241 Retinal disease: Exploring risk factors and mechanisms

Monday, May 04, 2015 11:00 AM–12:45 PM
Exhibit Hall Poster Session
Program #/Board # Range: 1779–1819/A0212–A0252
Organizing Section: Clinical/Epidemiologic Research
Contributing Section(s): Genetics, Immunology/Microbiology, Multidisciplinary Ophthalmic Imaging, Physiology/Pharmacology, Retina, Visual Neuroscience

Program Number: 1779 Poster Board Number: A0212
Presentation Time: 11:00 AM–12:45 PM

Barriers to Genetic Testing in Pediatric Retinitis Pigmentosa
Courtney K. Pollard1, 2, Emily A. McCourt1, 2, Kelsey Zegar2.
1University of Colorado, Denver, CO; 2Pediatric Ophthalmology, Children’s Hospital Colorado, Aurora, CO.

Purpose:
Retinitis Pigmentosa is a complex disease with dominant, X-linked, and polygenic causes. Genetic testing of pediatric RP patients is important because it provides data to further therapeutic development, allows parents to make future family planning decisions, directs testing of asymptomatic siblings, may define a syndromic cause, and can help predict rate of severe vision loss. Children can be offered genetic testing in order to categorize their disease, predict visual outcomes, and identify groups of patients who may benefit from future genetic therapies. Despite the benefits, many patients do not undergo genetic testing. This study was designed to elucidate the reasons why testing does not occur.

Methods:
Patients with a diagnosis of retinal dystrophy were identified by ICD-9 diagnosis codes in the electronic medical record of Children’s Hospital Colorado (CHC). 214 pediatric patients seen in the last 15 years with a diagnosis of retinal dystrophy were identified. Exam notes, telephone encounter documentation and letters to the families were reviewed. Of the identified 66 pediatric RP patients, 28 did not undergo genetic testing. Reasons for not pursuing genetic testing were coded and summed to determine the most common barriers to testing. Reasons included: cost of test, loss to follow up, parental refusal, enrollment in a study that did not use the patient’s blood sample, or the patient had multiple genetic diseases and the family chose to pursue non-RP genetic testing.

Results:
The most common barriers to genetic testing in the pediatric RP population at CHC were: patient lost to follow up (32.18%), inability of the family to afford the cost of the test (17.86%), and testing not documented as offered to the family (14.29%).

Conclusions:
The most common reason patients do not pursue genetic testing in the pediatric RP population at CHC is that they are lost to follow up. Given that CHC is a large tertiary referral center to which patients travel many miles for care, this finding is not surprising and is likely relatable to other large centers. However it is important because understanding the reasons patients are not tested can guide providers to develop protocols and systems to reach out to families to aid genetic characterization of individual RP disease types and to increase the pool of data for genetic research about RP.

Commercial Relationships: Courtney K. Pollard, None; Emily A. McCourt, None; Kelsey Zegar, None

©2015, Copyright by the Association for Research in Vision and Ophthalmology, Inc., all rights reserved. Go to iovs.org to access the version of record. For permission to reproduce any abstract, contact the ARVO Office at pubs@arvo.org.
of morphological abnormalities and visual impairment in a large population of children and adults.

**Methods:** Stargardt patients aged ≥ 6 yrs. with one or more pathogenic ABCA4 mutations, at least one area of well demarcated atrophy, visual acuity (VA) ≥ 20/400 (prospective study), and a clinical phenotype of Stargardt disease were enrolled. Fundus autofluorescence, spectral domain OCT, microperimetry, VA, and clinical examinations from ≥ 2 prior clinic visits 2-5 yrs. apart were submitted for the retrospective study. In the prospective study, participants complete the imaging and psychophysical tests described for the retrospective study in the clinic every 6 months over 2 yrs.

**Results:** 242 participants (442 eyes) are enrolled to date in the retrospective study with a mean ± standard deviation (SD) follow-up of 3.8 ± 1.6 years. Mean ± SD age at the earliest visit was 30.3 ± 17.6 yrs. and age at symptom onset is 21.9 ± 13.0 yrs. Participants are predominantly female (58.3%) and Caucasian (70.7%); 9.5% reported Vitamin A use. Mean (interquartile range) VA at the earliest visit was 20/125 (20/50, 20/200). Retinal pigment epithelium (RPE) atrophy and RPE pigmentation abnormalities were identified in 97.0% and 80.6% of eyes respectively. Flecks within and outside the arcades were present in 83.5% and 45.5% of eyes.

210 participants (393 eyes) are enrolled to date in the prospective study. Mean ± SD age at baseline and age of onset are 34 ± 15.5 yrs. and 23 ± 13.4 yrs. Participants are predominantly female (53.3%) and Caucasian (83.3%); 15.7% reported Vitamin A use. Mean ± SD best corrected LogMAR VA at baseline was 0.78 ± 0.32. RPE atrophy and RPE pigmentation abnormalities were present in 92.0% and 66.8% of eyes. Flecks within and outside the arcades were present in 90.8% and 45.0% of eyes. Prospective study follow-up visits are ongoing.

**Conclusions:** The results of the ProgStar studies will inform the development of clinically meaningful efficacy measures for future therapeutic trials to treat Stargardt disease.

**Commercial Relationships:** Ann-Margret Ervin, None; Beatriz E. Munoz, None; Rupert W. Strauss, None; Yulia Wolfson, None; Xiangrong Kong, None; Sheila K. West, None; Hendrik P. Scholl, QLT, Inc. (C), QLT, Inc. (F), Sanofi-Fovea Pharmaceuticals (C), Vision Medicines, Inc. (C).

**Support:** Foundation Fighting Blindness Clinical Research Institute

**Program Number:** 1782 **Poster Board Number:** A0215 **Presentation Time:** 11:00 AM–12:45 PM

**Exploring the Importance of the ELM as a Transient Biomarker in the Natural History of Early-Onset Stargardt Disease with SD OCT and UWF-AF**

Jerome Sherman1, Jennifer Lee2, Danica Yang2, K Bailey Freund4, 5.
1 Clinical Sciences, SUNY College of Optometry, New York, NY; 2 SUNY College of Optometry, New York, NY; 3 SUNY Eye Institute, New York, NY; 4 Ophthalmology, New York University School of Medicine, New York, NY; 5 Ophthalmology, Vitreous Retina Macula Consultants NY, New York, NY.

**Purpose:** To document the temporal changes in SD OCT and AF findings in 3 young siblings initially seen at ages 4, 5 and 8, with genetically confirmed Stargardt Disease (STGD).

**Methods:** Serial evaluation of 3 siblings with fundus photography, OCT, full field ERGs, ultra-widefield auto fluorescence (UWF-AF) and genetic testing.

**Result:** At initial presentation, only the 8 yo brother had visual symptoms with VA reduced to 20/200 in each eye. Although ophthalmoscopy appeared normal, SD OCT showed profound macula thinning and loss of much of the outer retina. FAF revealed hyper AF within the arcades as well as small hyper and hypo AF pisciform lesions that were quite symmetric in both eyes. ERGs were normal and genetic testing revealed an ABCA4 (Pro1380Leu) mutation.

Both the 4 and 5 yo sisters had no visual symptoms initially, VA of 20/25 in each eye, normal fundi, but each demonstrated a thickened, hyper-reflective ELM (external limiting membrane) and attenuated EZ (ellipsoid zone) on SD OCT. The 8 yo brother had no detectable ELM or EZ in the central 4 mm of the scans.

Over the next 2 yrs the brother’s VA worsened to 20/400 OU as did both the OCT and UWF AF abnormalities. The older sister did not appear to change significantly during the first year of follow-up but about a year later (at age 7) showed marked changes on SD OCT. The ELM, which 1 and 2 years earlier was grossly thickened throughout the entire 6 mm scan was almost completely absent in the central macula except at the fovea as a concave protuberance. Less dramatic was the loss of the EZ in the central macula in both eyes. At presentation, only the older sister had an obvious bull’s eye on AF OU. All 3 siblings had progressive AF changes.

**Conclusions:** In this pedigree, the thickened ELM was a transient biomarker for STGD that was imaged in a 4 and 5 year old. The thickened ELM occurred both before symptoms and VA loss. Since treatment for STGD may well be a reality in the near future, knowledge of this biomarker and its natural course during the first decade may be helpful in deciding who to treat and to determine drug efficacy.

**Commercial Relationships:** Jerome Sherman, None; Jennifer Lee, None; Danica Yang, None; K Bailey Freund, None

**Program Number:** 1783 **Poster Board Number:** A0216 **Presentation Time:** 11:00 AM–12:45 PM

**Phenotypic variability of retinal degeneration within a consanguineous family**

Marcela P. Perez Araya1, 2, Ajoy Vincent1, Carol A. Westall3, 4, Thomas Wright5, Heather Trang2, 6, Chelsea Roadhouse3, 4, Elise Heon1, 2.
1 Ophthalmology and Vision Sciences, The Hospital for Sick Children, Toronto, ON, Canada; 2 Genetics and Genomics Biology, The Hospital for Sick Children, Toronto, ON, Canada; 3 Ophthalmology and Vision Sciences, University of Toronto, Toronto, ON, Canada; 4 Neurosciences and Mental Health, The Hospital for Sick Children, Toronto, ON, Canada.

**Purpose:** To characterize the genotype(s) of individuals from a highly consanguineous family of Iraqi descent, affected with a range of retinal dystrophy phenotypes.

**Methods:** Eight members of a two generation family with vision loss (5 affected) underwent detailed ophthalmologival evaluation, including best corrected visual acuity (BCVA; n=7), color vision (n=5) and contrast sensitivity (n=5) measurements. All family members had fundus imaging, fundus auto-fluorescence testing
Investigation on cone structure and function in a family affected by occult macular dystrophy

Lucia Ziccardi1, Daniela Giannini2, Giuseppe Lombardo3, 5, Sebastiano Serrao2, Roberto Dell’Omo4, Annalisa Nicoletti6, Matteo Bertelli6, Marco Lombardo.

Commercial Relationships: Lucia Ziccardi, None; Daniela Giannini, None; Giuseppe Lombardo, None; Sebastiano Serrao, None; Roberto Dell’Omo, None; Annalisa Nicoletti, None; Matteo Bertelli, None; Marco Lombardo, None

Program Number: 1785 Poster Board Number: A0217
Presentation Time: 11:00 AM–12:45 PM

In 2017, we reported the retinal phenotype and genetic results in a large autosomal dominant kindred with North Carolina macular dystrophy (NCMD) like disease. Six affected members of a Caucasian family (age range: 12 – 47 years) underwent detailed ophthalmological evaluation that included best corrected visual acuity (BCVA) measurement, color vision testing and fundus examination. Fundus autofluorescence (FAF) imaging, spectral-domain optical coherence tomography (SD-OCT), full-field electroretinography (ERG) and electro-oculography (EOG) were performed in 5 cases. The proband (IV-4) had genetic testing, specifically a 25 gene maculopathy/cone-rod dystrophy panel. The proband’s son (V-1) was tested a large sequencing panel of 131 retinal dystrophy genes.

Program Number: 1784 Poster Board Number: A0217
Presentation Time: 11:00 AM–12:45 PM

To report the retinal phenotype and genetic results in a large autosomal dominant kindred with North Carolina macular dystrophy (NCMD) like disease

Methods: Six affected members of a Caucasian family (age range: 12 – 47 years) underwent detailed ophthalmological evaluation that included best corrected visual acuity (BCVA) measurement, color vision testing and fundus examination. Fundus autofluorescence (FAF) imaging, spectral-domain optical coherence tomography (SD-OCT), full-field electroretinography (ERG) and electro-oculography (EOG) were performed in 5 cases. The proband (IV-4) had genetic testing, specifically a 25 gene maculopathy/cone-rod dystrophy panel. The proband’s son (V-1) was tested a large sequencing panel of 131 retinal dystrophy genes.

Results: Grade-1 NCMD defined as fine drusen or mild retinal pigment epithelial (RPE) changes confined to the central macula was noted in III-4, IV-5 and the right eye (RE) of V-2. Grade-2 NCMD characterized by confluent elevated subretinal material with or without pigmentary changes was noted in the left eyes of V-2 and III-2. Grade-3 NCMD described as central macular chorioretinal atrophy with fibrous tissue and pigmentation along the rim of the atrophy was noted in IV-4, V-1 and the RE of III-2. The BCVA ranged between 0.3 and 3.0 logMAR in grade-3 eyes; and between 0.0 and 0.86 logMAR in grade-1 and 2 eyes. Color vision was normal or showed mild deficits. Radial, peripheral-retinal yellowish deposits that hyper-fluoresced on FAF were noted in 2 cases. Grade-1 and 2 eyes showed hyper-fluorescent macular lesions. The atrophic lesions in grade-3 eyes hypo-fluoresced on FAF, but its rim demonstrated hyper-fluorescence. On SD-OCT, grade-1 eyes showed subtle drusenoid deposition at the RPE with minimal disruption of photoreceptor layer. Grade-2 eyes showed large hyper/iso-reflective lesions at the RPE.
Progression of hydroxychloroquine (HCQ) retinopathy has been documented before and after cessation of the drug, in proportion to the severity of damage. Several papers have implicated involvement of inner as well as outer retina. We use a new topographic segmentation of the retina to independently assess inner and outer damage both during and after usage of HCQ.

**Methods:** A new automated image analysis system developed at Stanford has been applied to produce pixel-by-pixel OCT analysis of different retinal layers across the entire macula. OCT records from a prior clinical study of HCQ patients with retinopathy were reanalyzed to show inner and outer retinal integrity at different stages of retinopathy, and progression after the cessation of therapy.

**Results:** The topographic images confirmed a prior finding that in early and moderate retinopathy (no RPE damage), the retina gets slightly thinner only during the first year after HCQ is stopped. However, we found this change resulted entirely from damage to the outer retina, and inner retinal thickness was essentially unaffected by HCQ (even in severe retinopathy with a visible bull’s eye). Prior reports might have recorded inner retinal deformation as it fills in focal parfoveal outer retinal damage. Our topographic images revealed that outer retinal thinning after drug cessation was not limited to a parfoveal bull’s eye zone, but occurred diffusely across the macula. The development of bull’s eye thinning occurred primarily while patients were taking the drug, and before the damage reached the RPE level.

**Conclusions:** Topographic segmentation shows clearly that inner retina is not affected by HCQ to any major degree. It also shows that while HCQ toxicity targets the parafovea as it develops during drug exposure, damage after the HCQ is stopped is diffuse across the macula. Finally, it confirms the clinical observations that while visible bull’s eye maculopathy may progress for years after stopping HCQ, progression of HCQ retinopathy is very limited if detected before a stage of RPE damage. This provides a strong rationale for regular screening with sensitive procedures.

**Commercial Relationships:** Michael F. Marmor, None; Luis de Sisternes, None; Julia Hu, None; Daniel L. Rubin, None

**Support:** Spectrum-SPADA innovation grant, Stanford University

©2015, Copyright by the Association for Research in Vision and Ophthalmology, Inc., all rights reserved. Go to iovs.org to access the version of record. For permission to reproduce any abstract, contact the ARVO Office at pubs@arvo.org.
LONGITUDINAL EVALUATION OF HYDROXYCHLOROQUINE RETINAL TOXICITY USING OPTICAL COHERENCE TOMOGRAPHY

Fabio Scarinci1, 2, Amr Shaarawy1, 3, Lee M. Jampol1, Amani A. Fawzi1. 1Ophthal-Feinberg School of Med, Northwestern University, Chicago, IL; 2Ophthalmology, Fondazione G.B. Bietti -IRCCS, Rome, Italy; 3Ophthalmology, Alexandria Faculty of Medicine, Alexandria, Egypt.

Purpose: The hallmark of hydroxychloroquine retinal (HCQ) damage is bilateral pigmentary retinopathy due to long term effect of the drug on the photoreceptors. We performed a retrospective, SD-OCT clinical study to quantify the disruption of the external limiting membrane (ELM) and the volumetric photoreceptors changes in eyes with HCQ toxic effects after discontinuation of drug therapy.

Methods: A retrospective medical record review identified patients taking HCQ who were diagnosed with HCQ toxic effects at the ophthalmology department of Northwestern University. The SD-OCT images were obtained using the Spectralis HRA-OCT (Heidelberg Engineering, Heidelberg, Germany) and the images were analysed with Image J software (United States of National Institutes of Health). Individual b-scans from the volumetric scans were examined and manually marked for ELM disruption (Fig 1), as well as measure the volume (mm3) of the area between the ELM and Bruch’s Membrane (BM) (Fig 2) at baseline, intermediate follow up and final visit. Two trained graders marked these changes and intraclass correlation coefficients (ICCs) were calculated in order to assess inter-observer variability of the OCT measurements.

Results: Eighteen eyes of 9 patients were identified as having HCQ toxic effects and were included. The mean treatment duration was 11.2 years ±5.3. The mean cumulative dose of HCQ was 1671.62 g ±843.6. The mean follow up was 35.3 months. 12 out of 18 (66.6%) eyes showed damaged ELM at baseline, which showed progressive loss in 4/12 eyes over time. 6 of 3 patients did not have any ELM damaged during the entire follow up. Looking at the overall results for ELM disruption 3 types of effects was identified: 1) progressive worsening (4/18), 2) stable disruption (8/18), and 3) eyes with no ELM damage (6/18). Overall, the mean percentage photoreceptor volume change was -5.8% ±21.6 between baseline and the last visit. 7 out of 18 eyes showed progressive volumetric thinning of the photoreceptors during follow up. ICCs of the manually measurement of ELM disruption and the volume were reliable (0.94 and 0.96, respectively).

Conclusions: Using quantitative measurements on SD-OCT, this study showed that measuring the ELM disruption and the volume of the area between the ELM and the BM seems to be an appropriate tool for evaluating the course of HCQ lesions over time, identifying three patterns of outer retinal affection.
Impact of the Revised American Academy of Ophthalmology Guidelines for Hydroxychloroquine Retinopathy Screening at an Tertiary Care Academic Institution

Vishal Parikh1, Adrian Au2, Yasha Modi3, Rishi P. Singh1.
1Ophthalmology, Cleveland Clinic Cole Eye Institute, Cleveland, OH; 2Case Western Reserve School of Medicine, Cleveland, OH.

Purpose: The purpose of this study was to determine the hydroxychloroquine (HCQ) retinopathy screening practice patterns following the revised HCQ retinopathy screening recommendations published by the American Academy of Ophthalmology (AAO) in 2011.

Methods: This was an observational, retrospective study and approval from the institutional review board was obtained. 756 patients presenting to the Cole Eye Institute were identified as taking HCQ between 2011 and 2014 from their medication lists within the electronic medical record. Screening tests and follow-up intervals for all patients were analyzed and stratified by ophthalmic subspecialty. Per the 2011 guidelines, an appropriate screening visit was defined as having an objective (SD-OCT, mfERG, FAF) and a subjective test (HVF). Screenings were classified as “appropriate,” “over-screened,” “under-screened,” or “inappropriate.” The treating physician established diagnosis of toxicity, indeterminate findings, or a normal exam.

Results: After classifying screening visits, 228 (31.0%) patients were appropriately screened, (7.6%) patients were “over-screened,” 163 (22.2%) patients were “under-screened,” and 288 (39.2%) patients were inappropriately screened. Differences between subspecialties in screening include: 1) comprehensive ophthalmologists were more likely to order an Amsler test (p=0.0001); 2) glaucoma specialists were more likely to order the 24-2 HVF (p=0.002); 3) neuro-ophthalmologists were more likely to order the 30-2 HVF (p=0.008); 4) retina specialists were more likely to order the SD-OCT (p=0.0001), FAF (p=0.0001), FA (p=0.005), and fundus photos (p<0.0001). Twelve (1.6%) patients had definite toxicity. Eight (11.1%) patients had an abnormal or indeterminate exam concerning for HCQ toxicity. Of the patients with definite toxicity, eight (66.7%) had a cumulative dose >1 kg, seven (58.3%) exceeded 6.5 mg/kg/day based on ideal body weight, and two (16.7%) had comorbid renal or liver disease.

Conclusions: Screening for HCQ varied widely with 31% of patients undergoing appropriate screening, indicating a large percentage of screenings deviated from the recommended algorithm. Cumulative dosing is the most consistent risk factor for developing HCQ toxicity. SD-OCT was the primary screening tool coupled with the 10-2 HVF, with FAF and mf-ERG as additional tests if needed.

Commercial Relationships: Vishal Parikh, None; Adrian Au, None; Yasha Modi, None; Rishi P. Singh, None

Sensitivity and Specificity of Multifocal ERG in detection of chloroquine and hydroxychloroquine toxicity

Stuart G. Coupland, Sina Ahmadi, Chloe Gottlieb, John Hamilton.
Ophthalmology, Univ of Ottawa Eye Institute, Ottawa, ON, Canada.

Purpose: To calculate the sensitivity and specificity of multifocal electroretinography (mfERG) in detection of chloroquine (CQ) and hydroxychloroquine (HCQ) retinal toxicity and to find the relationship between the cellular mechanisms of toxicity and clinically recordable abnormalities of retinal electrophysiology testing. A cross sectional study was performed on patients referred for screening of CQ and HCQ retinal toxicity.

Methods: The results of 10-2 Humphrey automated visual field (10-2 AVF), fundus auto fluorescence (FAF), spectral domain optical coherence tomography (sdOCT) and mfERG were recorded in 120 eyes of 63 patients taking HCQ or CQ. Mean age was 60.06 years. The results of sdOCT and mfERG were also obtained from an age and sex-matched control group of subjects of mean age of 56 years that did not have any known autoimmune disease and never received CQ or HCQ. A combination of 10-2 AVF and sdOCT results was used as the reference test for the calculation of mfERG sensitivity and specificity. Correlation between the HCQ cumulative dose and 10-2 AVF mean deviation (MD), pattern standard deviation (PSD), and mfERG implicit time, and P1 amplitude R5 ring ratios was investigated using linear regression analysis.

Results: The sensitivity and specificity of mfERG relative to the reference test were 87% and 86.5% respectively. The “false positive” group exhibited significantly reduced mfERG P1 amplitude R5 ring ratios compared to the normal group in the parafoveal ring 2 (P<0.0002). This difference was not observed in other rings. The abnormal mfERG group also exhibited significantly reduced P1 amplitude R2/R5 (P<0.0001) and R3/R5 (P<0.0002) compared to the normal group. HCQ cumulative dose was negatively correlated with all of the mfERG P1 amplitude R5 ring ratios, but the correlation was strongest in ring 2 (P<0.0006). There was no statistically significant correlation between HCQ cumulative dose and any of 10-2 AVF mean deviation (MD), pattern standard deviation (PSD), or average sdOCT thickness.

Conclusions: mfERG is more sensitive than the combination of 10-2 AVF and sdOCT in early detection of CQ/HCQ retinal toxicity. There is a relationship between clinically recordable electrotoretinal dysfunction and the cellular disturbances resulting from accumulation of CQ and HCQ in the retinal neurons.

Commercial Relationships: Stuart G. Coupland, None; Sina Ahmadi, None; Chloe Gottlieb, None; John Hamilton, None
Support: University of Ottawa UMRF

The Incidence of Hydroxychloroquine (HCQ) Retinal Toxicity in the Veteran Affairs (VA) Patient Population

Salman A. Rahman, Diem K. Bui, Robert Coffee. Ophthalmology, Baylor College of Medicine, Houston, TX.

Purpose: To assess the incidence of HCQ retinal toxicity in the VA patient population.

Methods: Retrospectively evaluate the medical records of all the patients at the Houston VA who were started on HCQ therapy between January 2003 and December 2012. Inclusion criteria include duration of HCQ therapy > 1 year. Exclusion criteria include duration of HCQ therapy < 1 year or unknown duration of therapy, no documented dilated eye exams at least 1 year after the initiation of therapy or existing macular pathology prior to the initiation of therapy.

Results: 454 patients were initiated on HCQ therapy between Jan 2003 and December 2012 at the Houston VA. Of these 454 patients, 211 patients met the inclusion criteria. 63.0% of patients were on HCQ therapy for less than 5 years. 25.1% of patients were on HCQ for 5-10 years and 11.8% of patients were on HCQ therapy for more than 10 years. Of the 211 patients who were included in the study, 1 patient developed probable HCQ retinal toxicity after 8 years of therapy and a cumulative dose of 1168 g of HCQ.

Conclusions: The incidence of HCQ retinopathy at the Houston VA between 2003-2012 was 0.47% (1 out of 211 patients). This is consistent with previously reported rate of 0.5% to 0.65%. Given the small sample size, it is difficult to draw any definite conclusions regarding
the risk factors associated with HCQ retinopathy. However, it is observed that the risk for toxicity sharply increases with cumulative dose above 1000 g of HCQ which is also consistent with previously reported findings.

Commercial Relationships: Salman A. Rahman, None; Diem K. Bui, None; Robert Coffee, None

Program Number: 1792 Poster Board Number: A0225
Presentation Time: 11:00 AM–12:45 PM

Hydroxychloroquine Screening and Toxicity: A Comparison Between Screening Modalities
Yasha Modi, Vishal Parikh, Adrian Au, Rishi P. Singh. Ophthalmology, Cole Eye Institute, Cleveland, OH.

Purpose: We identify patients with hydroxychloroquine (HCQ) toxicity and compare detection rates between different screening modalities as suggested by the 2011 updated screening guidelines.

Methods: This was a retrospective, observational study, evaluating patients taking HCQ between 2011 and 2014 at a single academic institution.

Results: A total of 756 patients were screened for HCQ toxicity. Twenty (2.6%) patients had abnormal screenings and 12 (1.6%) were determined to have HCQ toxicity by the treating physician. While 9/12 (75%) were appropriately receiving less than 6.5 mg/kg (ideal body weight)/day, 8/12 (66.7%) had received a lifetime dose exceeding 1 kg. Five of the 12 (41.7%) were symptomatic on presentation with 3 reporting intermittent blurry vision and 2 reporting persistent blurry vision. Two presented with classic bull’s eye maculopathy and 8/12 (66.7%) had nonspecific retinal pigment epithelial (RPE) changes. Twelve (100%) had an abnormal SD-OCT demonstrating parafoveal loss or thinning of the ellipsoid zone, external limiting membrane, and outer plexiform layer. Eleven of 12 patients had a HVF 10-2, of which 4/11 were unreliable. Eight/11 (72.7%) had paracentral defects; 3/11 (27.3%) had central depression. FAF was performed in 9/12 patients and 8/9 (88.9%) demonstrated hypoautofluorescence patterns while the remaining 1 had a normal autofluorescence pattern. Multifocal ERG was not performed in any of the 12 patients.

At diagnosis, 1/12 had previously stopped HCQ and 11 were encouraged to stop immediately.

Conclusions: HCQ toxicity is a rare entity. As only 42% were symptomatic on presentation, early detection with sensitive screening modalities is essential. SD-OCT demonstrated the most consistent abnormalities with 100% presenting with characteristic parafoveal outer retinal thinning. While the subjective component of HVF may yield unreliable results, all patients in this study had either paracentral visual field loss or central depression. Fundus autofluorescence did not uniformly demonstrate a deficit and mfERG was not performed in any patient with toxicity.

Given the recommendations of the 2011 screening guidelines, it is reasonable to use SD-OCT as an anatomic test coupled with HVF 10-2 as a functional test to assess maculopathy. FAF may be better utilized as a confirmatory test rather than a stand-alone screening test as not all patients demonstrated abnormal findings.

Commercial Relationships: Yasha Modi, None; Vishal Parikh, None; Adrian Au, None; Rishi P. Singh, Alcon (C), Genentech (C), Regeneron (C), Regeneron (F)
2 Humphrey Field Analyzer), FAF, and SD-OCT. HCQ retinopathy was categorized as early, moderate, or severe according to the prior criteria.

**Results:** Three hundred and ten patients with exposure to HCQ were finally included. The mean age of patients was 44.5 years; a total of 286 patients (92.3%) were female. Mean duration of HCQ use was 72.0 months and mean cumulative exposure of HCQ was 624.8g. Among the overall 310 patients, 10 patients (3.2%) showed clinically evident HCQ retinopathy with characteristic visual field loss or photoreceptor damage in SD-OCT. Among the 172 patients with HCQ use ≥ 5 years, the prevalence of HCQ retinopathy was 5.8%. All the 10 patients with HCQ retinopathy were asymptomatic at the time of screening exam. In patients with HCQ retinopathy, mean duration of HCQ use was 110.5 months and mean cumulative exposure of HCQ was 945.6 g. Of the 10 patients, 4 patients showed severe HCQ retinopathy, 3 patients showed moderate retinopathy, and 3 patients showed early retinopathy.

**Conclusions:** In Korean patients, HCQ retinopathy detected by revised AAO recommendations is more common than previously recognized, especially in cases with long duration of use. This study highlights the importance of screening for HCQ retinopathy by revised screening system with objective imaging modalities.

**Commercial Relationships:** Doo-ri Eo, None; Mingyu Lee, None; Sang Jin Kim, None

**Program Number:** 1795 Poster Board Number: A0228
**Presentation Time:** 11:00 AM–12:45 PM

**Lamotrigine associated retinal phototoxicity**

April Harris1, Fatimah Gilani.1 Retina Associates, Tucson, AR; 1Ophthalmology, University of Arizona, Tucson, AZ.

**Purpose:** Lamotrigine [3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine] is an anticonvulsant drug. FDA approved for the treatment of epilepsy and bipolar disorder. It is also utilized off label for clinical depression. Lamotrigine absorbs ultraviolet(UV) light and generates free oxygen radicals potentially leading to cellular damage. We describe two patients using lamotrigine that experienced retinal phototoxicity during uncomplicated vitreoretinal procedures involving routine light exposure.

**Methods:** Two patients on lamotrigine were examined and treated at a community based vitreoretinal practice. They were subsequently identified with symptoms consistent with retinal phototoxicity. The first patient noted central scotoma after vitrectomy for vitreous opacities. The second patient experienced a profound decrease in vision after photodynamic therapy for chronic central serous retinopathy. Both patients were examined with multi-modal imaging including fundus photography, spectral domain optical coherence tomography(SD-OCT) imaging, fluorescein and indocyanine green angiography.

**Results:** The patients noted permanent visual changes after routine vitreoretinal procedures that would not be ordinarily be expected to induce light toxicity. In the first patient, fundus autofluorescence showed foveal hypoorfluorescence with surrounding ring of hyperautofluorescence and OCT imaging revealed subtle disturbance of the inner and outer segment(IS/OS) junction of the photoreceptors. The second patient clearly had yellow foveal lesion on fundus photography and full thickness hyperreflectivity at the fovea with disruption of the external limiting membrane and IS/OS junction.

**Conclusions:** This is the first report of lamotrigine associated retinal phototoxicity. Lamotrigine is a photosensitizer that is known to potentially lead to a photochemical reaction manifested as severe sunburn and may as well induce retinal phototoxicity during routine vitreoretinal procedures. Care should be taken to screen patients for use of this drug and consider discontinuing the drug prior to any planned vitreoretinal procedure involving light exposure. Exposure to even routine levels of light during treatment may lead to permanent and irreversible damage.

**Commercial Relationships:** April Harris, None; Fatimah Gilani, None

**Program Number:** 1796 Poster Board Number: A0229
**Presentation Time:** 11:00 AM–12:45 PM

**Central Serous Chorioretinopathy: Clinical Characteristics Associated with Visual Outcomes**


**Purpose:** To identify clinical characteristics associated with poor visual acuity in central serous chorioretinopathy.

**Methods:** All charts coded with a diagnosis of central serous chorioretinopathy between December 1, 2001 and September 30, 2013 were reviewed to confirm the diagnosis. Those with a confirmed diagnosis and at least two office visits over a minimum one month follow-up period were included, and the subjects’ charts were reviewed retrospectively. Multivariate logistic regression analyses were performed to assess the relationship between several clinical characteristics and final visual acuity.

**Results:** 353 subjects were confirmed to have central serous chorioretinopathy. Of these, 258 had a minimum of two clinical assessments and adequate follow-up. Multivariate analysis showed that the following clinical factors were significantly associated with worse final visual acuity: older age at diagnosis, a history of treatment with photodynamic therapy, choroidal neovascularization, hypertensive, and a history of either prostate cancer or benign prostatic hypertrophy. Diabetes mellitus was associated with better final visual acuity. In an a subgroup analysis of 151 subjects with at least one year of follow-up, the following factors were significantly associated with worsening of visual acuity over the study period: choroidal neovascularization, use of a psychiatric medication at presentation, hypertension, and gastroesophageal reflux disease.

**Conclusions:** Poor visual outcomes in central serous chorioretinopathy are associated with older age at diagnosis, choroidal neovascularization, hypertension, and a history of prostate disease. Several clinical characteristics that have been identified as risk factors for developing central serous also appear to be associated with worse visual outcomes.

**Commercial Relationships:** Benjamin Nicholson, None; Amrou Ali Idris, None; Alan D. Marmorstein, None; Sophie J. Bakri, None

**Program Number:** 1797 Poster Board Number: A0230
**Presentation Time:** 11:00 AM–12:45 PM

**Recent Central Serous Chorioretinopathy with Steroids**

Dipal Shah1, Ronni M. Lieberman.2 Ophthalmology, North Shore - Long Island Jewish Health System, Great Neck, NY; 2Ophthalmology, Mount Sinai Medical Center, New York, NY.

**Purpose:** To determine if a subset of patients with central serous chorioretinopathy (CSCR) secondary to exogenous steroid use have anatomic and functional resolution of their symptoms after steroids are discontinued and to evaluate whether their symptoms recur. To determine if once resolved, the neurosensory detachment recurred without the exogenous steroid and to examine the role of treatment in these cases.

**Methods:** Retrospective chart review of 40 patients seen between January 2013 and October 2014 with CSCR was conducted. Patients who initially developed CSCR while on steroids were evaluated. Data from these patients was reviewed for demographics, systemic disease,
route of steroid administration, initial best corrected visual acuity (BCVA), and initial optical coherence tomography (OCT). Outcome measures after steroids were discontinued included development of recurrent fluid, time to recurrence, number of recurrences, type and timing of intervention, final BCVA and OCT findings. 

**Results:** Eleven (11) eyes from 7 patients were included in the study. Five (5) patients were on oral steroids, 1 on an inhaled steroid and 1 on a topical preparation. Initial VA ranged from 20/20 to counting fingers (CF). Eight eyes (72%) showed no improvement at 3 months after steroids were discontinued, necessitating treatment. This included intravitreal anti-VEGF injections in 7 eyes (64%) and/or focal laser photocoagulation (3 eyes [27%]). Without steroids, 8 eyes developed a recurrence of fluid, at times ranging from 2 to 7 months. The number of recurrences ranged from 1 to 3, with 1 eye never completely resolving. Patients were followed for an average of 32.8 months (range 15-59). All but 2 eyes achieved a BCVA of ≥20/50 (range 20/20 to CF). 72% (8) of the eyes had flat OCTs on most recent exam.

**Conclusions:** CSCR secondary to steroids is generally assumed to resolve and not recur once steroids are tapered and discontinued. Our patient population was found to have a high rate of recurrence of fluid, in addition to a tendency toward multiple recurrences, even after steroids had been discontinued. Although a larger study is needed, these patients need to be monitored closely.

**Commercial Relationships:** Dipal Shah, None; Ronni M. Lieberman, None

**Program Number:** 1798 Poster Board Number: A0231
**Presentation Time:** 11:00 AM–12:45 PM

The multifocal electroretinogram may predict functional retinal deterioration in patients with birdshot chorioretinopathy

**Adrian C. Tsang, Paul Bastianelli, John Hamilton, Stuart G. Coupland, Chloe Gottlieb.** University of Ottawa Eye Institute, The Ottawa Hospital, Ottawa, ON, Canada

**Purpose:** To characterize multifocal electroretinogram (mfERG) findings in patients with birdshot chorioretinopathy (BCR) over the clinical course of the disease. A retrospective chart review was conducted to compare findings on mfERG to clinical indicators of uveitis activity, Goldmann visual field (GVF) findings, and structural findings on spectral domain optical coherence tomography (sdOCT) throughout the clinical course of BCR.

**Methods:** A review of 14 eyes of 7 patients presenting to the uveitis service at the University of Ottawa Eye Institute with BCR and documented mfERG, GVF, sdOCT, and clinical exam between September 2010 and December 2013. Time since diagnosis, pharmacological therapy, best corrected visual acuity (BCVA), anterior chamber and vitreous cell grading, mfERG ring ratios, GVF maps, and structural changes on sdOCT were recorded from each clinical appointment and compared over the duration of follow-up.

**Results:** Mean age at presentation was 55 years (range 41-71 years). There were five females and two males, all Caucasian. Average duration of follow-up was 29.4 months. All patients developed electroretinal dysfunction of the cone system within the central 30 degrees detected on mfERG regardless of the morphology of choroidal lesions. In 4 of 7 patients, mfERG abnormalities preceded detectable changes in the degree of inflammation, BCVA, GVF, and macular thickness on sdOCT. In one patient, the onset of mfERG findings coincided with abnormal clinical, GVF, and sdOCT findings. Two patients were referred late in the disease course and their mfERG results were abnormal from baseline. Four patients were treated with cyclosporine and prednisone, two patients were treated with mycophenolate mofetil, and one with adalimumab. All patients showed an improvement of at least one line in Snellen visual acuity from baseline.

**Conclusions:** This is the first report in the literature illustrating the potential utility of mfERG in detecting declining retinal function earlier in the course of BCR than is otherwise detected by history, clinical indicators of uveitis activity, GVF, or macular thickness on sdOCT. Further prospective trials are required to determine if use of mfERG to detect early functional decline in the retina may assist clinicians in initiating immune modulatory therapy or optimizing treatment to improve patient outcomes in the treatment of BCR.

**Commercial Relationships:** Adrian C. Tsang, None; Paul Bastianelli, None; John Hamilton, None; Stuart G. Coupland, None; Chloe Gottlieb, None

**Program Number:** 1799 Poster Board Number: A0232
**Presentation Time:** 11:00 AM–12:45 PM

Sleep disorders : a risk factor of central serous chorioretinopathy

**Mariam Dhundass1, elodie bouquets1, Mathieu Lehmann1, Pierre-Raphael Rothschild2, Antoine P. Brezin1, Francine Behar Cohen1.** 1ophthalmology, HOSPITAL HOTEL DIEU, Paris, France; 2Ophthalmology, Lausanne, Switzerland.

**Purpose:** Based on clinical observation, we hypothesized that sleep disorders and staggered work hours are risk factors for central serous chorioretinopathy (CSC)

**Methods:** 38 patients with active acute CSC and 30 controls were included in this prospective case control study. The Insomnia Severity Index (ISI), a validate screening device for insomnia research, was administered to all the patients and controls with a cut off score of 10. The other risk factor (stress, steroids, profession, work shift) were measured with an additional questionnaire. Patients from two groups matched for age and sex.

**Results:** Mean age in CSC group was 44±8.5 versus 42±10.2 years in the control group (p=0.4). 84% and 80% of patients were male in CRSC and control group (p=0.8). An ISI score >10 was found in 58% of patients with CSC compared to 17% in the control group (OR : 6.9 [2.25 ; 21] ; p=0.001). In CSC group, 45% of patients had staggered work hours compared to 10% in the control group (OR : 7.3 [2.62] ; p=0.002). Steroids use was significantly increased in CSC patients as compared to controls (60.5% versus 26.7%, OR : 4.2 [1.5 ; 11.7] ; p=0.005) and stress was significantly more frequent in CSC patients (65% versus 13% OR : 12.5 [3.8 ; 41.4] ; p=0.001).

**Conclusions:** Sleep disorders, different from sleep apnea and staggered works hours could be newly identified risk factors for CSC. The relation between circadian rythm disruption, cortisol rythmicity and CSC should be analyzed.

**Commercial Relationships:** Mariam Dhundass, None; elodie bouquets, None; Mathieu Lehmann, None; Pierre-Raphael Rothschild, None; Antoine P. Brezin, None; Francine Behar Cohen, None

**Program Number:** 1800 Poster Board Number: A0233
**Presentation Time:** 11:00 AM–12:45 PM

Long-term effects of anti-VEGF injections on intraocular pressure in patients with age-related macular degeneration and diabetic macular edema

**Blake Williams1, Shriishira Nairani1, Shrishir Poudyal1, Seenu M. Hariprasad2.** 1Pritzker School of Medicine, University of Chicago, Chicago, IL; 2Ophthalmology, University of Chicago, Chicago, IL; 3University of Chicago, Chicago, IL.

**Purpose:** There is debate in the ophthalmology community about whether anti-VEGF injections result in a long-term increase in intraocular pressure (IOP). Some studies have identified risk factors...
(i.e. number of injections, interval between injections) that are associated with elevated IOP, while other studies have shown that intravitreal anti-VEGF injections do not lead to elevated IOP. We performed a retrospective, observational clinical study to investigate how the number and timing of intravitreal injections for patients with age-related macular degeneration (AMD) and diabetic macular edema (DME) affect IOP over time.

**Methods:** After receiving IRB approval, we collected long-term IOP data on patients receiving anti-VEGF injections at the University of Chicago. Patients over the age of 40 who received the injections for AMD (n = 76) or DME (n = 55) were included in the study; those receiving injections for retinal vein occlusion were excluded. Patients were grouped according to indication for injection as well as number of injections received (1-3, 4-6, 7-9, or 10+ injections). IOP measurements were then placed into time points (0-6, 6-12, 12-18, 18-24, or 24+ months after first injection) and compared to the pre-injection IOP. One-tailed t-tests were used for statistical analysis.

**Results:** For patients with DME, average initial IOP was 15.7 mmHg. At 24+ months after injection, the average IOP was 15.2 (95% CI: 13.8-16.6, p = 0.68) for patients receiving 1-3 injections, 16.8 (15.3-18.3, p = 0.23) for 4-6 injections, and 14.4 (13.8 – 15.0, p = 0.66) for 7-9 injections. For patients with AMD, average initial IOP was 15.6 mmHg. At 24+ months after injection, the average IOP was 12.6 (95% CI: 10.8-14.4, p = 0.97) for patients receiving 1-3 injections, 14.9 (13.7-16.1, p = 0.96) for 4-6 injections, 14.8 (12.4-17.2, p = 0.84) for 7-9 injections, and 15.7 (14.0-17.4, p=0.56) for 10+ injections.

**Conclusions:** There was no statistically significant increase in IOP over time for AMD or DME patients, regardless of the number of injections received. Ours is the only study we are aware of to track progression of IOP over a period of greater than two years and to stratify by number of injections received. It is notable that neither of these variables affected IOP, as they have been proposed as potential factors contributing to increased IOP after injections.
Kaplan-Meier graph, showing that patients with retinal neovascularization above the internal limiting membrane present significantly slower regression of the neovascularization after panretinal photocoagulation in comparison with those having the neovascularization below the internal limiting membrane.

**Commercial Relationships:** Irini Chatziralli, None; Sobha Sivaprasad, Allergan (F), Allergan (R), Bayer (F), Bayer (R), Novartis (F), Novartis (R), Roche (F), Roche (R)

**Program Number:** 1802 Poster Board Number: A0235
**Presentation Time:** 11:00 AM–12:45 PM
**Correspondence between central mfERG changes and thinning of Ganglion Cells and Retinal Nerve Fiber layers in the initial stages of Diabetic Retinopathy**

**Purpose:** To evaluate the presence of multifocal ERG (mfERG) changes and retinal cells layers changes in eyes of patients with diabetes type 2, using Spectral Domain Optical Coherence Tomography (SD-OCT), in order to identify the correspondence between functional mfERG changes and retinal structural changes.

**Methods:** 211 out of 450 diabetic type 2 patients enrolled in the EUROCONDOR study (NCT01726075) and that performed SD-OCT Cirrus (Zeiss Meditec, Dublin, CA, USA) were considered for analysis: 109 patients with Diabetic Retinopathy (DR) ETDRS level 10 and 102 patients with DR ETDRS level 35. All patients performed mfERG (103 hexagons) and SD-OCT at baseline. P1 amplitude and implicit time (IT) of mfERG central rings (rings 1, 2 and 3) were analyzed by the number of hexagons with altered z-scores (z-score \( \geq 2 \)) for IT and \( \leq -2 \) for amplitude. The number of altered hexagons was compared with retinal cells layers changes detected by SD-OCT.

**Results:** Mean age and duration of diabetes in these patients were 63.9 and 11.3 years, respectively; 71% were males and 29% were females. In the 109 eyes classified as having ETDRS level 10 (without microaneurysms) there were central mfERG changes in 57% of eyes. A decrease of thickness in the Ganglion Cells (GC) or Retinal Nerve Fiber (RNF) layers was observed in 13% of the eyes. 64% of eyes with thinning of GC or RNF layers showed correspondence with mfERG changes. In the 102 eyes with ETDRS level 35 (mild nonproliferative DR), central mfERG response was altered in 68% of eyes and GC and RNF layers thinning was present in 12% of the eyes. Correspondence between mfERG changes and GC or RNF thinning was present in all cases (100%; \( p=0.011 \)).

A good correspondence between mfERG changes and thinning of the GC and RNF layers.

**Conclusions:** There is good correspondence between central mfERG changes (ring 1, 2 and 3) and thinning of GC and RNF layers in the initial stages of DR in patients with diabetes type 2. Therefore, functional and structural measurements used for assessing neurodegeneration run in parallel in the early stages of DR.

**Commercial Relationships:** Ana Rita Santos, None
**Support:** EC-FP7-278040
**Clinical Trial:** NCT01726075

**Program Number:** 1803 Poster Board Number: A0236
**Presentation Time:** 11:00 AM–12:45 PM
**Retinal Vascular Fractals Correlate With Early Neurodegeneration in Patients With Type 2 Diabetes Mellitus**

**Purpose:** To investigate the correlation between early retinal vascular and neurodegenerative changes in diabetic retinopathy (DR).

**Methods:** Altogether 105 patients with type 2 diabetes mellitus (T2DM) with no or mild DR were examined. Forty nine patients were recruited from the baseline population of the EUROCONDOR study, the rest from the local DR screening. Retinal vascular fractal analysis is a global measurement of the density and complexity of the retinal vascular system. Fractal dimension (Fd) using a disc-centered cropped Optos 200T x image (Optos plc, Dunfermline, Scotland, UK) were used. In a randomly selected eye of each patient, Fd was calculated using SIVA-Fractal (Singapore University, Singapore), a specialized semi-automatic software. Retinal neurodegeneration was evaluated by Topcon 3D OCT-2000 Spectral Domain OCT (Topcon, Tokyo, Japan) and by a RETI-scan multifocal ERG system (Roland Consult, Brandenburg a.d.Havel, Germany) in ring 1–6. Level of DR was determined by a single trained grader in 7-field fundus photos using the Early Treatment Diabetic Retinopathy Scale (ETDRS). Diabetic neuropathy was defined by the presence of neuropathic symptoms or a current patient diagnosis.

**Results:** Mean age and duration of T2DM were 62.4 and 11.7 years, respectively; 45.7% were men. Mean Fd was 1.413 (range 1.278–1.509) and ETDRS levels were 10 (42.3%), 20 (34.6%) and 35 (23.1%), respectively. In univariate models, significant correlations were found between Fd and multifocal ERG implicit time of ring 1 (\( r=0.25 \), \( p=0.01 \)) and OCT ganglion cell layer (GCL) thickness (\( r=0.20 \), \( p=0.04 \)). In a multivariable linear regression model, Fd showed statistically significant correlation with multifocal ERG implicit time of ring 1 (\( r=0.25, p=0.01 \)) and OCT ganglion cell layer (GCL) thickness (\( r=0.20, p=0.04 \)). There were no correlations between Fd and age, sex, duration of diabetes, hypertension, BMI, nephropathy or other OCT and multifocal ERG parameters.

**Conclusions:** In patients with T2DM and no/mild DR, independent correlations were found between early vascular and neurogenic changes. Decreased retinal vascular fractal dimension and GCL-loss as well as prolonged central implicit time seem to be early events in DR. Thus, retinal fractal analysis might help to identify patients with early neurodegenerative changes.
Commercial Relationships: Ulrik Frydkjaer-Olsen, None; Rasmus Soegaard Hansen, None; Knud Pedersen, None; Jose G. Cunha-Vaz, None; Rafael Simó, None; Tunde Peto, None; Jakob Grauslund, None

Program Number: 1804 Poster Board Number: A0237
Presentation Time: 11:00 AM–12:45 PM
Electrophysiology in the evaluation of neuroprotective effect in early diabetic retinopathy – a pilot study
Balazs Varsanyi1, Zsolt Biro1, János Fehér2.
11:00 AM–12:45 PM
1804
None
Grauslund
Tunde Peto
None;
Cunha-Vaz
None;
Rafael Simó
None;
Balazs Varsanyi
Commercial Relationships:
Zsolt Biro
None;
János Fehér
None;
Patents

Purpose: Diabetic retinopathy (DR) is a leading cause of preventable blindness. Evidence suggests that retinal neurodegeneration (ND) plays a role in the genesis of DR. Our aim is to study ND process and long-term effect of neuroprotection with electrophysiological methods in patients with diabetes (DM).
Methods: 24 patients with DM (without diabetic macular edema and severe DR) are involved in this study (age: 34-65 ys). 12 patients have taken probiotic vitamin supplements with supposed neuroprotective effect (Group 1), while the other 12 patients remained on their previous diet (Group 2). Beside routine ophthalmological examinations, electrophysiological tests (RetiPort/ RetiScan, Roland Consult GmbH) and optical coherence tomography (OCT – Topcon 3D 2000, Topcon Inc.) are performed at baseline and every 6 months. Electrophysiological test are repeated within 1 week and average values are analyzed. The observed parameters are best corrected visual acuity (BCVA), central retinal thickness (CRT), retinal nerve fiber layer thickness (RNFL), multifocal ERG (mfERG) implicit times, pattern ERG (PERG) P50 and N95 amplitudes, visual evoked potential (VEP) P100 amplitude and latency. The changes from the baseline of these parameters are compared between the two groups.
Results: After 6 months, there were no change in the BCVA in any of the patients. Changes of the OCT parameters (CRT, RNFL) were within ±5 mm, thus considered absent. The overall changes from baseline in mfERG implicit time were 0.03 and 0.04 ms in Group 1 and 2, respectively. PERG P50 amplitudes became 0.15 and 0.23 mV lower, while there was a decrease of 0.11 vs 0.19 mV in the N95 amplitudes in Group 1 and 2, respectively. The changes in VEP amplitudes were -0.39 and -0.62 mV in the two groups. None of these changes or the differences were statistically significant (p>0.05).
Conclusions: In the first 6 months of follow-up no statistically significant changes were detected in either parameters. This time is definitely too short to detect significant changes, however a tendency of worsening parameters was observed. These changes were slightly more remarkable in the control group and above the expected normal progression. The design of the study seems suitable for the long term evaluation of ND and neuroprotection in patients with early diabetic retinopathy, so continuation of the follow-up and enrollment of more patients are in prospect.
Commercial Relationships: Balazs Varsanyi, None; Zsolt Biro, None; János Fehér, Nutripharma Kft. (P)

Program Number: 1805 Poster Board Number: A0238
Presentation Time: 11:00 AM–12:45 PM
Age and sex distribution of retinal layer thickness from spectral domain optical coherence tomography (SD-OCT) macular scans in the Beaver Dam Eye Study (BDES)
Stacy M. Meuer1, Kyungmoo Lee1 2, Andreas Wahle1 2, Kristine E. Lee1, Anurita Kulkarni1, Barbara E. Klein1, Milan Sonka1 2, Michael D. Abramoff1 2, Ronald Klein1.1 Ophthalmology & Visual Sciences, University of Wisconsin-Madison, Madison, WI; 2Electrical and Computer Engineering, University of Iowa, Iowa City, IA; 3Iowa Institute for Biomedical Imaging, University of Iowa, Iowa City, IA; 4Ophthalmology and Visual Sciences, University of Iowa, Iowa City, IA.
Purpose: To describe retinal layer thickness by age, sex and location in the macula in a large population based study of older adults.
Methods: SD-OCT imaging was performed in participants aged 63-100 years at the 2008-2010 BDES examination (n=1913). These images (3038 gradable scans in 1538 people) were automatically segmented using the Iowa Reference Algorithms which identify 10 retinal layers: nerve fiber (NFL), ganglion cell (GCL), inner plexiform (IPL), inner nuclear (INL), outer plexiform (OPL), outer nuclear (ONL), inner segment/outer segment (ISOS), outer segment junction (OSJ), outer photo receptor (OPR) and retinal pigment epithelial (RPE). Mean thickness of each layer was calculated by averaging the thicknesses of the 4 subfields in the inner ring of the Early Treatment Diabetic Retinopathy Study grid. Scans where macular degeneration, diabetic retinopathy, macular holes, epiretinal membranes or other pathology was identified and scans with a low tissue contrast score or other artifacts (severe motion, Z-plane offset) affecting segmentation were excluded.
Results: The average (standard deviation) thickness in the inner ring was 25.7 (2.9), 44.0 (7.3) 40.0 (3.0), 34.5 (3.3), 32.1 (3.6), 39.8 (8.4) 12.4 (0.7), 12.0 (1.8), 16.5 (2.3) and 18.8 (1.7) µm for the NFL, GCL, IPL, INL, OPL, ONL, ISOS, OSI, OPR, and the RPE, respectively. The figure shows the thickness z-score by age. With the exception of the ISOS and RPE, the layers were thinner with age and in females (not statistically different for GCL). The ISOS and RPE were slightly thicker with age and in females. No associations between age or sex and the OPL were identified. The GCL thickness decreased from 45.8 µm in persons aged <70 years to 39.5 µm in those aged ≥ 85 years, or a 0.28 µm decrease per 1 year increase in age. Equivalent but smaller decreases in thickness of other retinal layers with age were found. Trends were similar for the central subfield and outer ring.
Conclusions: Age related thinning of the retina was present in most retinal layers. The differences between layers, correlates and functional implications of these findings will be further explored.

Thickness measures (z-score) for each layer with lines connecting 5 age groups (<70, 70-74, 75-79, 80-84 and ≥85 years).
Program Number: 1807 Poster Board Number: A0240
Presentation Time: 11:00 AM–12:45 PM
Spatial distribution of early thickness changes in the inner retinal layer in adolescents with Type 1 diabetes
Al Alan M. Poon1, 2, Thomas Wright3, Annie Dupuis4, 5, Zhihong Hu5, Srinivas R. Sadda5, 6, Carol A. Westall2, 7. 1Institute of Medical Science, University of Toronto, Toronto, AB, Canada; 2Department of Ophthalmology and Vision Sciences, The Hospital for Sick Children, Toronto, ON, Canada; 3Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada; 4Clinical Research Services, The Hospital for Sick Children, Toronto, ON, Canada; 5Doheny Eye Institute, Los Angeles, CA; 6University of California, Los Angeles, Los Angeles, CA; 7Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, ON, Canada.

Purpose: Diabetic retinopathy (DR) is clinically defined by vascular lesions that develop in the multilayered retina. By the time vascular lesions appear and are clinically detectable, there may already be irreversible damage and permanent vision loss. Inner retinal layer (IRL) thickness changes precede the development of vascular lesions and may serve as an early biomarker of DR. It is unknown whether IRL thickness changes are evenly distributed or localized to discrete regions across the retina.

We hypothesize that in diabetes, IRL thickness changes are localized to specific regions. The objective of this prospective, cross-sectional observational study was to determine if there are regional changes in IRL thickness in adolescents with Type 1 diabetes compared with controls.

Methods: Participants were adolescents with Type 1 diabetes (T1D) with no or minimal DR (patient group), and adolescents with no diabetes with healthy eyes (control group). At the time of testing, blood glucose levels were maintained within 4-10mmol/L. Standard eye examination and fundus photography ensured adherence to inclusion criteria.

Using spectral-domain optical coherence tomography (OCT), we obtained high resolution cross-section images of the retina in vivo. A 6x6mm area centered on the fovea was imaged using Cirrus HD-OCT 5000 (Carl Zeiss Meditec). Automated segmentation software was applied to unprocessed OCT images to discriminate individual retina layers. The distance between the upper and lower boundaries of the IRL gives the thickness at that location.

Results: A total of 6536 evenly distributed IRL thicknesses were obtained per participant, achieving up to 11.7 and 2.0μm resolutions in the lateral and axial dimensions, respectively. Currently, single eyes from 5 patients (mean age 23.0±1.7y) and 8 controls (mean age 23.4±4.7y) have been analyzed. Natural variation was observed in each participant. Analysis revealed no significant difference in total IRL thickness between patient and control groups although the patient group showed greater variance. Regionally, patient foveas were thicker, superior perifoveas thinner, and inferior perifoveas thicker, than controls.

Conclusions: This is the first study to maintain high resolution segmentation of retinal layer thickness throughout the analyses. These data show certain regions that are prone to changes in diabetes.
Utilizing Spectral-Domain Optical Coherence Tomography to Measure Panretinal Photocoagulation’s Effect on Retinal Nerve Fiber Layer Thickness in Patients with Proliferative Diabetic Retinopathy

Adam C. Janot1, Jessica Randolph1, 2, Vikram Brar1. 1Ophthalmology, VCU, Richmond, VA; 2Texas Retina, Houston, TX.

**Purpose:** Panretinal photocoagulation (PRP) is the standard of care in the treatment of proliferative diabetic retinopathy (PDR). Prior studies have attempted to measure PRP’s effect on peripapillary retinal nerve fiber layer (RNFL) thickness using older optical coherence tomography (OCT) technology, but have shown inconsistent results. We utilized a prospective-cohort study design to quantify the RNFL’s response to PRP using spectral-domain optical coherence tomography (SD-OCT) with image registration, allowing scans to align precisely with prior scans and facilitate more accurate measurements over time.

**Methods:** Study inclusion criteria were patients who underwent a single treatment of first-time PRP, with a minimum of 1000 spots and a 360-degree fashion. Exclusion criteria included any history of optic neuropathy, glaucoma, ocular hypertension, and poor scans that could not be re-segmented. Pre-PRP SD-OCTs were completed, using a Heidelberg Spectralis OCT, in all patients and compared to SD-OCTs done at all follow-up visits. To compare the data over time, the SD-OCTs were divided in 6 post-PRP groups (1-60, 61-120, 121-240, 241-360, 361-480, and >480 days). Data was normalized to pre-PRP values. A two-sided, pairwise t-test for the mean was used to determine the significance of RNFL changes from baseline.

**Results:** 22 eyes from 17 patients were enrolled in the study. The 1-60 day post-PRP scans showed statistically significant RNFL thickening in global thickness (10.8±0.9%, p=0.004) as well as the inferonasal (10.1±1.0%, p=0.002), inferotemporal (11.1±1.0%, p=0.001), temporal (13.0±1.5%, p=0.007), and supratemporal (7.1±0.7%, p=0.003) regions. After 60 days, there was a return to baseline RNFL thickness that was maintained throughout the follow-up period (see figure 1).

**Conclusions:** Following PRP, there is an initial thickening of the peripapillary RNFL followed by a return to pre-PRP thickness. In patients with PDR and glaucoma, RNFL thickness measured by SD-OCT can be used reliably to monitor for progression of disease beginning 60 days after PRP, especially in those whose laser pattern may affect visual field results.

![Mean Change in Global RNFL Thickness After PRP](image_url)

**Figure 1:** A statistically significant increase in global RNFL thickness is seen after PRP, followed by a return to baseline.

**Commercial Relationships:** Adam C. Janot, None; Jessica Randolph, None; Vikram Brar, None

**Program Number:** 1808 Poster Board Number: A0241
**Presentation Time:** 11:00 AM–12:45 PM

A novel approach in the assessment of the photoreceptor layer in eyes with macular diseases using texture-based analysis of SD-OCT data

Daniela Giannini1, Giuseppe Lombardo1, 4, Sebastiano Serrao2, Maurizio Vichi1, Marco Lombardo1, 4. 1Statistical Sciences, University of Rome “La Sapienza”, Mentana, Italy; 2Fondazione G.B. Bietti IRCCS, Rome, Italy; 3CNR-IPCF Unit of Support Cosenza, Rende, Italy; 4Vision Engineering Italy srl, Rome, Italy.

**Purpose:** To evaluate a texture analysis method to assess the integrity of the photoreceptor layer (PRL) in spectral domain - optical coherence tomography (SD-OCT) images of patients suffering from inherited and acquired macular diseases.

**Methods:** High-quality SD-OCT images were acquired over a 10°x15° retinal area centered on the fovea in four patients suffering from macular diseases, two of which had a previous diagnosis of age-related macular degeneration and the others of rod-cone dystrophy. Eight age-matched healthy subjects were used as controls. After automated segmentation of the PRL, a sliding box algorithm was used to calculate the Gray Level Co-occurrence Matrix (GLCM) over the PRL. From the GLCM matrix, three texture parameters were computed, which included the contrast, the local homogeneity, and the correlation (256 gray levels; directions 0°, 45°, 90° and 135°). The raw data were used to generate three statistical descriptors of the PRL integrity, such as the ratio of contrast, the ratio of homogeneity and the ratio of correlation; all the parameters were calculated as the ratio between 0° and 90° directions. Texture analysis of the PRL was then performed over the foveola (0.25 mm diameter) and other regions of interests (ROIs) across the temporal and nasal meridians, such as the parafovea (0.26-0.86 mm), the perifovea (0.87-2.00 mm) and the mid-periphery (2.01-2.36 mm).

**Results:** GLCM analysis was valuable to characterize the structure and texture of the regular horizontal stratification of the PRL in SD-OCT images. The method was highly sensitive for assessing the pathological changes of the ellipsoid zone in patients compared with age-matched controls. In patients, all the statistical descriptors based on texture analysis of the PRL were far below the 95% confidence interval of controls in all ROIs, except for the mid-periphery.
Conclusions: The GLCM based imaging biomarkers showed to be valuable to assess quantitatively the pathological disruption of the PRL. Texture analysis of the PRL in high-resolution SD-OCT images of the retina represents a valuable objective tool for monitoring and assessing the integrity of photoreceptors in patients.

Commercial Relationships: Daniela Giannini, None; Giuseppe Lombardo, None; Sebastiano Serrao, None; Maurizio Vichi, None; Marco Lombardo, None

Support: 5x1000 funding - Italian Ministry of Health

Program Number: 1810 Poster Board Number: A0243
Presentation Time: 11:00 AM–12:45 PM
Relationship between metamorphopsia and foveal microstructure in patients with cystoid macular edema caused by branch retinal vein occlusion

Tomoya Murakami, Fumiki Okamoto, Yoshimi Sugiuara, Yoshifumi Okamoto, Takahiro Hiraoka, Tetsuro Oshika, University of Tsukuba, Tsukuba, Japan.

Purpose: To investigate the relationship between severity of metamorphopsia and the foveal microstructure measured with spectral-domain optical coherence tomography (SD-OCT) in patients with cystoid macular edema caused by branch retinal vein occlusion (BRVO-CME).

Methods: The study included 23 eyes of 23 patients with BRVO-CME. We examined the logarithm of the minimum angle of resolution best-corrected visual acuity (logMAR BCVA) and the severity of metamorphopsia using M-CHARTS. Central foveal thickness, central retinal thickness at the fovea (CRT-1mm), and macular volume were measured with SD-OCT software. Based on the obtained OCT image, the status of ellipsoid zone, external limiting membrane (ELM), outer retinal cyst and inner retinal cyst was also evaluated.

Results: The mean metamorphopsia score was 0.91 ± 0.57, with 22 of 23 patients having metamorphopsia (metamorphopsia score ≥ 0.2). The vertical metamorphopsia score (1.0 ± 0.6) was significantly higher than the horizontal metamorphopsia score (0.8 ± 0.6) (p < 0.05). The status of ellipsoid zone and ELM were significantly associated with logMAR BCVA, but not with the severity of metamorphopsia. The mean metamorphopsia score was significantly related to CRT-1mm (r = 0.595, p < 0.05) and the presence of inner retinal cyst (p < 0.05).

Conclusions: In patients with BRVO-CME, metamorphopsia was severer in the vertical than in the horizontal direction. The severity of metamorphopsia was significantly associated with central retinal thickness and the presence of inner retinal cyst.

Commercial Relationships: Tomoya Murakami, None; Fumiki Okamoto, None; Yoshimi Sugiuara, None; Yoshifumi Okamoto, None; Takahiro Hiraoka, None; Tetsuro Oshika, None

Program Number: 1811 Poster Board Number: A0244
Presentation Time: 11:00 AM–12:45 PM
The results of intravitreal bevacizumab (Avastin) therapy in patients with retinal venous occlusion


Purpose: To evaluate the functional and anatomical results of anti-VEGF (bevacizumab) treatment in patients with retinal venous occlusion.

Methods: Retrospective data analysis of 20 patients (10 men, 10 women, mean age 62 years) suffering from retinal venous occlusion (10 CRVO, 10 BRVO) treated with intravitreal bevacizumab injections at the Department of Ophthalmology, Faculty of Medicine, University of Pécs, Hungary between July 2012 and May 2014. The mean follow-up time was 12 (5-22) months. The visual acuity was determined by ETDRS chart, the retinal thickness by SD OCT (Topcon).

Results: The mean best corrected visual acuity improved by 15 ETDRS letters (from 55 to 70). The central retinal thickness decreased from 521 μms to 322 μms in average by the end of the follow-up period. The mean number of injections was 7 during the follow-up time.

Conclusions: Intravitreal bevacizumab therapy in patients with retinal venous occlusion showed functional and anatomical results during one year follow up.

Commercial Relationships: Zsofia Kolkedi, None; Adrienn Horvath, None; Zsolt Biro, None

Program Number: 1812 Poster Board Number: A0245
Presentation Time: 11:00 AM–12:45 PM
Efficacy and Safety of Rituximab in the Treatment of Ophthalmic Complications of Systemic Vasculitis

Shams Ilyas1, Christopher Holmes3, Hema Kolli1, Efrosini Papagiannuli2, Susan Mollan2, Matthew Morgan2, Alastair Denniston1. 1Ophthalmology, Wolverhampton Eye Infirmary, Birmingham, United Kingdom; 2University Hospital Birmingham, Birmingham, United Kingdom; 3Birmingham Midland Eye Centre, Birmingham, United Kingdom.

Purpose: Rituximab, a monoclonal antibody against CD-20 expressing B-cells, is increasingly used in systemic vasculitis, but there is limited data on its utility in ocular inflammation associated with these conditions. To evaluate the efficacy and safety of rituximab in the treatment of inflammatory eye disease associated with systemic vasculitis.

Methods: Patients receiving rituximab for non-cancer indications were identified from the pharmacy chemotherapeutic register between 2005-2014. Indication for treatment, eye involvement, response to therapy, reduction of corticosteroid and adverse events/discontinuation were recorded. The primary outcome was control of inflammation.

Results: 119 patients received rituximab for non-cancer indications, with 91 classified as systemic vasculitis (52 Granulomatosis with Polyangiitis (GPA), 29 Systemic Lupus Erythematosus (SLE) and 10 Other). In total 25 patients had ophthalmic involvement. The leading type of ophthalmic involvement were scleritis (n = 9). Sustained control of inflammation (for at least 28 days) was 38% within 6 months, and 80% within 12 months. Of those previously on a dose of greater than 10mg prednisolone, reduction to 10 mg or less was achieved by 36% at 6 months and by 62% by at 12 months respectively. Rituximab was discontinued prematurely in two patients because of adverse events, one for facial swelling the other for possible serum sickness reaction.

©2015, Copyright by the Association for Research in Vision and Ophthalmology, Inc., all rights reserved. Go to iovs.org to access the version of record. For permission to reproduce any abstract, contact the ARVO Office at pubs@arvo.org.
Conclusions: Our data suggests that rituximab is effective for the majority of patients with inflammatory eye disease associated with systemic vasculitis. The rate of adverse events were low.

Commercial Relationships: Shams Ilyas, None; Christopher Holmes, None; Hema Kolli, None; Efrosini Papagiannuli, None; Susan Mollan, None; Matthew Morgan, None; Alastair Denniston, None

Program Number: 1813 Poster Board Number: A0246
Presentation Time: 11:00 AM–12:45 PM

Nutrition Intake and Retinal Microvasculature in Pregnant Women during the Mid-Late Pregnancy:
Ling Jun Li, Mary Foong-Foong Chong, Ryan Man, Ecosse Lamoureux, Yap Seng Chong, Peter Gluckman, Kenneth Kwek, Seang-Mei Saw, Tien Y. Wong, Carol Y. Cheung. 1 Epidemiology and Public Health, National University of Singapore, Singapore; 2 Singapore Eye Research Institute, Singapore National Eye Centre, Singapore, Singapore; 3 Singapore institute for clinical sciences A*STAR, Singapore, Singapore; 4 O&G, National University Hospital, Singapore, Singapore; 5 KK Women’s and Children’s Hospital, Singapore, Singapore.

Purpose: Both over-nutrition (e.g. high fat intake) and under-nutrition (e.g. low protein and carbohydrate intake) in the mothers during pregnancy may lead to reduced uterine-placental blood flows and eventually stunt fetal growth. The mechanism, of how maternal suboptimal nutritional problems affect uterine-placental vasculature and further stunt utero-placental blood flow and fetal growth, is still unknown. Retinal microvasculature can be examined non-invasively and used as a reliable tool to assess microcirculation in vivo, thus, our study investigated the association between maternal nutrition intake and retinal microvasculature, which may indirectly reflect the uterine-placental circulation during pregnancy.

Methods: A total number of 1163 pregnant women aged 18-46 years were recruited during their early pregnancy to GUSTO birth cohort. Dietary intake was ascertained and retinal photography was performed at 26-28 weeks gestation. Intakes of protein, fat and carbohydrate (all in grams) were calculated based on an interviewer-administered 24-hour food recall. Healthy eating index (HEI) was scored from 0-100 within GUSTO cohort specific-intakes of different food components, and it was used to assess the dietary quality. Higher HEI score shows a better dietary pattern during pregnancy. Retinal vascular parameters were quantitatively measured by a semi-automated computer program (Singapore I Vessel Assessment [SIVA], version 3.0).

Results: There were 614 pregnant women in this study. In non-adjusted model, each unit increase in log-transformed protein intake and each 10-score increase in HEI was associated with a 6.08 μm (p=0.03) and a 1.23 μm (p=0.002) decrease in retinal venular caliber, respectively. After adjusting for age, ethnicity, maternal education, birth order, prenatal comorbidity, BMI at 26-28 weeks, smoking and alcohol drinking history and gestational diameter mellitus diagnosis, per 10 scores increase in HEI was marginally associated with a 0.93 μm (p=0.046) decrease in retinal venular caliber, yet the significance of unadjusted association between protein intake and retinal venular caliber narrowing was attenuated.

Conclusions: Our data suggest that mothers with better dietary quality tend to have smaller retinal venular caliber, which is an indicator of healthy retinal vasculature. These results provide insights into how maternal nutrition may affect the microvasculature in pregnancy.

Commercial Relationships: Ling Jun Li, None; Mary Foong-Foong Chong, None; Ryan Man, None; Ecosse Lamoureux, None; Yap Seng Chong, None; Peter Gluckman, None; Kenneth Kwek, None; Seang-Mei Saw, None; Tien Y. Wong, None; Carol Y. Cheung, None

Support: This study is funded by the National Medical Research Council, Singapore, NMRC/TCR/004-NUS/2008, NMRC/CG/SERI/2010, and NMRC/STaR/0003/2008

Program Number: 1814 Poster Board Number: A0247
Presentation Time: 11:00 AM–12:45 PM

Prevalence and progression of sickle cell retinopathy among children at Yale
Daniel Lee1, Farzana Pashankar2, Martin D. Slade1, Ron A. Adelman1, Kathleen M. Stoessel1. 1 Ophthalmology and Visual Science, Yale School of Medicine, New Haven, CT; 2Pediatric Hematology & Oncology, Yale School of Medicine, New Haven, CT; 3Occupational and Environmental Medicine, Yale School of Medicine, New Haven, CT.

Purpose: To determine the prevalence of sickle retinopathy in pediatric patients seen at Yale and to identify factors that modifies risk for the onset and progression of sickle retinopathy.

Methods: A retrospective chart review and analysis of consecutive pediatric patients (ages 6-21) referred to Yale for sickle retinopathy from January 1, 2003 to December 31, 2012. 135 patients were reviewed for the onset of retinopathy, time to progression, gender, genotype, fetal hemoglobin (HgF) level, and history of monthly transfusions.

Results: Of the 135 patients, 81 patients had SS genotype, 38 had SC genotype, and 15 had SB-thalassemia genotype. Among patients with SS genotype, 35 (43.2%) and 11 (13.6%) had non-proliferative and proliferative sickle retinopathy respectively. The mean age at diagnosis was 13.4 (SD 6.16) for NPSR and 16.8 (SD 2.50) for PSR. Of the patients with SC genotype, 14 (36.8%) had NPSR and 12 (31.6%) had PSR with a mean age of diagnosis of 11.5 (SD 5.15) and 12.5 (SD 4.04) respectively.

Patients with SS genotype were stratified by hemoglobin F (HgF) levels of 0.19 mg/dL, 2.4 mg/dL, 2.7 mg/dL and 9.8 mg/dL with 4, 3, 15 and 19 patients in each group respectively. Subjects undergoing monthly transfusions were excluded from the analysis. There was a 5.3 fold increase (CI 95% 1.9-14.9, p=0.001) in the incidence of sickle retinopathy in patients with HgF less than 4.0mg/dL. There was a statistically significant inverse correlation of sickle retinopathy with HbF levels using spearman correlation (r=-0.22, p=0.0028). Patients undergoing monthly scheduled transfusions had 7.07 fold (CI 95% 1.61 to 31.0, P=0.0096) decreased risk for progression of retinopathy while receiving treatment. The one patient who demonstrated progression despite monthly transfusions died secondary to complications related to her SCD.

Conclusions: Our patient cohort agrees with previous studies with the tendency of the SC genotype having a more rapid onset and progression of SR compared to SS. Low HgF levels correlated with a statistically significant increased incidence of sickle retinopathy. Higher levels of HgF seem to be protective against onset and progression of SR. Patients undergoing monthly transfusions had a statistically significant reduction in risk for progression of disease. Progression in the setting of transfusion is rare and may be a poor prognostic indicator.

Commercial Relationships: Daniel Lee, None; Farzana Pashankar, None; Martin D. Slade, None; Ron A. Adelman, None; Kathleen M. Stoessel, None

©2015, Copyright by the Association for Research in Vision and Ophthalmology, Inc., all rights reserved. Go to iovs.org to access the version of record. For permission to reproduce any abstract, contact the ARVO Office at pubs@arvo.org.
Program Number: 1815 Poster Board Number: A0248
Presentation Time: 11:00 AM–12:45 PM
36-months follow-up of the Phase 1 clinical trial of the use ciliary neurotrophic factor (CNTF) for Macular Telangiectasia Type 2 (MacTel)
Tunde Peto1, Traci E. Clemons2, Emily Y. Chew1, Irene Leung1, Ferenc Sallo1, Alan C. Bird1. 1MEH and IoO, NIHR Biomedical Rsch Ctr for Ophthal., London, United Kingdom; 2EMMES Corporation, Rockdale, MD; 3National Eye Institute, Rockdale, MD.
Purpose: MacTel is a slowly progressing disease of the macula where both vascular and neuronal layers of the retina are involved. There is currently no known safe and effective treatment for MacTel. The CNTF Phase 1 trial is a non-randomised uncontrolled trial that has completed 3 years of safety follow-up. The purpose of this study is to describe the imaging safety outcomes at 36-months as per independent and objective Reading Centre (RC) evaluation where all personnel are masked to the treatment status of the participants’ eyes.
Methods: One eye (eye with worse visual acuity) of each patient was implanted and the patients were followed up biannually, the most recent of which is the 3-year follow-up. After clinical examination and electrodiagnostics, standard imaging battery including colour fundus photography, fluorescein angiogram, optical coherence tomography, fundus autofluorescence imaging and microperimetry were carried out on both eyes. The deidentified images were sent to the RC at Moorfields Eye Hospital, London, UK where the images were read by masked trained and certified MacTel graders.
Results: Seven participants were enrolled (2 males; 48-67 years of age). None had neovascular stage MacTel at enrolment or at 36-months. On image analysis, there was no significant progression of any MacTel related characteristics (opacification of the retina, telangiectasias, blunted vessels, pigmentary changes) in either eye of the participants. The mean retinal thickness in eyes with CNTF implant showed a marked increase in ETDRS zones 6-9 (20-23 micron), while the untreated eyes showed minimal increase of 6-11 micron. On en-face imaging, the main break area did not change in either eye significantly (mean difference in area -0.04±0.07; 95%CI: -0.22–0.16; p=0.58). Microperimetry showed no statistically significant difference between the mean change in sensitivity from baseline to 36-months between eyes (mean±SE difference=-0.9±0.5 dB; 95%CI:0.3–2.2; p=0.12), and this level of change is within the expected level of variability for this test modality.
Conclusions: So far there has been no safety identified on any imaging modalities used for this trial. A Phase 2 trial is ongoing to establish efficacy of CNTF in MacTel.
Commercial Relationships: Tunde Peto, None; Traci E. Clemons, None; Emily Y. Chew, None; Irene Leung, None; Ferenc Sallo, None; Alan C. Bird, None
Support: Lowy Medical Research Foundation
Clinical Trial: NCT01327911

Program Number: 1816 Poster Board Number: A0249
Presentation Time: 11:00 AM–12:45 PM
The study on the correlation between fundus changes and the risk of cerebral stroke
Li Zhang1,2, Liang Xu1,2, Hua Yang1,2, Qisheng You1,2.
1Ophthalmology, Beijing Institute of Ophthalmology, Beijing, China; 2Ophthalmology, Beijing Tongren Hospital, Beijing, China.
Purpose: To explore the correlation between fundus changes and the risk of cerebral stroke, and to find out the risk factors or early-warming indicators for stroke.
Methods: This is a case-control study. 450 patients with cerebral stroke (stroke group) and 566 non-stroke subjects (controlled group) selected from Beijing Eye Study were enrolled. Two groups matched for age. 1016 cases of fundus photographs were evaluated to find out the correlation between fundus indicators and the risk of stroke. Main outcome measures were retinal nerve fiber layer defect (RNFLD), retinal microvascular abnormalities (arterial narrowing, vein dilatation), retinopathy (cotton wool spot, and retinal hemorrhage), optic nerve changes and macular diseases. Logistic regression statistic method was used to analysis the correlation between fundus changes and stroke. Orange 2 analysis software was used to visualization the data results.
Results: The mean age of stroke group was (63.64±10.16) years old, 258 males (57.3%), 192 females (42.7%). The mean age of non-stroke group was (62.45±8.68) years old, 250 males (44.2%), 316 females (55.8%). Two groups matched for age (P=0.063). Gender, RNFLD, retinal vein dilatation, macular diseases were correlated with stroke significantly (P=0.000), RNFLD (OR=4.163, 95%CI 2.792–6.208) and retinal vein dilatation (OR=3.443, 95%CI 2.333–5.082) were highly correlated with stroke particularly. Except for gender having negative correlation with stroke (being compared with females, males a for more cases susceptible risk to stroke), RNFLD and retinal vein dilatation, macular diseases having positive correlation with stroke. Fundus indicators of retinal arterial narrowing, vein dilatation and RNFLD coexisting were correlated with high risk of stroke.
Conclusions: RNFLD, retinal arterial narrowing, vein dilatation correlated with high risk of cerebral stroke, can be regarded as early-warming indicators for stroke. Fundus changes reflect cerebrovascular changes relating to stroke. The ability to assess the retinal circulation and nerve fiber layer in vivo offers potential advantages over other cerebral imaging techniques, which tend to be expensive and not necessarily widely available.

Commercial Relationships: Li Zhang, None; Liang Xu, None; Hua Yang, None; Qisheng You, None
Influence of systemic hypertension on macular thickness measured with optical coherence tomography

Don-II Ham1, Mingui Kong1, Young K. Kwun1, Joohon Sung1, Yun-Mi Song1. 1Samsung Medical Center, Ophthalmology, Sungkyunkwan Univ Sch of Med, Seoul, Korea (the Republic of); 2Epidemiology and Institute of Environment and Health, Seoul National University, School of Public Health, Seoul, Korea (the Republic of); 3Family Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea (the Republic of).

Purpose: To investigate the association between systemic hypertension and macular thickness.

Methods: Clinical data of 889 Korean participants in previous Korean Twin Study were reviewed. All subjects underwent ocula examination, axial length measurement, and optical coherence tomography (OCT) using Stratus OCT. Body mass index (BMI), blood pressure, blood level of glucose and cholesterol, were measured.

Results: Age, sex, axial length-adjusted analysis revealed that hypertension was associated with a significant decrease in macular thickness in 8 of 9 ETDRS ring subfields (P<0.01), except the central subfield. The further adjustment for BMI, diabetes, and smoking showed similar association except the central and outer nasal subfield.LDL, HDL, presence of diabetes, and smoking history showed no significant association.

Conclusions: The thickness in most of macular area is reduced in subjects having systemic hypertension. The central subfield isthe area not affected by systemic hypertension.

Commercial Relationships: Don-II Ham, None; Mingui Kong, None; Young K. Kwun, None; Joohon Sung, None; Yun-Mi Song, None

Program Number: 1818 Poster Board Number: A0251
Presentation Time: 11:00 AM–12:45 PM

Using OCT and a novel grading method to investigate the prevalence and severity of epiretinal membranes in an optometric practice in Norway


Purpose: The introduction of OCT in optometric practice has improved detection and diagnosis of epiretinal membranes (ERM). However, the occurrence of ERM in Norway is unknown. In this cross-sectional study, we investigated the prevalence and distribution of ERM stages imaged by OCT in optometric patients.

Methods: 120 healthy patients, age > 50 yrs, were enrolled from one optometric practice in Trondheim, Norway, during a period of 6 months. All underwent a full optometric examination followed by SD-OCT (Topcon 3D OCT-2000). Repeated volume scans (128 B-scans, 512 A-scans) were obtained from the posterior pole of both eyes. ERM was identified (I), classified (C) and graded (G) based on: I) the occurrence and extension of hyperreflective bands, C) location of ERM relative to the fovea (fovea, parafovea, macula), and G1) any concomitant deformation of the underlying retinal structures (with and without involvement of the receptor layer) and G2) deformation of the foveal profile (2 levels of flattening, 2 levels of steepening).

Results: 4 months into the study 182 eyes of 91 patients were included (F: 64, mean age 66.5 yrs). The prevalence of ERM in one or both eyes was 30.8 % (CI 21.3 – 40.3) and 7.7 % (CI 2.2 – 13.2), respectively. Patients with ERM were significantly older than patients with no ERM (+ 9 yrs, p < 0.001). However, both genders were equally affected. Among eyes with ERM the distribution of foveal-, parafoveal- and macular ERM (C) were 8.6 %, 42.9 % and 100.0 %, respectively. Retinal deformation without receptor layer involvement (G1) was found in 68.6 % of these eyes. None showed signs of receptor layer involvement. 42.9 % of the eyes with ERM had deformed foveal profiles (G2) ranging from slightly- (17.1 %) to markedly flattened (8.6 %), or from slightly- (8.6 %) to markedly steepened (8.6 %). The frequency of ERM classified as foveal was 12.5 % for eyes with deformed retina and 26.7 % of eyes with both deformed retina and foveal profile.

Conclusions: This is the first report on the prevalence and severity of ERM imaged by OCT in optometric patients in Norway. Results indicate that ERM imaged by OCT may be encountered more frequently than expected from the literature, however with limited involvement of the retinal structures and foveal profile. Further studies to understand the implications for monitoring in optometric practice is warranted.

Commercial Relationships: Tina Wammer, None; Per O. Lundmark, None
Support: C-optikk grant

Program Number: 1819 Poster Board Number: A0252
Presentation Time: 11:00 AM–12:45 PM

Visual Acuity and Prevalence of Fundus Diseases in Japanese Elderly: Baseline Findings of Fujiwara-Kyo Cohort Study

Kimie Miyata1, Tomo Nishi1, Taiji Hasegawa1, Takeshi Kobayashi1, Masahiro Okamoto1, Masashi Mine1, Toyoaki Matsuura1, Nozomi Okamoto1, Norio Kurumatani1, Nahoko Ogata1. 1Ophthalmology, Nara Medical University School of Medicine, Kashihara, Japan; 2Community Health and Epidemiology, Nara Medical University School of Medicine, Kashihara, Japan.

Purpose: Japan is considered to be one of the most super-aged country in the world. In this elderly community, it is very important to maintain good visual functions to maintain a good quality of life. The purpose of this study was to determine the baseline visual functions and the prevalence of fundus diseases in an elderly Japanese population.

Methods: This was a population based, cross-sectional study conducted in 2012 in Nara, Japan and named the Fujiwara-Kyo study. The study included 2873 individuals ≥70-years-of-age who were independent walkers. The best-corrected visual acuity (BCVA) and intraocular pressure (IOP) were measured, the fundus photographs and optical coherence tomographic (OCT) images were examined, and the self-reported ophthalmological history was analyzed. The associations between the visual acuity and the history of cataract surgery and fundus diseases were also analyzed.

Results: There were 1514 men (52.7%) and the mean age was 76.3±4.9 (mean ± standard deviation) years. The mean BCVA was 0.048 ± 0.26 logMAR units, and the IOP was 12.3 ± 3.0 mmHg. Both the BCVA and IOP decreased with increasing age. Of the 5453 eyes, 1174 (21.5%) had undergone cataract surgery, and these eyes had better visual acuity by 0.02 logMAR units than eyes without cataract surgery. The prevalence of late age-related macular degeneration was 1.1%, epiretinal macular membrane was 6.7%, diabetic retinopathy was 0.7%, and retinal vein occlusion was 0.8%. The prevalence of ERM was greater than that previously reported.

Conclusions: Individuals ≥70 years who have independent walking ability in the Fujiwara-Kyo study have the good visual acuity. Fundus examinations by ophthalmoscopy and OCT were important in detecting fundus diseases.

Commercial Relationships: Kimie Miyata, None; Tomo Nishi, None; Taiji Hasegawa, None; Takeshi Kobayashi, None; Masahiro Okamoto, None; Masashi Mine, None; Toyoaki Matsuura, None; Nozomi Okamoto, None; Norio Kurumatani, None; Nahoko Ogata, None

©2015, Copyright by the Association for Research in Vision and Ophthalmology, Inc., all rights reserved. Go to iovs.org to access the version of record. For permission to reproduce any abstract, contact the ARVO Office at pubs@arvo.org.