**Conclusions:** To our knowledge, this is the first analysis of the role of anti-VEGF therapy in the CT of DR patients. Eyes treated with anti-VEGF showed a significant positive correlation between the number of PRP spots and CCT in 6 of the 13 measures in central B-domain OCT Enhanced depth imaging protocol (OCT). The laser parameters were different between two groups and were as follows: mean number of treatments=2.4 and 3.4, mean total number of laser burns=1960 and 1371, mean duration of laser=26 and 216ms, mean laser power=394 and 216 mW in PASCAL and conventional laser group, respectively (p<0.001). The laser parameters were different between two groups and were as follows: mean number of treatments=2.4 and 3.4, mean total number of laser burns=1960 and 1371, mean duration of laser=26 and 216ms, mean laser power=394 and 216 mW in PASCAL and conventional laser group, respectively (p<0.001 in all laser parameters).

**Conclusions:** Both PASCAL and conventional PRP showed similar effect on inducing and maintaining regression of retinal neovascularization over 12 months in treatment-naïve PDR with the laser parameters used in this study. On the other hand, incidence of ME was lower in PASCAL group than conventional PRP group (171/219 eyes, 78.1%) (p<0.001). The laser parameters were different between two groups and were as follows: mean number of treatments=2.4 and 3.4, mean total number of laser burns=1960 and 1371, mean duration of laser=26 and 216ms, mean laser power=394 and 216 mW in PASCAL and conventional laser group, respectively (p<0.001 in all laser parameters).

**Conclusions:** The prevalence of retinal vasculopathy in diabetic and non-diabetic persons with increased BMI has been described. The purpose of this investigation was to describe the prevalence and spectrum of retinal vasculopathy in morbidly obese and to determine if diabetes or BMI is associated with prevalence of retinopathy.

**Methods:** One hundred morbidly obese patients (BMI>40 kg/m2 or BMI>30 kg/m2 and waist circumference>102 cm for men and >88 cm for women) were recruited and classified in two groups. Preoperative systemic and ocular data were similar between two groups. However, the incidence of VH, NVI, and ME was lower in PASCAL group than conventional PRP group (171/219 eyes, 78.1%) (p<0.001). The laser parameters were different between two groups and were as follows: mean number of treatments=2.4 and 3.4, mean total number of laser burns=1960 and 1371, mean duration of laser=26 and 216ms, mean laser power=394 and 216 mW in PASCAL and conventional laser group, respectively (p<0.001 in all laser parameters).
BMI >35 kg/m² with significant co-morbidity were recruited into this prospective study. Clinical data included age, gender, presence and duration of diabetes, BMI, and dilated fundus photography. Microvascular retinopathy was graded by two independent observers using the Early Treatment Diabetic Retinopathy Study (ETDRS) retinopathy grades. Arterial-venule ratio (AVR) was used to evaluate microvascular retinopathy and calculated using Knudson’s revised formulas. Prevalence of microvascular retinopathy (and 95% confidence intervals) was calculated for those with and without diabetes. Mean AVR was calculated for the entire population, compared between patients with and without diabetes, and was correlated with BMI using Pearson correlation.

**Results:** Patients included 30 males and 70 females with a mean age of 49 years (range=25, 71). Forty-five (45%) of the patients were diabetic with a duration of diabetes ranging from 1 month to 30 years (mean=8 years). BMI ranged from 35 kg/m² to 97 kg/m² with a mean of 48.5 kg/m² (SD=9.3). Microvascular retinopathy was present in 17 of 45 diabetics (37.8%, 95% CI=[23.8%, 53.5%]) and in 2 of 55 non-diabetics (3.6%, 95% CI=[0.1%, 11.8%]). ETDRS grades in affected patients ranged from 3 to 35. The mean AVR for the 100 patients was 0.664 (95% CI=[0.654, 0.674]). Mean AVR was not significantly different between patients with and without diabetes (diabetes mean=0.670, no diabetes mean = 0.659, two-sample t-test p-value = 0.290). AVR was not significantly correlated with BMI (r = -0.02, p-value=0.830).

**Conclusions:** The prevalence of retinal vasculopathy, which in this population included only non-proliferative diabetic, is greater in morbidly obese diabetics than non-diabetics, and exceeds those reported for obese diabetics with lower BMI. BMI was not correlated with AVR.

**Commercial Relationships:** Tamara R. Vrabec, None; Tatiana C. Franco, None; Christopher Still, None; Craig Wood, None; Vincent F. Baldassano, None

**Support:** Internal Funding, ACR, Geisinger Medical Center, Danville, PA

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National Diabetic Screening Programme for M1 maculopathy were imaged with both non-stereo Fundus Photographs (FP) (Zeiss Visucam Pro NM) and Multicolor Spectralis (McS) (Heidelberg Engineering) in an hospital based OCT virtual clinic. FP were graded as sharp, unsharp or ungradable. Ungradable FP were excluded. A retinal photographer (MC) and ophthalmologist (EC) graded in a masked fashion the presence of exudates on FP and McS. Cohen’s Kappa statistic was used to ascertain the level of agreement between the two imaging modalities and between observers. Fundus photographs and the ophthalmologist’s observations were set as gold standard for analysis purposes. A senior ophthalmologist (SP) more familiar with McS reviewed the disagreements and graded HE as being significant on FP if HE were ≥ than ETDRS Standard Photo 3.

**Results:** McS and FP matched detection of HE in 83 eyes for the ophthalmologist observations. The mismatch were due in 14 cases to McS failing to identify HE and in 3 cases to McS detecting HE not visible on unsharp, lower quality FP. Interobserver agreement was highest for detection of any HE on fundus photos with K=0.71. Agreement between McS and FP achieved K=0.61 for the ophthalmologist and K=0.45 for the photographer. Senior ophthalmologist arbitration reduced the McS and FP disagreement to 4 cases, of which only 2 had significant HE. Confounding factors causing disagreement were questionable or dot HE, abnormal reflectance from ERM and unsharp FP.

**Conclusions:** McS seems to need more clinically experienced observers to match detection of HE on FP. Conversely, assessment of HE on fundus photos seems to be less influenced by operator expertise. Correctly interpreting green reflectance helped in confirming presence of HE on McS. In some cases McS achieved sharper fundus images than FP. The use of McS as a single equipment to assess HE in the absence of fundus photographs in M1 maculopathy OCT virtual clinics needs further evaluation and validation.

**Commercial Relationships:** Sergio Pagliarini, Novartis (R), Allergan (R), Bayer (R); Elisa Carini, None; Mariano Cozzi, None
Quantitative Evaluation of Perifoveal Capillary Network in Young Diabetes Mellitus Type I Patients

Zoi Kapsala¹, Aristofanis Pallikaris², Vassileia Maniadi¹, Vassiliki Louvari¹, Dimitrios Mamooulakis¹, Miltiadis K. Tsilimbaris², ³
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Purpose: To develop an algorithm for the quantitative assessment of the retinal capillary microcirculation in diabetes mellitus type I (DM I) patients.

Methods: Thirty-two images of 32 eyes (16 eyes of 9 DM I patients and 16 eyes of 10 non DM patients) were chosen from the University Hospital of Heraklion digital fluorescein angiography database. The age was 18±5 years for the patient group (range: 12-26 years) and 17±7 years (range: 6-26 years) for the control group. For each eye a high resolution image was chosen and underwent a processing procedure using a commercial software (MatLab R2011a; The MathWorks Inc.). The so far developed algorithm traces both manually (by choosing with the cursor) and automatically the perifoveal capillary network in a subimage of field 20°×20° of the original one and provides measurements of the foveal avascular zone (FAZ) surface, the capillary density and the branch point density in the mentioned area.

Results: The capillary mapping revealed a FAZ area of 0.23±0.06 degrees² in the DM I group versus 0.22±0.05 degrees² in the control group. The capillary density (capillary length in degrees/total area in square degrees) was 2.48±0.55 degrees⁻¹ and 2.76±0.21 degrees⁻¹ in each group, respectively. The last metric estimated, the branch point density, was 2.86±0.73 branch points/degrees² in the diabetic group and 3.14±0.7 branch points/degrees² in the control group. It seems that there is a slight reduction of these indexes in DM I patients when comparing with controls but none of these differences were statistically significant.

Conclusions: This approach constitutes our first attempt in order to develop an algorithm for the quantification of retinal microvessel alterations in young DM I patients. Further improvement of the algorithm will help us optimize the detection module and develop automated metrics for the quantification of diabetic retinal microangiopathy.

Commercial Relationships: Zoi Kapsala, None; Aristofanis Pallikaris, None; Vassileia Maniadi, None; Vassiliki Louvari, None; Dimitrios Mamooulakis, None; Miltiadis K. Tsilimbaris, None

Program Number: 196 Poster Board Number: D0007
Presentation Time: 8:30 AM - 10:15 AM

Retinal arterial and venous oxygen saturation is altered in diabetic patients with and without retinopathy

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¹Ophthalmology, LSUHSC, New Orleans, LA; ²Neuroscience, Tulane University, New Orleans, LA; ³CytoViva, Inc., Auburn, AL.

Purpose: To test the hypothesis that oxygen saturation is altered in retinal arteries and veins in diabetic patients.

Methods: A retinal oximeter (Oxymap e hf., Reykjavik, Iceland) was used to measure oxygen saturation in all major retinal arteries and veins in healthy subjects and in patients with and without diabetic retinopathy. Oxygen-sensitive (605 nm) and oxygen-insensitive (586 nm) wavelengths were employed by the retinal oximeter. The oxygen saturation values in all major arteries and veins in each subject were averaged and then all subject values in each category were averaged.

Results: In healthy subjects, retinal oxygen saturation values for arteries and veins were 92.3 ± 4.2 and 57.2 ± 6, respectively (n=14). The analogous values in diabetic patients with no signs of retinopathy were 96.3 ± 8.6 and 58.7 ± 7.5 (n=45). In patients with varying degrees of pathology from mild to severe nonproliferative to proliferative retinopathy, these values were 99.8 ± 10 in arteries and 63.2 ± 8 in veins (n=48). The difference between healthy subjects and diabetic patients without and with retinopathy was statistically significant. The arterial p-values were 0.02 and 0.0001, respectively. The venous p-values were 0.4 and 0.03, respectively. The difference between all levels of retinopathy and no retinopathy in diabetic patients is significant only for a p-value of 0.03 for arteries. The corresponding p-value for veins is 0.07. All five subgroups of diabetic patients (non-diabetic-retinopathy, mild, moderate to severe nonproliferative diabetic retinopathy and proliferative diabetic retinopathy) had higher saturation values than healthy subjects.

Conclusions: Based on our study, we believe the dual-wavelength retinal oximeter will significantly aid in the screening of DR by identifying those at risk for retinal vascular changes.

Commercial Relationships: Bahram Khooobehi, None; Kim A. Firn, None; Reinoso Maria, None; O’Sullivan Patrick, None; James M. Beach, Oximap (I); Amol Sura, None; John F. Green, None

Support: Research to Prevent Blindness, Inc.
compared clinical characteristics and visual outcomes in each groups. In addition, we classified according to retinal component in SD-OCT, compared the clinical characteristics and surgical outcome in each groups.

**Results:** Of 20 eyes, group 1 had 12 eyes and group 2 had 8 eyes. There are no statistically differences in age, best corrected visual acuity (BCVA) before and after the operation and mean spherical equivalent. Group 2 had longer axial length than group 1 (p=0.029). In Group 1, 9 eyes (75%) had the BCVA after vitrectomy and 4 eyes (42%) had final visual acuity more than 0.4. Group 2 had only 4 eyes (40%) with improving BCVA after vitrectomy and 2 eyes (25%) with final BCVA more than 0.4. Regardless of group, SD-OCT represents component of sponge, bridging columnar, saw tooth, cystoid macular edema and retinoschisis. The eyes with cyst component have poor visual outcome. Of 9 eyes have performed SD-OCT after vitrectomy, there are remained sponge component in 8 eyes, saw tooth component in 7 eyes, and cyst component in 3 eyes. These components decreased as time passed after vitrectomy. There are no remained bridging columnar component.

**Conclusions:** Each group has BCVA improvement with vitrectomy and removal of tractional membrane and release the tractional force. However, the eyes with TRD has poor surgical outcome compared with the eyes without TRD. SD-OCT is useful tool for presenting the change of retina like sponge, bridging columnar, saw tooth, cystoid macular edema and retinoschisis components from tractional elevation, and it helps understanding of tractional elevation in proliferative diabetic retinopathy.

**Commercial Relationships:** Kwang-Soo Kim, None; Rebecca Kim, None; Yu Cheol Kim, None

**Program Number:** 198 Poster Board Number: D0009

**Presentation Time:** 8:30 AM - 10:15 AM

**Effectiveness of prophylactic intravitreal bevacizumab injection in preventing complications after vitrectomy for proliferative diabetic retinopathy**

Kinya Tsubota, Yoshihiro Wakabayashi, Shunichiro Ueda, Yoshihiko Usui, Jun Suzuki, Hiroshi Goto. Ophthalmology, Tokyo Medical University, Nishishinjuku, Japan.

**Purpose:** We previously reported that high intraocular VEGF concentration before vitrectomy for proliferative diabetic retinopathy (PDR) was associated with a high incidence of post-vitrectomy complications such as early vitreous hemorrhage (VH) and neovascular glaucoma (NVG) (Wakabayashi et al. IOVS 2012). In this study, we examined the effectiveness of intravitreal bevacizumab (IVB) injection given to patients with elevated preoperative intraocular VEGF concentration for the prevention of postoperative complications of PDR.

**Methods:** We studied 27 patients (28 eyes) with PDR who underwent vitrectomy first time at the Department of Ophthalmology, Tokyo Medical University Hospital between April and October 2012. The mean postoperative follow-up period was 3.4 months (1-6 months). The VEGF concentration in the vitreous humor collected at the time of vitrectomy was measured by ELISA. IVB injection was conducted after operation in patients with vitreous VEGF levels exceeding 1,000 pg/ml. The incidence of early VH and newly developed NVG after vitrectomy was investigated. New bleeding occurring within 1 month after operation was defined as early VH. investigated. New bleeding occurring within 1 month after operation was defined as early VH.

**Results:** IVB injection was performed in 5 eyes (18%) in which vitreous VEGF concentrations exceeded 1,000 pg/ml. The mean duration from vitrectomy to IVB injection was 7.4 days (3-12 days). None of the 5 eyes that received IVB developed early VH and NVG. All 23 eyes (82%) with vitreous VEGF concentrations lower than 1,000 pg/ml also had no postoperative complications.

**Conclusions:** Prophylactic IVB given to patients with elevated preoperative intraocular VEGF concentration is effective for preventing postoperative early VH and NVG.

**Commercial Relationships:** Kinya Tsubota, Tokyo Medical University (E); Yoshihiro Wakabayashi, None; Shunichiro Ueda, None; Yoshihiko Usui, None; Jun Suzuki, None; Hiroshi Goto, None

**Support:** We don't have financial support.

**Program Number:** 199 Poster Board Number: D0010

**Presentation Time:** 8:30 AM - 10:15 AM

**Assessment of retinal perfusion using ultra wide filed (UWF) imaging in patients with diabetic retinopathy treated with intravitreal bevacizumab (IVB)**

Shulamit Schwartz1, Scott Oliver2, Regina Victoria1, Ramanath Bhandari1, Naresh Mandava2, Hugo Quiroz-Mercado1.

1Ophthalmology, Denver Health Medical Center affiliated with University of Colorado, Denver, CO; 2ophthalmology, University of Colorado, Aurora, CO.

**Purpose:** To evaluate retinal perfusion in diabetic retinopathy before and after treatment with monthly IVB injections over a medium term follow up, using UWF retinal imaging.

**Methods:** A retrospective, interventional, non comparative case series. Diabetic patients with newly diagnosed proliferative diabetic retinopathy (PDR) and/or macular edema (ME) were included. All were treated with IVB injections every 4-6 weeks, if pan retinal photocoagulation (PRP) could be deferred for at least four weeks at physician discretion. Patients with previous treatment with laser or angiogenic therapy, media opacity or PDR complications were excluded. Follow up included fluorescein angiography (FA) using UWF laser scanning ophthalmoscope technology (Optomap 200Tx, Optos®) that allowed for high resolution visualization of the retina up to 200 degree in one frame. The main outcome measure was the extent of retinal perfusion. Secondary outcomes were regression of neovascularization (NV), macular ischemia, BCVA and need for PRP or vitrectomy.

**Results:** Twelve eyes of six patients were enrolled in the study. Mean age was 54.8± 8.1 years. Eleven eyes were diagnosed with PDR and eight eyes with ME. Patients received on average 3 injections and followed for an average of 16.5 ± 3.2 weeks. IVB allowed for regression of NV in 11 eyes, demonstrated on FA a month after first injection. The average ischemic area decreased significantly from 86.2%± 4.9% to 77.2%± 10.7% and the average perfused area increased significantly by 66.5% (P=0.0024) during the follow up period. Two eyes showed minimal reduction in ischemic area after treatment and one of them developed mild persistent vitreous hemorrhage without evidence of active NV. Macular ischemia didn't evolve in any of the study eyes. None of the eyes developed DR complications that required rescue with PRP or vitrectomy. Average BCVA improved significantly from 0.48 log MAR before to 0.26 log MAR after treatment (p=0.0036).

**Conclusions:** IVB injections improved retinal perfusion in a small series of patients with DR over a medium term follow up. Further prospective large scale studies are needed to determine the role of IVB in PDR.

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Retinal Microglia Activity Mirrors the Progression of Diabetic Retinopathy. An in vivo Spectral Domain OCT Study

Carlo Torrazza1, Simonetta Guidelli Guidi1, Mariachiara Morara1, Chiara Veronesi1, Francesco Pichi2, Antonio P. Ciardella1.

1Ophthalmology Unit, Policlinico S Orsola Malpighi, Bologna, Italy; 2Department of Ophthalmology, University of Padova, Padova, Italy; 1GB Bietti Foundation, IRCCS, Roma, Italy.

Purpose: To evaluate in vivo if retinal microglia activity mirrors the progression of diabetic retinopathy (DR).

Methods: 40 subjects were enrolled: 30 subjects were affected by diabetes mellitus and 10 normals served as controls. Proliferative DR, previous laser photocoagulation, intracocular surgery or intravitreal injection, glaucoma or ocular hypertension and neurodegenerative diseases were the main exclusion criteria. One eye of each subject had mild non proliferative DR (Mi-NPDR), 10 severe NPDR (Se-NPDR) group and 10 severe NPDR (Se-NPDR). Full ophthalmic examination including spectral domain-OCT (SD-OCT) were performed in all eyes. After segmentation of retinal layers by SD-OCT, retinal images were analyzed for reflectivity changes (hyperreflectivity spots) at the level of: internal limiting membrane plus retinal nerve fiber layer (ILM+RNFL), inner nuclear layer plus outer plexiform layer (INL + OPL) and outer nuclear layer, where ganglial cells are located in the human retina. Hyperreflective spots were analyzed in a full retinal section between 500 and 1500 µm from the foveal center. All examinations were performed twice, by two independent masked graders.

Conclusions: No statistically significant differences were found for age among all groups and for glycemic control between diabetic groups. The inter-grader agreement was at least substantial for all measurement. In DR eyes hyperreflective spots (discrete microaggregates) were systematically detected at the level of ILM+RNFL (75% vs 87% vs 98% in Mi-NPDR vs Mo-NPDR vs Se-NPDR, respectively; p<0.0001) and their expression significantly progressed toward outer retinal layers with the progression of NPDR steps (p< 0.005 for INL+OPL in the three groups; p< 0.001 for ONL in the three DR groups).

Conclusion: The presence of retinal discrete microaggregates, documented as hyperreflective spots, in areas corresponding to microglial cells may represent an in vivo biomarker of retinal progression of diabetic retinopathy.
microglial activation in diabetes. The increase in number and the significant migration toward outer retinal layers of the (hyperreflective) microaggregates, mirrors the progression of DR, confirming the importance of neuroinflammation in the development and progression of DR. Microglial activation may be detected by spectral domain OCT using refined retinal layers analysis.

**Purpose:** To assess the prognosis and prognostic factors of patients undergoing vitrectomy for tractional retinal detachment (TRD) in eyes with proliferative diabetic retinopathy (PDR)

**Methods:** Retrospective chart review of patients with diabetic tractional retinal detachment who underwent pars plana vitrectomy (PPV) between November 2008 and April 2012. Subjects were 86 consecutive cases of 72 patients who had follow-up for at least 6 months. Variables assessed were: age, gender, hemoglobin A1c (HbA1c), macular involvement, anatomical retinal status, visual acuity, surgical methods, post-operative retinal status and visual acuity, and surgical complications. The mean post-operative follow-up duration was 19.8 ± 11.3 months (range, 6 to 44 months). We detected an inter-group difference using Fisher’s exact probability test.

**Results:** There were 65 men, 21 women with an average age of 50.8±12.0 years old. The mean HbA1c was 8.0±2.2%. The average logMAR visual acuity before operation was 1.4±0.79 and macula-involving RD was found in 34 eyes. The final postoperative visual acuity was improved more than 0.2 logMAR in 64 eyes (74.4%), was unchanged in 14 eyes (16.3%) and decreased in 8 eyes (9.3%). Air or SF6 were used in 43 eyes (50.0%), while in 12 eyes (14.0%) we used silicone oil for retinal tamponade, while retinas in 37 eyes (43.0%) SF6 were used in 43 eyes (50.0%), while in 12 eyes (14.0%) we used air. Acuity was improved more than 0.2 logMAR in 64 eyes (74.4%), was unchanged in 14 eyes (16.3%) and decreased in 8 eyes (9.3%). Air or SF6 were used in 43 eyes (50.0%), while in 12 eyes (14.0%) we used silicone oil for retinal tamponade, while retinas in 37 eyes (43.0%) were reattached without gas or silicone oil tamponade. Final retinal reattachment was achieved in 82 eyes (95.3%). Re-attachment was required in 18 eyes (20.9%). Neovascular glaucoma (NVG) following vitrectomy occurred in 3 eyes (3.5%) and proliferative vitreoretinopathy (PVR) following vitrectomy occurred in 13 eyes (15.1%). Cases without panphotocoagulation (PRP) before vitrectomy, cases with macula-involving RD, cases with TRD extending beyond the quadrant, cases with TRD in temporal retina, cases with proliferative PVR, and cases occurred NVG following vitrectomy were significantly associated with poorer of final postoperative visual acuity (p<0.05).

**Conclusions:** The poor prognostic factors of TRD in eyes with PDR were pre-operative PRP, macula-involving TRD, TRD on the temporal side, and TRD complications following vitrectomy, in particular, NVG and PVR.

**Commercial Relationships:** Ayumi Usui, None; Masatoshi Kiyokawa, None; Toshiro Sakuma, Rei Ito, Nobuyuki Ebihara, None

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**Program Number:** D0015  
**Presentation Time:** 8:30 AM - 10:15 AM  
**Surgical and visual outcome and prognostic factors following vitrectomy in diabetic tractional retinal detachment**

Kiyokawa, Rei, Nobuyuki Ebihara, None; Stela Vujosevic, None; Edoardo Midena, None

**Purpose:** To assess the prognosis and prognostic factors of patients undergoing vitrectomy for tractional retinal detachment (TRD) in eyes with proliferative diabetic retinopathy (PDR)

**Methods:** Retrospective chart review of patients with diabetic tractional retinal detachment who underwent pars plana vitrectomy (PPV) between November 2008 and April 2012. Subjects were 86 consecutive cases of 72 patients who had follow-up for at least 6 months. Variables assessed were: age, gender, hemoglobin A1c (HbA1c), macular involvement, anatomical retinal status, visual acuity, surgical methods, post-operative retinal status and visual acuity, and surgical complications. The mean post-operative follow-up duration was 19.8 ± 11.3 months (range, 6 to 44 months). We detected an inter-group difference using Fisher’s exact probability test.

**Results:** There were 65 men, 21 women with an average age of 50.8±12.0 years old. The mean HbA1c was 8.0±2.2%. The average logMAR visual acuity before operation was 1.4±0.79 and macula-involving RD was found in 34 eyes. The final postoperative visual acuity was improved more than 0.2 logMAR in 64 eyes (74.4%), was unchanged in 14 eyes (16.3%) and decreased in 8 eyes (9.3%). Air or SF6 were used in 43 eyes (50.0%), while in 12 eyes (14.0%) we used silicone oil for retinal tamponade, while retinas in 37 eyes (43.0%) were reattached without gas or silicone oil tamponade. Final retinal reattachment was achieved in 82 eyes (95.3%). Re-operation was required in 18 eyes (20.9%). Neovascular glaucoma (NVG) following vitrectomy occurred in 3 eyes (3.5%) and proliferative vitreoretinopathy (PVR) following vitrectomy occurred in 13 eyes (15.1%). Cases without panphotocoagulation (PRP) before vitrectomy, cases with macula-involving RD, cases with TRD extending beyond the quadrant, cases with TRD in temporal retina, cases with proliferative PVR, and cases occurred NVG following vitrectomy were significantly associated with poorer of final postoperative visual acuity (p<0.05).

**Conclusions:** The poor prognostic factors of TRD in eyes with PDR were pre-operative PRP, macula-involving TRD, TRD on the temporal side, and TRD complications following vitrectomy, in particular, NVG and PVR.

**Commercial Relationships:** Ayumi Usui, None; Masatoshi Kiyokawa, None; Toshiro Sakuma, Rei Ito, Nobuyuki Ebihara, None

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**Program Number:** D0014  
**Presentation Time:** 8:30 AM - 10:15 AM  
**Adaptive optics imaging of diabetic retinopathy**

Jonathan Benesty, None; Sarah Ayello-Scheer, None; Jose A. Sahel, UPMC/Essilor (P), Second Sight (F); Michel Paques, MerckSerono (C), Roche (C), Sanofi (C)

**Support:** ANR_09_TECS_009_01_iPhot

**Clinical Trial:** C10-03

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**Program Number:** D0015  
**Presentation Time:** 8:30 AM - 10:15 AM  
**Choroidal circulation before and after panretinal photocoagulation using a Pattern Scanning Laser for Diabetic Retinopathy**


**Purpose:** To evaluate the choroidal circulation before and after panretinal photocoagulation (PRP) for diabetic retinopathy (DR).

**Methods:** This study was conducted in 34 eyes of 26 patients. Choroidal blood velocity at the macula was evaluated as mean blur rate (MBR) by laser speckle flowgraphy (LSFG). PRP was performed using a pattern scanning laser (PASCAL). Choroidal blood velocity was imaged before and during PRP, and at monthly intervals for 6 months after PRP. Patients with prior PRP, vitrectomy, diagnosis of extensive vitreous hemorrhage or mature cataracts were excluded. LSFG was performed with a new external laser unit (wavelength, 830 nm) for wider illumination of the retina.

**Results:** Mean choroidal velocity decreased to 79.6±15% (P<0.001) after PRP as measured by LSFG. PRP reduced choroidal circulation to 82.9±14%, 80.1±14% and 82.9±17% (P<0.001 each) at 1, 3 and 6 months after PRP, respectively, compared with before PRP. None of the present cases developed exacerbation of DR after PRP.

**Conclusions:** Our previous reports have indicated that PRP reduces retinal blood flow to 71.2±15%, compared with initial value. In this study, choroidal circulation similarly reduced retinal blood flow after PRP. The number of laser spots correlated with decreases in mean blood velocity (R=0.31, p<0.021). LSFG may be useful for clarifying the optimal number of laser spots for DR. If adequate PRP was enforced, retinal blood flow and choroidal circulation decreased to 71% and 79% compared to before PRP.

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Commercial Relationships: Naoko Onizuka, None; Kiyoshi Suzuki, None; Masafumi Uematsu, None; Yoshishita Yamada, None; Takashi Kitaoka, None

Program Number: 205 Poster Board Number: D0016
Presentation Time: 8:30 AM - 10:15 AM
A Randomized Trial Evaluating Intravitreal Ranibizumab or Intravitreal Saline for Vitreous Hemorrhage from Proliferative Diabetic Retinopathy
Abdhisra R. Bhavsar. Retina Center of Minnesota, Minneapolis, MN.
Purpose: To evaluate intravitreal ranibizumab compared with intravitreal saline injections on vitrectomy rates for eyes with vitreous hemorrhage from proliferative diabetic retinopathy (PDR).
Methods: Eligible eyes had vitreous hemorrhage from PDR precluding panretinal photocoagulation (PRP) completion. Eyes were randomly assigned to 0.5-mg intravitreal ranibizumab (N = 125) or intravitreal saline (N = 136) at baseline, 4, and 8 weeks. Injections were deferred at 4 and 8 weeks if vitrectomy had already been performed or the hemorrhage had cleared such that complete PRP could be given (or it was determined that complete PRP was already given). Study participants and all study personnel were masked to treatment assignment. At each visit the study eye was assessed to determine whether vitrectomy was indicated based on protocol guidelines.
Results: The cumulative probability of vitrectomy by 16 weeks was 12% with ranibizumab versus 17% with saline (hazard ratio 0.74, 95% confidence interval (C.I.) 0.38-1.43, P = 0.37). The treatment group difference in the cumulative probability of vitrectomy was 4% (95% C.I. (−4%, 13%)). The cumulative probability of complete PRP without vitrectomy by 16-weeks was 44% and 31% respectively (P = 0.05). The mean (±SD) visual acuity improvement from baseline to 12 weeks was 22±23 letters and 16±31 letters respectively (P = 0.04). Recurrent vitreous hemorrhage occurred within 16 weeks in 6% and 17% respectively (P = 0.01). One eye developed endophthalmitis after a saline injection. Eight eyes (6%) in the ranibizumab group and 9 eyes (7%) in the saline group had a traction retinal detachment (P>0.99). Rheximatogenous retinal detachments were reported in one eye (<1%) in the ranibizumab injection group and 2 eyes (2%) in the saline injection group. One additional eye in the ranibizumab injection group reported a combination of traction and rhegmatogenous retinal detachment.
Conclusions: While the study suggests little likelihood of a clinically important difference between ranibizumab and saline on the rate of vitrectomy by 16 weeks in eyes with vitreous hemorrhage from PDR, short term secondary outcomes including visual acuity improvement, increased PRP completion rates, and reduced recurrent hemorrhage rates suggest biologic activity of ranibizumab without an increased risk of traction retinal detachment.

Commercial Relationships: Abdhisra R. Bhavsar. Regeneron (F), Genentech (F)
Support: Cooperative agreement from the National Eye Institute and the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Department of Health and Human Services EY14231, EY018817
Clinical Trial: NCT00996437

Program Number: 206 Poster Board Number: D0017
Presentation Time: 8:30 AM - 10:15 AM
Telemedicine for diabetic retinopathy screening: a pilot program for Italian hospitals
Alessandro Invernizzi1, Maurizio T. Bevilacqua2, Mariano Cozzi1, Carlo D. Bianchi1, Alessandro Pagani1, Mario V. Cigada1, Giovanni Staurenghi1. "Eye Clinic, Luigi Sacco Hospital, University of Milan, Milano, Italy; 2Endocrinology-Diabetology, Luigi Sacco Hospital, University of Milan, Milano, Italy.
Purpose: To assess the clinical reliability and economic impact of a semi-automatic fundsus photography screening program for diabetic retinopathy in Italian population
Methods: A semi automatic fundus camera (DRS, Centervue Padua, Italy) was installed into the endocrinology unit at the Sacco Hospital of Milan. For 3 months, all the patients referring to the diabetic service, in addition to the standard systemic clinical evaluation, underwent a semi-automatic three fields fundus photographs set (FP) before and after pupil dilation. The pictures were then read by an expert ophthalmologist to assess the presence of diabetic retinopathy (DR). Rules to refer patients to the Retina clinic for fundus oculi (FO) examinations were: sign of diabetic retinopathy of any level, unreadable pictures.
To test the sensitivity and specificity of the DRS fundus camera, a subset of patients independently of FP findings, also underwent FO examination.
The costs and benefits evaluation of this telemedicine approach compared to the present screening method based on FO examination only in the Retina clinic was than conducted.
The economical analysis was done on 3 months duration trial and one year projection was generated by these data.
Results: 347 patients underwent the semi-automatic FP screening program.
FP examination without dilation results: 8.94%=presence of DR; 19.92%=absence of DR; 71.74%=unreadable pictures (UP); 80.08%=patients referred to the retinal unit (DR+UP). FP examination after pupil dilation results: 19.51%=presence of DR; 65.85%=absence of DR; 14.63%=UP; 34.15%=patients referred to the retinal unit (DR+UP). SE and SP of the non miidriatic FP, assessed on a sample of 246 subjects, resulted respectively 96% and 24%; after pupil dilation they both resulted 78%.
All the false negative patients generated by FP showed mild diabetic retinopathy at clinical FO examination. According to the annual projection, FP approach could increase the total number of screened patients for DR by 33%. Supposing the number of screened patients being equal, screening costs would be 20% less using miosis FP and 66% using miidriatic FP when compared to the present approach.
Conclusions: Semi-automatic FP could be considered as a screening tool for DR in Italian population. Telemedicine could reduce costs of screening programs but the method should be improved to achieve a better cost-benefits balance.
Commercial Relationships: Alessandro Invernizzi, None; Maurizio T. Bevilacqua, None; Mariano Cozzi, None; Carlo D. Bianchi, None; Alessandro Pagani, None; Mario V. Cigada, None; Giovanni Staurenghi, Ocular Instruments (P), GSK (C), Novartis (C), Alcon (C), Allergan (C), Bayer (C), Roche (C), Heidelberg Engineering (C), OD-OS (C), QLT (C), Optos (C)
Support: Novartis Grant Support

Program Number: 207 Poster Board Number: D0018
Presentation Time: 8:30 AM - 10:15 AM
Serum uric acid and newly developed diabetic retinopathy in type 2 diabetes mellitus—a 3 years prospective study
Shih-Hao Wang, Jong-Jer Lee, Hsi-Kung Kuo, I-Hui Yang. Ophthalmology, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung City, Taiwan.
Purpose: Hyperuricemia is a risk factor of diabetic nephropathy and cardiovascular mortality. The aim of this study was to explore the role of uric acid in diabetic retinopathy (DR) of type 2 diabetes
Hemorrhage After Vitrectomy for Diabetic Retinopathy

Purpose: To describe our experience using intravitreal bevacizumab for eyes with recurrent vitreous hemorrhage after vitrectomy for proliferative diabetic retinopathy.

Methods: The patient database of Illinois Retina Associates was searched for patients who had received vitrectomy for diabetic retinopathy and at least one bevacizumab injection to the operative eye for post-operative vitreous hemorrhage (VH). Patients who had less than 6 months follow-up after vitrectomy were excluded. Snellen visual acuity measurements were converted to logMAR visual acuity for analysis and then converted back to report results.

Results: There were 12 eyes of 9 patients that were included in the study. Follow-up after primary vitrectomy had mean of 24.5 months (median 18.5 months, range of 8 to 52.5 months). Two eyes with severe vitreous hemorrhages had a second vitrectomy and one of these also had an outpatient fluid-air exchange early in the post-operative period. A mean of 8.75 bevacizumab injections (median 7, range 1-19 injections) were given in the post-operative period for recurrent VHs. During the post-operative period the mean number of recurrent VHs was 4 (median 3, range 2-8). Of the 12 eyes, 10 had total resolution of the VH by the last post-operative visit. The visual acuity before the first bevacizumab injection had mean of counting fingers (median counting fingers, range 20/100 to hand motions). Final visual acuity had mean of 20/80 (median 20/60 and range 20/20 to CF).

Conclusions: Intravitreal bevacizumab is a useful adjunct for the management of recurrent VH in eyes that had undergone vitrectomy for PDR. Patients often required multiple injections and had recurrent VH when the treatment was stopped, however the need for treatment declined over time. Repeat vitrectomy or fluid-air exchange was not required for most eyes and, when employed, was only used in the early post-operative period for the most severe cases.

Commercial Relationships: Kevin Ferenchak, None; Renaud Duval, None; Jack A. Cohen, None; Mathew MacCumber, Genentech (C), Regeneron (C), Allergan (C), Thrombogenics (C), Optos (C), Sequenom (C), ArcticDx (C)

Program Number: 209 Poster Board Number: D0020
Presentation Time: 8:30 AM - 10:15 AM

Assessment of macular function using the SKILL card in adult patients with Type 2 Diabetes


Purpose: To evaluate vision function at reduced contrast and reduced luminance using the Smith-Kettlewell Institute Low Luminance (SKILL) card in adult patients with type 2 diabetes and with or without retinopathy.

Methods: We studied 13 participants with no retinopathy (NoRet group), 13 participants with moderate to severe retinopathy (NPDR group) and 40 healthy control subjects (control group). Their mean ages were 54.0 ± 10.5, 54.4 ± 9.1, and 41.8 ± 12.2 yrs for the NoRet, NPDR and control groups, respectively. All the participants with diabetes had diabetes duration of at least 10 yrs and an HbA1c above 7%. All the participants had 20/20 or better-corrected visual acuity. Monocular high contrast and low contrast, low luminance (1 log unit less than the white chart) near visual acuity were tested using light and dark sides of the SKILL card at a distance of 40 cm. The SKILL score was calculated as the difference in performance on the low-contrast dark versus the high-contrast light side adjusted for the age difference between the controls and diabetic groups. T-tests were performed to examine whether the subject groups differed. Linear regressions were performed to examine effects of age, HbA1c, central macular thickness, and duration of diabetes on SKILL score.

Results: The SKILL score was higher (reflecting reduced performance on the low contrast, low luminance chart) in both of the diabetic groups as compared to the controls but was significantly different only between controls and the NPDR group (P<0.05). There was no statistically significant correlation between HbA1c or duration of diabetes and SKILL score (P>0.5 for both). Age was positively correlated with SKILL score in controls and in NoRet group (both P<0.03) but not in the NPDR group (P>0.5).

Conclusions: The SKILL card sensitively assesses vision function change in diabetes when acuity is still good. Diabetic retinopathy leads to an increased SKILL score i.e. reduced performance, while visual acuity is unaffected. The SKILL score can provide different information about mechanisms of diabetic retinal damage than regular visual acuity charts.

Commercial Relationships: Kavita P. Dhamdhere, None; Marilyn E. Schneck, None; Wendy Lam, None; Shirin Barez, None; Marcus A. Bearse, None; Anthony J. Adams, None
Support: EY021811

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Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom; "Vitreo-Retinal Service, Cheltenham General Hospital, Cheltenham, United Kingdom.

**Purpose:** To characterize active and inactive new vessels at the disc (NVD) or elsewhere (NVE) and its associated vitreoretinal features in diabetic patients with proliferative diabetic retinopathy using Spectral Domain Optical Coherence Tomography (SD-OCT).

**Methods:** Retrospective cross-sectional study of 20 non-consecutive patients with proliferative diabetic retinopathy that were assessed in the Medical Retina Department of Moorfields Eye Hospital, London, UK, between July and November 2012. SD-OCT (SPECTRALIS®, Heidelberg Engineering, Heidelberg, Germany) was performed in areas of active or inactive NVE and NVD. New vessel activity was assessed using clinical and angiographic criteria.

**Results:** A total of 38 SD-OCT scans of new vessel complexes were analysed from 28 eyes of 20 patients. The mean age was 56 (SD:25-73), and 11 (55%) were male. 6 patients had type 1 and 14 type 2 diabetes. 13 scans were of NVD and 25 of NVE. 5 eyes had both NVD and NVE and 4 eyes had more than one foci of NVE. 20 scans (52.6%) had active neovascularization (NV) and 18 (47.4%) were quiescent. In SD-OCT scans across the new vessels, tissue contracture was noted in 18 scans (47.3%). Similarly, intraretinal fluid was noted in 7 scans (18.4%) and hyperreflective dots within the NV complex in 9 scans (23.7%). (Table 1) (Figure 1). The presence of tissue contracture was significantly greater in quiescent vs active NV (p<0.01). Although the presence of intraretinal fluid and hyperreflective dots was more frequent in active NV, this was not statistically significant (p=0.878 and p=0.560, respectively). The presence of hyperreflectivity within the NV complex or vitreous invasion did not differ between groups (p=0.898 and p=0.068, respectively).

**Conclusions:** SD-OCT can be used to assess retinal neovascularization and associated vitreoretinal features. Tissue contracture was significantly different between active and quiescent disease. Such parameters may be useful in differentiating active from quiescent disease.

**Table 1- SD-OCT features of active and quiescent NV.**

<table>
<thead>
<tr>
<th>SD-OCT features of NV</th>
<th>Active NV</th>
<th>Quiescent NV</th>
<th>Chi- square</th>
<th>P- value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue contracture</td>
<td>0 (20.0%)</td>
<td>11 (72.2%)</td>
<td>4.698 0.049</td>
<td></td>
</tr>
<tr>
<td>Intraretinal fluid</td>
<td>4 (20.0%)</td>
<td>1 (16.7%)</td>
<td>0.034 0.867</td>
<td></td>
</tr>
<tr>
<td>Hyperreflective dots</td>
<td>6 (30.0%)</td>
<td>3 (16.7%)</td>
<td>0.340 0.569</td>
<td></td>
</tr>
<tr>
<td>Vitreous invasion</td>
<td>12 (60.0%)</td>
<td>17 (94.4%)</td>
<td>3.220 0.072</td>
<td></td>
</tr>
<tr>
<td>Hyperreflectivity</td>
<td>13 (65.0%)</td>
<td>11 (72.2%)</td>
<td>0.017 0.913</td>
<td></td>
</tr>
<tr>
<td>Breakthrough dots</td>
<td>16 (80.0%)</td>
<td>10 (100%)</td>
<td>2.180 0.139</td>
<td></td>
</tr>
<tr>
<td>Posterior projection</td>
<td>17 (85.0%)</td>
<td>10 (100%)</td>
<td>1.227 0.270</td>
<td></td>
</tr>
</tbody>
</table>

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Deterioration.

dmi progression itself, was also independently predictive of VA

great severity, and ranges from 5 to 10% of baseline FAZ area per year. A

Conclusions: The rate of FAZ enlargement increases with DMI
severity, and ranges from 5 to 10% of baseline FAZ area per year. A
greater ETDRS-DMI grade and worsening VA were independently predictive for DMI progression in eyes with established ischemia. DMI progression itself, was also independently predictive of VA deterioration.

Commercial Relationships: Dawn A. Sim, None; Pearse A. Keane, None; Javier Zarranz-Ventura, None; Catey Bunce, None; Marcus Fruttiger, AstraZeneca (F), Novartis (F), Novartis (C), Amakem (F); Praveen J. Patel, Allergan (R), Bayer (C), Novartis UK (C), Heidelberg UK (R), Topcon UK (R), Thrombogenics (C); Adnan Tufail, Allergan (C), Bayer (C), GSK (C), Oculogics (C), Pfizer (C), Thrombogenics (C), Amakem (C), Heidelberg Engineering (R), Novartis/Alcon (C), Sanofi/Genzyme (C); Catherine A. Egan, Bayer (S), Oculogics (S), Novartis (S), Allergan (S), Novartis (F)

Support: Fight For Sight UK, Grant 1987

Program Number: 212 Poster Board Number: D0023

Presentation Time: 8:30 AM - 10:15 AM

Intravitreal Ranibizumab for Diabetic Macular Edema with Prompt vs Deferred Laser Treatment: 3-year Randomized Trial Results Presenter: Michael E. Rauser, M.D. for the Diabetic Retinopathy Clinical Research Network

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the disc and macula. If they did it could be concluded that they would also lie outside the 45° screening program images.

**Results:** 225 patches of NVE and 20 patches of NVD were noted in the 69 eyes analysed. 178 patches of new vessels occurred within 50° FFA images centred on the disc and macula. 70 patches did not occur within these central images. The difference in the distribution of the vessels was significant (p<0.005; unpaired t-test).

Out of the 225 patches of NVE, 50 were supero-temporal, 74 infero-temporal, 42 supero-nasal, and 59 infero-nasal. ANOVA showed there to be no significant difference in this distribution (p=0.08). The position of vessels did not vary whether the NVE were within the central 50° images or not (p>0.05 by 2 test).

Out of the 69 eyes analysed, 36 had all their new vessels, 27 had some new vessels and 6 had no new vessels within FFA images centred on the disc and macula. Therefore, in the screening program, new vessels would have been missed in 6 eyes giving a 91% sensitivity.

**Conclusions:** The majority of eyes analysed had at least some central new vessels that would be likely to be picked up by screening photographs. With hospital eye services under pressure this study helps provide evidence that it would be safe to discharge treated R3 patients to the community. NVE arising in these patients appear to be randomly distributed between quadrants meaning screeners need to analyse all quadrants with equal effort.

**Commercial Relationships:** Guy S. Negretti, None; Gilli C. Vafidis, None

**Program Number:** 214 Poster Board Number: D0025
**Presentation Time:** 8:30 AM - 10:15 AM
**Front or Back?:** Intracameral vs. Intravitreal Injection of Bevacizumab for Neovascular Glaucoma

*Larry Putphenparambil, Yu-Guang He.* Ophthalmology, UT Southwestern, Dallas, TX.

**Purpose:** Anti-VEGF agents such as Bevacizumab are used for neovascular glaucoma in order to reduce the VEGF burden. Giving this agent into the posterior segment increases the intraocular pressure which leads to an anterior chamber paracentesis. Placing this agent into the anterior chamber has effect on the neovascularization of the iris and angle and has less effect on the intraocular pressure. This study compares the differences in the intraocular pressure and reduction in neovascularization between intracameral bevacizumab (ICB) and intravitreal Bevacizumab (IVB).

**Methods:** This is a retrospective study done at Parkland Memorial Hospital to look at the differences in the vision, pressure and neovascularization changes between IVB and ICB. There were 19 patients total that fit the criteria that were required such as IOP measurement before and after injection. Nine patients received intravitreal injections and ten patients received intracameral injections.

**Results:** The primary endpoints was looking at intraocular pressure pre and post injection as well as regression of neovascularization. Secondary endpoint was need for anterior chamber paracentesis. The mean intraocular pressure in intracameral Bevacizumab patients was lower than the intravitreal Bevacizumab and it was statistically significant. The number of anterior chamber paracentesis required for the intracameral group was much lower than the intravitreal group.

**Conclusions:** Intracameral Bevacizumab has been previously shown to reduce neovascularization due to neovascular glaucoma, but no study has compared intravitreal to intracameral bevacizumab. The advantages to doing intracameral injections versus intravitreal injections are two-fold. One is that there is not a sudden increase in intraocular pressure causing discomfort to the patient and placing the optic nerve at further risk of damage. The other advantage is to not have to place a needle into the eye twice, therefore not exposing the eye to excess pathogens.

The results show a statistically significant difference in the intraocular pressures before and after injection in the two groups.

**Intraocular pressure between intracameral and intravitreal Bevacizumab injections.**

**Commercial Relationships:** Larry Putphenparambil, None; Yu-Guang He, None

**Program Number:** 215 Poster Board Number: D0026
**Presentation Time:** 8:30 AM - 10:15 AM
**Educational and Personal Reminders to Improve Follow-Up to Vision Care in Patients with Diabetes: A Prospective, Randomized Trial**

*Camila Zangalli1, 2, Ann P. Murchison1, 2, Nicole Hale1, Yang Dai1, 2, Lisa A. Hark1, 2, Laura Pizzi1, 2, Benjamin Leiby1, 2, Philip P. Storey1, Julia A. Haller1, 2.* Research, Wills Eye Institute, Philadelphia, PA; 2Thomas Jefferson University, Philadelphia, PA.

**Purpose:** To evaluate the effectiveness of a personalized educational and telephone-based intervention on dilated fundus examinations (DFE) follow-up in patients with diabetes.

**Methods:** Prospective study of adults with diabetes who were recommended for a follow-up DFE. Over 7 months, 522 patients were randomly assigned to usual care or the intervention group. Usual care group (n=260) received a standard form letter reminding them to make an appointment and, once an appointment was made, they received an automated reminder phone call one day prior to their scheduled follow-up visit. Patients in the intervention group (n=262) received an educational brochure about diabetic eye disease and a personalized letter encouraging them to schedule an eye exam. Two weeks after the letter and brochure were mailed, a research assistant called to provide personal assistance to schedule a follow-up eye exam. Barriers to care utilization were also captured. Once an appointment was made, patients in the intervention group received a reminder letter 3 weeks prior to their appointment and an automated phone call one day prior to the scheduled follow-up visit.

**Results:** Patients in the intervention and control groups had similar demographics with regards to gender, race, and age. Overall, the majority of patients were female (66%) and African-American (70%). The mean age was 61 years (range 19-95 years). Patients in the intervention group were more likely to schedule an appointment (68% vs. 44%; relative risk 1.55; 95% confidence interval 1.29-1.79; p <0.0001) compared to the usual care group. Patients in the intervention group were equally likely to keep their appointment once scheduled compared to the usual care group (73.3% vs. 71.3%; p
Retinopathy Vitamin B Intervention in Non-Proliferative Diabetic Retinopathy with or without pre-surgical intravitreal bevacizumab

Sumihiro Kawano, Toshifumi Yamashita, Yasushi Sonoda, Keita Yamakiri, Taiji Sakamoto. ophtalmology, kagoshima Univ Faculty of medicine, Kagoshima, Japan.

Purpose: To evaluate the effect of pre-surgical intravitreal bevacizumab (IVB) on vitrectomy for proliferative diabetic retinopathy (PDR).

Methods: IVB was done for PDR eyes (12 consecutive eyes, IVB group) within one week prior to vitrectomy. Those received vitrectomy for PDR without IVB were used as a control (15 eyes, control group). Baseline characteristics of two groups, visual outcome, post-operative hemorrhage were investigated.

Results: There were no significant difference in the rate of increase of intraocular pressure (IVB group vs control group; 5 eyes VS 6 eyes, P=0.93), macular edema (IVB group vs control group: 11 eyes VS 13 eyes, P=0.69) and visual outcome (pre-operative logMAR: 1.46 VS 1.13 P=0.18, post-operative logMAR: 0.44 VS 0.52 P=0.62) between groups. Frequency of post-operative hemorrhage after 1 month were 4 times/15eyes, in IVB group and 0 times/12eyes in control group (P=0.057). No adverse events related to IVB such as retinal detachment, endophthalmitis, and MAIA testing foveal edema were seen once per month for 6 months. All subjects gave informed consent.

Conclusions: There were no adverse effects with the IVB treatment, and the IVB was effective for PDR eyes postoperative hemorrhage.

Commercial Relationships: None in the Support

Support: None in the Support

Program Number: 216 Poster Board Number: D0027
Presentation Time: 8:30 AM - 10:15 AM

Clinical Utility of Multifocal Pupillographic Objective Perimetry in Type 1 Diabetes

Ted Maddess, Lauren J. Baker, Andrew C. James, Caitlin Coombes, Veronica Cheung, Melody Melody Chiu, Maria Kolic, Christopher Nolan, Faran Sabeti. ARC Vision Centre, Eccles Inst Neurosci, Australian National University, Canberra, ACT, Australia.

Purpose: To evaluate the sensitivity and specificity of five variants of multifocal pupillographic objective perimetry (mfPOP) for discriminating controls from patients with type 1 diabetes (T1D) presenting with nil to non-proliferative diabetic retinopathy (NPDR). Pupillary contraction amplitudes and times-to-peak responses to red/green, yellow and blue dichoptic stimuli with 44 test regions/eye extending, to either ±15° or ±30°. Disease severity was based on either ETDRS scores from fundus photos; or scores based or factors from correlations between 18 patient variables, which were mainly based on blood analyses, but included peripheral neuropathy, and advanced glycation end-products.

Results: Factor scores based mainly on renal function, HBA1c and...
BIM were the best indicator of diabetic damage as measured by miPOP. In eyes with no or mild NPDR, red/green miPOP stimuli extending to ±30° achieved the highest ROC area under the curve (AUC) of 0.95 ± 0.05 (mean ± SE) for delay deviations and 0.91 ± 0.05 when amplitude deviations were considered. In moderate NPDR eyes diagnostic accuracy improved to 1.00 ± 0.05 for blue and yellow protocols.

**Conclusions:** The results suggest that red/green stimuli presented within the central 30° of fixation achieved good diagnostic power to determine diabetes status in eyes with minimal to no retinopathy. MiPOP may be a useful clinical tool in evaluating and monitoring eyes with early NPDR.

**Commercial Relationships:** Ted Maddess, Seeing Machines (F); Seeing Machines (P), EyeCo (I); Lauren J. Baker, None; Andrew C. James, Seeing Machines, Inc (P); Caitlin Coombe, None; Veronica Cheung, None; Melody Melody Chiu, None; Maria Kolic, Seeing Machines Ltd (E); Christopher Nolan, None; Faran Sabeti, None

**Support:** ARC CE0561903

**Program Number:** 219 Poster Board Number: D0030

**Presentation Time:** 8:30 AM - 10:15 AM

**Contribution of Breakdown of Outer Blood-retinal Barrier (BOBRB) to Diabetic Macular Edema**

Weiye Li1, Mansi Patel1, Behnaz Rouhani1, Raza Shah1, Fang Wang2, Liumei Hu2, Yaprap B. Unver1, 2. 2Ophthalmology, Drexel University College of Medicine, Philadelphia, PA; 1Ophthalmology, Tenth People's Hospital of Tongi University, Shanghai, China; 1Ophthalmology, Birinci Eye Hospital, Istanbul, Turkey.

**Purpose:** Despite the substantial evidence of the BOBRB as a pathogenic component of experimental diabetic retinopathy, the contribution of the BOBRB to clinical diabetic retinopathy has largely been neglected. This study has provided clinical evidence to support this concept.

**Methods:** A cohort study of 34 patients, 19 male and 15 female, with diabetic macular edema (DME), ranging from 43 to 82 years of age, were included in this study. All patients were evaluated by SD-OCT showing DME with subfoveal fluid, subretinal fluid (SRF), and clearly identifiable outer retina layers including the external limited membrane (ELM), photoreceptor (IS/OS), and retinal pigment epithelium (RPE). The affected eyes were also evaluated with overlay fundus photos, fundus auto fluorescence (FAF), fluorescein angiography (FA), and SD-OCT with enhanced depth imaging (EDI) to measure the underlying RPE thickness and overlaying IS/OS integrity corresponding to the area of SRF.

**Results:** All of the tested eyes showed an intact ELM, indicating a lack of fluid communication between the inner and outer retina. The FAs demonstrated isolated hyperfluorescent spots in the early phase with limited oozing into the subfoveal space during the late phase in only a few patients. The overlay FAF examination showed either hyper- or hypo-AF, indicating an accumulation of lipofuscin or a loss of RPE cells, respectively. By using SD-OCT with EDI, the trend of a thinning and more irregular RPE and IS/OS was observed.

**Conclusions:** The major hurdle for the insufficiency in detecting the role of OBRB is the difficulty to measure the OBRB-specific leakage in DME. The combination of current advances in retinal imaging studies enables us to specifically characterize the BOBRB clinically. This approach has provided evidence that dysfunction of OBRB contributes to DME formation. Therefore, these findings merit serious consideration of the BOBRB as a therapeutic target in DME.

**Commercial Relationships:** Weiye Li, None; Mansi Patel, None; Behnaz Rouhani, None; Raza Shah, None; Fang Wang, None; Liumei Hu, None; Yaprap B. Unver, None

**Support:** RFP Grant, Drexel University

**111 Macular Edema**

**Program Number:** 252 Poster Board Number: D0097

**Presentation Time:** 8:30 AM - 10:15 AM

**Correlations Between Functional and Structural Changes in Treatment of Macular Edema Secondary to Branch Retinal Vein Occlusion**

Gokcen Gokce1, Gunorg Sobaci2, Ali Hakan Durukan3, Fazil Cuneyt Erdurman2. 1Ophthalmology, Sarikamis Military Hospital, Kars, Turkey; 2Ophthalmology, Gulhane Military Medical Academy, Ankara, Turkey; 3Ophthalmology, Canakkale Military Hospital, Canakkale, Turkey.

**Purpose:** To elucidate values of optical coherence tomography (OCT) based macular thickness assessment methods in definition of correlations between best corrected visual acuity (BCVA) and macular thickness values in different treatment methods of macular edema secondary to branch retinal vein occlusion (BRVO).

**Methods:** Sixty-two patients treated with intravitreal triamcinolone (IVTA) (group 1, n=26), intravitreal bevacizumab (IVB) (group 2, n=36), for treatment-naive, chronic, center-involved, macular edema secondary to BRVO were included. In each group, correlation between changes in BCVA and central macular thickness (CMT) values recorded during 12 months (1-3-6-12) follow-up were defined, regarding four OCT assessment methods including absolute change in retinal thickness (ACRT), relative change in retinal thickness (RCRT), relative change in retinal thickening (RCRTing), and logarithmic changes in retinal thickness (LCRT).

**Results:** In IVTA group, the most correlated OCT parameters with the logMAR improvements were RCRTing in 1st month visit (r=0.38, p<0.05), LCRT and RCRT in 3rd month visit (r=0.51, p<0.01), ACRT (r=0.51, r=0.52 respectively p<0.01) in other visits. In IVB group the most correlated OCT parameters with the logMAR improvements were RCRTing in 1st, 3rd and 12th month visits (r=0.41, r=0.53 p<0.05 respectively; r=0.30 p=0.07), LCRT and RCRT in 6th month visit (r=0.31, p=0.06).

**Conclusions:** RCRTing in eyes treated with IVB seem to be the method of choice to analyse correlation between BCVA and CMT values in macular edema secondary to BRVO.

**Commercial Relationships:** Gokcen Gokce, None; Gunorg Sobaci, None; Ali Hakan Durukan, None; Fazil Cuneyt Erdurman, None
Snellen chart lines and the ‘non-gainer group’ consisted of eye with less than 2 lines improvement or which had worsened at the last follow-up visit. Comparative clinical characteristics were analyzed between the 2 groups. Total duration of ME was sum of period when ME were existed, not considering of discontinuous and consecutive duration of ME were duration of longest period when ME continuously maintained.

Results: Seventy-one eyes of 71 patients treated with intravitreal bevacizumab injection (18 patients), intravitreal triamcinolone acetonide injection (20 patients) and natural course (33 patients) were enrolled. The gainer group were 32 patients and non-gainer group were 39 patients. Age, duration of symptom, initial visual acuity, initial CMT and duration of follow up did not show significant difference between gainer group and non gainer group. But, total duration of ME in gainer group was shorter than non gainer group (4.23±2.29, 6.87±4.04 month, p=0.001). Especially, consecutive duration of ME was shorter in gainer group than non-gainer group (3.33±1.50, 4.23±2.29 month) and difference of which was more significant (p=0.000). After exclusion of macular ischemia, total duration of ME and consecutive duration of ME in gainer group were also shorter than non gainer group (p=0.010, p=0.025).

Conclusions: The duration of ME in non-gainer group was longer than the gainer group. Especially, the consecutive duration of ME was an important factor in determining the final visual outcome (p=0.001, p=0.000). Therefore, single injection of appropriate timing to reduce consecutive duration of ME could improve the visual outcome in BRVO.

Commercial Relationships: Hyo sung Yoon, None; In Won Park, None; Soon Il Kwon, None; Sung uk Baek, None

Program Number: 254 Poster Board Number: D0099
Presentation Time: 8:30 AM - 10:15 AM
Treatment of Macular Edema (secondary to vein occlusion) with Dexamethasone Implant (Ozurdex)
Nabil Jabbour1,2, Frank Ruda1, Adel S. Wahba3, 4, Frank Ruda1, 1 West Virginia University Eye Institute, Morgantown, WV; 2ForSight Foundation, Morgantown, WV; 3National Eye Institute - Cairo, Cairo, Egypt. Purpose: To assess the response & complications of treating macular edema (ME) secondary to vein occlusion (VO) with Ozurdex (IVO), especially in cases not responding to anti-VEGF treatment.

Methods: 40 eyes were treated with IVO & followed up for 6-24 months (an average of 12M) with additional treatment PRN. 7 (18%) were primary and 33 eyes (82%) were “rescue” (non-responders to Avastin and/or Lucentis).

Results: Overall, 94% showed full initial regression on OCT lasting an average of 4.2 months with 2 lines of improvement. 59% improved (14.2 letters), 10% worsened (6.7 letters) and 31% remained stable. 19% showed elevated intraocular pressure; all successfully treated with drops. The primary treatment group showed 100% regression with 13.3 letters of improvement; 86% improved and 14% remained stable. Only 20 (50%) required more than one treatment of IVO (average of 1.6 treatments per year). CRVO showed better anatomic & visual response than BRVO.

Conclusions: IVO seems to be an effective & safe treatment for VO, especially central. Many eyes that showed initial or latent “resistance” to anti-VEGF showed good response to IVO, making IVO a good “rescue” option for ME secondary to vein occlusion.

Commercial Relationships: Nabil Jabbour, None; Frank Ruda, None; Adel S. Wahba, None

Program Number: 255 Poster Board Number: D0100
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Optical Coherence Tomography Predictors of Visual Outcome in Macular Edema
Salma Radwan 1 2, Sohini RoyChowdhury 3, Julian Tokarev 4, Helen F. Roemhild 5, Keshab K. Parhi 6, Dara D. Koozekanani 7
1Ophthalmology, University of Minnesota, Minneapolis, MN; 2Ophthalmology, Cairo University, Cairo, Egypt; 3The Department of Electrical and Computer Engineering, University of Minnesota, Minneapolis, MN.

Purpose: To identify new biomarkers in spectral domain optical coherence tomography (SD-OCT) images to predict visual acuity (VA) outcome in patients with macular edema (ME).

Methods: Patients with center-involved intraretinal ME (N=38 eyes) that resolved within 1 year follow up were grouped by etiology. Group A (N=25 eyes) with diabetic macular edema (DME) and Group B (N=13 eyes) with ME due to other causes. ETDRS VA testing and macular imaging using Spectralis SD-OCT were done before and after edema resolution. Matlab and Adobe Photoshop softwares were used in the analysis of the central 1500 μ region. Internal reflectivity was calculated from raw data images. Image analyses included (i) recording of center (CST) and paracentral subfield thickness; (ii) quantification of outer retinal disruption, including the external limiting membrane (ELM), inner-segment/outer-segment junction (IS/OS), and cone outer segment tips (COST); (iii) analysis of inner retinal cysts and regions of disorganization, including size, reflectivity, and location.

Results: Baseline logMAR VA ranged from 0 to 1.6 and CST ranged from 322 to 600 μ. Regression analyses were done. In both groups, final VA correlated strongly with initial VA with no significant correlation with baseline CST. However, paracentral subfield thickness correlated significantly with final VA, especially for the inner and outer superior subfields in group A (p<0.05). After adjusting for baseline VA, the extent of IS/OS and ELM disruption correlated significantly with final VA (p<0.001) in both groups. In group A, inner retinal disorganization area, the number of scan lines involved, and presence of disorganization in the center line scan were significantly correlated with final VA (p<0.001, p=0.001, p<0.04 respectively). Cyst area was more highly correlated with VA outcome in group B than was in group A (p=0.047 vs. p=0.097). In group B, the extent and reflectivity of inner retinal disorganization correlated with final VA (p=0.0027, p=0.05 respectively). There was no correlation between cyst reflectivity, location, COST interruptions, epithelial membranes and final VA in either group.

Conclusions: Paracentral thickness correlated better with final VA than CST in DME. The extent of photoreceptor layer disruption & inner retinal disorganization correlated significantly with final VA in both groups. The markers discussed above can be used as potential predictors of VA outcome.

Commercial Relationships: Salma Radwan, None; Sohini RoyChowdhury, None; Julian Tokarev, None; Helen F. Roemhild, None; Keshab K. Parhi, Leanics Corporation (S), Leanics Corporation (E); Dara D. Koozekanani, None

Program Number: 257 Poster Board Number: D0102
Presentation Time: 8:30 AM - 10:15 AM

Assessment of Metamorphopsia in Patients with Central Serous Chorioretinopathy

Purpose: To evaluate the role of aqueous flare in pseudophakic eyes with cystoid macular edema (CME) and its relationship to best corrected visual acuity (BCVA) and retinal thickness.

Methods: 30 pseudophakic eyes with clinically significant CME as well as 46 healthy pseudophakic eyes and 97 healthy phakic eyes as controls were enrolled in this study. BCVA, aqueous flare measurements with a laser flare-cell meter (Kowa FM-500, Kowa Co. Ltd, Tokyo, Japan) and spectral domain optical coherence tomography (SD-OCT) volume scans were collected. Foveal central thickness (FCT) was assessed using custom software.

Results: Pseudophakic eyes with CME showed significantly higher flare values than healthy pseudophakic eyes (p<0.0001; median, 22.55 vs. 11.00 photon counts per millisecond (pc/ms)) and phakic eyes (p< 0.0001; median, 22.55 vs. 3.52 pc/ms). There was also a significant difference of flare values between pseudophakic and phakic healthy eyes (p<0.0001; median, 11.00 vs. 3.52 pc/ms). Among pseudophakic eyes, higher flare values correlated significantly with lower BCVA (p=0.041). Higher flare values also correlated with higher FCT (p<0.0001) in the pseudophakic group.

Conclusions: Analysis of aqueous flare values revealed significant differences between eyes with clinically significant CME and healthy controls indicating higher inflammation levels in the anterior chamber of affected eyes.

Commercial Relationships: Lebriz Ersoy, None; Albert Caramoy, Bausch & Lomb (F), Fluoron GmbH (F), Alamedics GmbH & Co. KG (F); Tina Ristau, Novartis (F); Bernd Kirchhof, None; Sascha Fauser, None

Program Number: 259 Poster Board Number: D0104
Presentation Time: 8:30 AM - 10:15 AM

Optical Coherence Tomography Assisted Enhanced Depth Imaging of Central Serous Chorioretinopathy
Lihong Yang 1, Jost B. Jonas 2, Wen Bin Wei 1, 3. Beijing Tongren Eye Center, Beijing Tongren Hospital, Beijing, China; 2Department of
Purpose: To describe characteristics of central serous chorioretinopathy (CSC) imaged by optical coherence tomography assisted enhanced depth imaging (EDI-OCT).

Methods: The prospective observational case series study consisted of patients with acute or chronic CSC. All subjects underwent fundus fluorescein angiography (FFA), indocyanine green angiography (ICGA), and EDI-OCT.

Results: The study included 68 eyes (68 patients) with 35 eyes showing signs of acute CSC. Mean subfoveal choroidal thickness was 478±14 μm was larger than the normative value from the Beijing Eye Study 2011 (254±107 μm) on the same ethnic group. In the hyperfluorescent ICGA areas, EDI-OCT revealed a thinning of the inner choroidal layers and enlargement of the underlying hyporeflective lumina in all eyes. The diameter of the hyporeflective lumina (mean:330±103 μm) was significantly (P<0.001) associated with subfoveal choroidal thickness (correlation coefficient r: 0.68).

Conclusions: CSC is characterized by thinned inner choroidal layer and enlarged underlying hyporeflective choroidal lumina in all eyes, in addition to a dome-shaped RPE elevation, a double layer sign of the RPE Bruchs membrane complex, and RPE microrips in some eyes. EDI OCT may be helpful in the diagnosis of CSC.
for controlling inflammatory conditions by intravitreal injection, mainly for uveitic patients, when all other treatment options did not show any benefit.

**Methods:** Data and history of 9 patients who were given 400 μg of methotrexate intravitreally up to three times for different conditions (4 with therapy refractory uveitic macular edema and one each with atypical retinopathia centralis serosa (RCS), persistent subretinal fluid after scleral buckling, anti-VEGF-refractory AMD, postoperative cystoid edema after macular hole and multiple glaucoma surgery) were retrospectively evaluated. Visual acuity, amount of intra- and subretinal fluid on SD-OCT, unwanted adverse events and time to recurrence were documented and are presented.

**Results:** One of the four uveitic patients responded with improvement of visual acuity and reduction in fluid, as did the patient with the atypical RCS. The effect was gone four to six weeks after injection. All other patients did not show constant benefit in respect to visual acuity or amount of fluid in OCT. Only one adverse event was seen (intraocular pressure elevation in the patient with the history of multiple glaucoma surgery).

**Conclusions:** Treatment of patients with intravitreal methotrexate might be effective in terms of reducing intraretinal or subretinal fluid and improving visual acuity, but the rate of response is poor. Our data suggest to use intravitreal methotrexate only when all other established therapies have proven futile and the condition in question is clearly inflammatory. Therefore patients need to be selected carefully for this treatment.

**Commercial Relationships:** Egbert Matthe, None; Dirk Sandner, Novartis (F), Novartis (R); Lutz E. Pillunat, None

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**Program Number:** 262 Poster Board Number: D0107
**Presentation Time:** 8:30 AM - 10:15 AM
**Results of Intravitreal Dexamethasone Implant 0.7mg (Ozurdex) in non-infectious posterior uveitis**

*Yew Chong Yap, Thomas Papathomas, Kamal Ahmed.*

Ophthalmology, Aintree University Hospital, Liverpool, United Kingdom.

**Purpose:** Purpose: To evaluate the safety and efficacy of Ozurdex implant in patients with posterior uveitis with CMO.

**Methods:** Methods: Retrospective analysis of patients reports with CMO secondary to uveitis treated with Ozurdex. Data included type of posterior uveitis, any systemic immunosuppressive therapy, Best Corrected Visual Acuity (BCVA), Central Macular Thickness (CMT) on OCT and signs of intraocular inflammation at baseline and then at 2 weeks postoperatively and monthly thereafter. Follow-up is up to 10 months. Any per-operative and post-operative complications were recorded.

**Results:** Results: Six eyes of 4 patients with CMO due to uveitis treated with Ozurdex implant. Diagnosis included idiopathic panuveitis, Birdshot choriororetinopathy, idiopathic intermediate uveitis and inflammation confirmed by Fluorescein Angiography. At baseline mean logMAR BCVA was 60 letters and mean CMT 566μ. At 2 weeks postoperatively mean logMAR BCVA improved to 70 letters and mean CMT to 303μ. All eyes showed clinical evidence of decreased inflammation. The duration of effect of the implant was 5 to 6 months and retreatment was required in 2 eyes. Two patients required antiglaucoma therapy for increased intraocular pressures. No other adverse effects were recorded.

**Conclusions:** Conclusions: In patients with non-infectious posterior uveitis Ozurdex implant can be a safe and effective treatment option for controlling intraocular inflammation.

**Commercial Relationships:** Yew Chong Yap, None; Thomas Papathomas, None; Kamal Ahmed, None

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**Program Number:** 263 Poster Board Number: D0108
**Presentation Time:** 8:30 AM - 10:15 AM
**Treatment Outcomes of Cystoid Macular Edema in Patients with Boston Type I Keratoprosthesis**

*Randee C. Miller, Kaitlyn M. Wallace, Joshua H. Hou, Clement C. Chow, Jose De la Cruz, Maria S. Cortina, Felix Y. Chau.* University of Illinois at Chicago, Chicago, IL.

**Purpose:** Cystoid macular edema (CME) is a common complication of Boston keratoprosthesis (Kpro) implantation, for which there is no standard treatment protocol. In this study we report our experience with several established therapies for CME.

**Methods:** Medical records of all patients who underwent implantation of Kpro at Illinois Eye and Ear Infirmary from Feb 2007- Nov 2012 were retrospectively reviewed. Eyes with CME as confirmed on spectral domain optical coherence tomography (SD-OCT) in the postoperative period were included. Outcome measures included visual acuity (VA), intraocular pressure, SD-OCT macular thickness, type, frequency, and duration of treatment including topical steroids and non-steroidal, posterior sub-tenon (PST) and intravitreal triamcinolone (IVT), intravitreal bevacizumab, and dexamethasone implant (Ozurdex). Structural outcomes were categorized into resolution (R), improvement (I), stable (S), or worsened (W).

**Results:** 105 Kpro were implanted into 91 eyes of 85 patients over a 5 year period. 19 of 91 eyes (21%) were diagnosed with CME postoperatively. The median time from Kpro to diagnosis of CME was 3 months. The median follow up time was 21.9 months. The median VA at time of CME diagnosis was 20/200 and the median initial OCT macular thickness was 519 μm. 10 eyes had topical treatment only (3R, 3I, 2S, 2W).

9 eyes had additional treatments with injections:
1 had intravitreal bevacizumab (S);
1 had PST and IVT (S);
1 had PST, IVT and bevacizumab (W);
3 had at least one Ozurdex (1R, 2I) and
3 had PST, IVT, and Ozurdex (3I).

The 8 steroid injected eyes received a median of 3 treatments over a median of 24.7 months. Overall, the median final VA was 20/250 (p= 0.25) and median final OCT macular thickness was 413 μm (p= 0.005). 4 eyes with pre-existing glaucoma had a transient pressure spike >30 mmHg following steroid injection; 3 were treated successfully with topical medication (3/4) and one required a glaucoma shunt procedure (1/4). There were no other ocular complications.

**Conclusions:** Treatment of CME following Kpro can be challenging. Corticosteroids remain a mainstay of treatment and anatomic improvement may occur in the absence of visual acuity improvement. Twelve of 19 eyes exhibited resolution or improvement of CME, including all 6 eyes treated with Ozurdex; four of these 12 eyes had improved visual acuity. Ozurdex may be beneficial in treating chronic Kpro CME.

**Commercial Relationships:** Randee C. Miller, None; Kaitlyn M. Wallace, None; Joshua H. Hou, None; Clement C. Chow, None; Jose De la Cruz, alcon (C), amo (C); Maria S. Cortina, None; Felix Y. Chau, None

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**115 Retinal Prosthesis I**

Sunday, May 05, 2013 10:30 AM-12:15 PM
6E Paper Session

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Extracellular recording of multiple retinal ganglion cells during epiretinal vs. subretinal electrical stimulation of isolated mouse retina with a high resolution stimulation device

Eyal Margalit1, 2, Sylvie Sim1, Robert Szalewski1, Lee J. Johnson1, Wallace B. Thoreson2, VA Nebraska-Western Iowa Health Care System, Omaha, NE; 2Ophthalmology and Visual Science, University of Nebraska Medical Center, Omaha, NE; 3Naval Research Laboratory, Washington, DC.

Purpose: To compare response patterns and electrical receptive fields (ERF) of retinal ganglion cells (RGCs) evoked by epiretinal vs. subretinal electrical stimulation (epi vs. sub) of isolated mouse retina with a novel stimulation device.

Methods: Retinae were isolated from 4-12 week old normal (C57BL6J) mice, and positioned ganglion cell down (epi), or up (sub), over a stimulation device with 3200 electrodes (Naval Research Laboratory, Washington DC) that is capable of stimulating single or multiple electrodes. Extracellular recording was performed from multiple RGCs using an array of sixteen recording electrodes (Alfa Omega, Alpharetta, GA).

Results: 46 and 59 RGCs were recorded during epi and sub, respectively. The thresholds for spikes evoked by stimuli increased with the square of distance between the stimulating electrode and the target cell.

Three response patterns were observed: a burst of activity immediately after stimulation (Type I cells, Jensen and Rizzo-2008), delayed bursts beginning >25 ms later (Type II), or a combination of both (Type III). Type I responses were produced more often by epi (83%) than sub (53%). Conversely, delayed responses observed in Type II and Type III cells were evoked more frequently by sub (18/59 cells, 31%) than epi (7/46 cells, 15%). Inhibitory responses were also observed more often with sub (17%) than epi (2%). These differences were significant (p=0.0012, chi-square test). In addition, the response delay was shorter for epi vs. sub (p=0.0099, chi-square test).

ERF was defined as a stimulating array’s surface area that can successfully stimulate spikes in a given RGC in either epi or sub. The area (in mm2) of ERFs obtained for short latency responses reflecting direct activation was smaller with sub (Type I 0.239±0.151, N=11; Type II 0.362±0.238, N=31) than epi (0.461±0.524, N=7; 0.733±0.773, N=38). The difference in the ERF size between epi vs. sub was significant (p=0.0052, ANOVA).

Conclusions: The greater frequency of delayed and inhibitory responses suggests that sub stimulation is more effective at activating intraretinal circuits than epi stimulation. The differences in epi vs. sub ERFs’ areas can be largely explained by the greater distance between stimulating electrodes and recorded RGCs due to the interposed retina in the sub configuration.

Commercial Relationships: Eyal Margalit, None; Sylvie Sim, None; Lee J. Johnson, None; Wallace B. Thoreson, None

Support: a Veterans Administration Merit Review Grant #C6583R, unrestricted grant from Research to Prevent Blindness, Nebraska Research Initiative, and NEI grant EY10542.
infra-red (NIR) light. Each pixel in the subretinal implant converts pulsed light into local electric current to stimulate the nearby inner retinal neurons. The study characterized the cortical responses to photovoltaic stimulation and compared them with responses elicited by visible light.

**Methods:** Subretinal photodiode array with pixels 70, 140 and 280μm in width were implanted in the subretinal space of wild type (WT) (n=12) and Royal College of Surgeon (RCS) rats with degenerated retina (n=15). Cortical responses were recorded over a 6 months follow-up period using three skull electrodes. The NIR (915nm) and visible (635nm) laser beams were projected onto the retina via a slit lamp. A VEP response threshold was defined as the signal 3 standard deviation above the noise level. Stimuli were modulated by pulse duration, peak power and repetition rate.

**Results:** The implant induced cortical responses (eVEP) at irradiance levels two orders of magnitude below the ocular safety limit for 915nm radiation. Average thresholds of eVEP were 0.43, 1.0 and 2.1 mW/mm² for pixel sizes of 280, 140 and 70μm, respectively, at 10ms pulse duration. Latency of the visible light-induced VEP decreased with increasing irradiance from 70 to 30ms, unlike the significantly shorter latency of eVEP, which did not vary with stimuli irradiance. In both rats type the eVEP amplitude increased with peak irradiance and pulse duration, and decreased with increasing frequency in the range of 2-20Hz, similar to the visible light response. However, from 20 to 40Hz the VEP continued to decreased while the eVEP did not change as much.

**Conclusions:** Robust cortical responses to photovoltaic subretinal stimulation and similarity in the eVEP modulation by NIR irradiance, pulse duration and frequency to VEP modulation by visible light suggest similarity in visual cortex processing of the retinal responses elicited by both types of stimuli. The small size and lack of wires makes photovoltaic arrays easy to implant and well tolerated in the subretinal space. Photovoltaic retinal prosthesis offers a promising approach to restoration of sight in patients blinded by retinal degenerative diseases.

**Commercial Relationships:** Yossi Mandel, None; Georges A. Goetz, None; Daniel Lavinsky, TMLS (C); Philip Huie, None; Keith Mathieson, None; Lele Wang, None; Theodore J. Kamins, None; Richard Manivanh, None; James Harris, None; Daniel V. Palanker, None.

**Support:** NIH Grant # 1R01EY018608, Stanford University Bio-X Research Grant, US Air Force Office of Scientific Research Grant, SU2P RCUK Science Bridges award Grant, Research to Prevent Blindness and the Department of Veterans Affairs

**Program Number:** 349
**Presentation Time:** 11:15 AM - 11:30 AM

**Recent Results from Second Sight’s Argus® II Retinal Prosthesis Study**

Mark S. Humayun1, Lyndon daCruz2, Gislin Dagnelie2, Paulo E. Stanga3, Allen C. Ho4, Robert J. Greenberg5, David G. Birch7, Jacque L. Duncan4, Jose A. Sahel6.

1Ophthalmology, Doheny Eye Institute - USC, Los Angeles, CA; 2NIHR Biomedical Research Centre for Ophthalmology, Moorfields Eye Hospital, London, United Kingdom; 3Lions Vision Research and Rehabilitation Center, Johns Hopkins University, Baltimore, MD; 4Manchester Royal Eye Hospital, Manchester, United Kingdom; 5Wills Eye Institute, Philadelphia, PA; 6Second Sight Medical Products, Inc., Sylmar, CA; 7Retina Foundation of the Southwest, Dallas, TX; 8University of California, San Francisco, San Francisco, CA; 9Center Hospitalier National d’Ophthalmologie des Quinze-Vingts, Paris, France.

**Purpose:** To provide an update on performance outcomes in the Argus II Retinal Prosthesis Study.

**Methods:** Subjects had bare light perception or worse vision due to retinitis pigmentosa. All subjects were implanted with a Second Sight Argus II implant (clinicaltrials.gov NCT00407602). Visual function was evaluated by a grating visual acuity test as well as by assessing the ability to determine the direction of motion of a line and the location of a square on an LCD screen. Orientation and mobility (O&M) tests were also given, which involved following a line and finding a door. The Functional Low-vision Observer Rated Assessment was used by low-vision rehabilitation experts to evaluate subjects’ functional vision and well-being.

**Results:** As of December 1, 2012, 30 subjects have been implanted at 10 centers (in the main study). Subjects have been implanted an average of 4.2 ± 1.0 years (range of 1.2 - 5.5), and all have used or are using the System at home. In this report we are only mentioning what we have learned new over the last year. Over the past year, the Argus II continues to work in all subjects except for one device which had exhibited intermittent communication link which subsequently failed at 4 years post-implant. There was one additional case of presumed endophthalmitis (culture negative) associated with an area of conjunctival erosion which resolved using intravitreal and topical antibiotics and with repair of the conjunctiva and did not require device removal. Additional research has demonstrated GVAs as high as 1.0 logMAR (20/200) using image processing algorithms. Functional vision O&M tests continue to demonstrate that subjects are significantly better at performing visual tasks with the System ON vs. OFF. In September 2012, the Argus II retinal prosthesis received a unanimous approval by an advisory panel convened by the FDA ophthalmic device division.

**Conclusions:** With over 125 cumulative patient-years of follow-up on 30 subjects, this is the largest study of a visual prosthesis to date. This year results continue to confirm previous reports on the ability of the Argus II prosthesis to provide visual function and functional vision over several years. The Argus II Retinal Prosthesis System has been commercially available in Europe since 2011 and FDA approval in the US is now pending. Funding information: NIH 1R01EY012893-10

**Commercial Relationships:** Mark S. Humayun, Bausch & Lomb (F), Bausch & Lomb (C), Bausch & Lomb (P), Bausch & Lomb (R), Bausch & Lomb (S), Alcon (C), Alcon (R), Iridex (P), Iridex (R), Replens (I), Replens (C), Replens (R), Replens (S), Second Sight (F), Second Sight (I), Second Sight (C), Second Sight (P), Second Sight (R), Second Sight (S), Regenerative Patch Technologies (I), Regenerative Patch Technologies (C); Lyndon daCruz, Second Sight Medical products Inc. (R); Gislin Dagnelie, None; Paulo E. Stanga, OPTOS PLC (C), OPTOS PLC (R), TOPCON CORP (F), TOPCON CORP (C), TOPCON CORP (R), SECOND SIGHT (F), SECOND SIGHT (R); Allen C. Ho, Second Sight (C), Second Sight (F); Robert J. Greenberg, Second Sight Medical Products, Inc. (I), Second Sight Medical Products, Inc. (E), Second Sight Medical Products, Inc. (P), Second Sight Medical Products, Inc. (S); David G. Birch, Acucela (C), QLT (C), Neurotech, USA (C); Jacque L. Duncan, None; Jose A. Sahel, UPMC/Essilor (P), Second Sight (F)

**Support:** NIH 5R01EY012893-10

**Clinical Trial:** NCT00407602

**Program Number:** 350
**Presentation Time:** 11:30 AM - 11:45 AM

**Electric Field Shaping Via Separatrices For Focused Electric Retinal Stimulation Via Retinal Implants**

Wolfgang Fink1, Erich W. Schmidt1, 2

1Visual & Autonomous Exploration Systems Research Laboratory, University of Arizona, Tucson, AZ; 2Visual & Autonomous Exploration Systems Research
Laboratory, California Institute of Technology, Pasadena, CA; 1Institute for Theoretical Physics, Eberhard Karls University, Tübingen, Germany.

**Purpose:** To introduce a method for shaping electric fields for focused stimulation of the retina via retinal implants. Phosphenes-based visual perception through electrical stimulation tacitly assumes that such stimulation is confined to prescribed target volumes. However, electric currents cannot be focused like a laser. State-of-the-art retinal implants use remote return electrodes, or adjacent return electrodes with an additional remote return electrode. Such configurations, especially with high electrode densities, are prone to crosstalk.

**Methods:** We are using multi-poles of electrodes and optimization of separatrices (i.e., mathematical surfaces between distinct bundles of field lines) to avoid crosstalk and to guide the stimulation field into the target volumes. As an example, in the electrode configuration of Fig. 1a, four dipoles (blue electrodes) form the guiding field, and the red electrodes the stimulation field. The stimulation field cannot penetrate into the guiding field because of the non-crossing rule of field lines (Fig. 1b). The separatix between the guiding field and stimulation field forms a ridge with peaks and saddle points. At the saddle points the stimulation field line density is maximal. Optimization routines are used for shifting the saddle points into the target volumes.

**Results:** In a hexagonal array of electrodes a ring of dipoles (blue electrodes) builds up a separatix that has the shape of a crater (Fig. 2a). The stimulation current emitted from the center electrode rises like a narrow fountain and spreads out above the crater rim (Fig. 2b). The time profiles of guiding and stimulation fields are chosen such that the stimulation field has a lower stimulation threshold than the guiding field (Schmid & Fink, arXiv:1210.5348v1); the guiding field is not shown in Fig. 2b.

**Conclusions:** Separatrices can focus electric stimulation currents into prescribed target volumes. The space and time profiles of the resulting electric currents are entirely determined by the spatial arrangement of the electrodes and by their respective activation potentials. The caveat is that one image-giving pixel is formed by a multi-pole. However, image resolution can be restored by switching the center of the pixel from electrode to electrode for subsequent stimulation events (i.e., local area scanning; arXiv:1210.5348v1).

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Protein Profiles in Patients with Retinopathy of Prematurity

To analyze the effect of ASC, postnatal day 7 neonatal immune compromised NSG mice along with nursing mothers were subjected to oxygen induced retinopathy (OIR). At p12 mice were randomized to receive human ASC (10,000 cells/eye/2μL) into the vitreous after birth. The mice were euthanized at p20, and the retinas were collected for analysis. The ASC were isolated from adipose tissue (ASC) are pluripotent stem cells, reside in perivascular niche, possess functional and phenotypic overlap with pericytes and improve ischemia reperfusion in-vivo. In this study, we hypothesized that ASC may stabilize vasculature and therapeutically rescue ROP features.

Methods: To analyze the effect of ASC, postnatal day 7 neonatal immune compromised NSG mice along with nursing mothers were subjected to oxygen induced retinopathy (OIR). At p12 mice were randomized to receive human ASC (10,000 cells/eye/2μL) into the left eye and saline into the right eye. At p17, mice were euthanized; retinal wholemounts were imaged by confocal microscopy and mRNA expression by qRT-PCR. In-vitro human retinal endothelial cells (HREC) subjected to hypoxia were co-cultured with ASC and

Purpose: Retinopathy of Prematurity (ROP) is a vaso-proliferative eye disease in premature babies with low gestational age (≤32 weeks) and birth weight (≤1,700g) and is characterized by abnormal retinal vascular development. The present study aimed to evaluate the levels of inflammatory and angiogenic factors in ROP for understanding their involvement in the disease process.

Methods: Vitreous humor (50-100μl) were collected from patients (n=30) with stage IV and V of ROP (classified as per ICROP guidelines) along with infants with congenital cataract as control subjects (n=30) undergoing vitrectomy, with prior informed consent from their parents. The concentrations of 28 proteins involved in neuro-degeneration, extracellular matrix (ECM) remodeling, angiogenesis and inflammatory pathways in pre-diluted vitreous (1:5) samples were evaluated using multiplex bead immunoasays based on Luminex xMAP technology. Differences between levels of these proteins were analyzed using appropriate statistical tests followed by validations by western blotting.

Results: Of the analytes evaluated, 21/28 could be detected in the vitreous humor of these subjects. Patients with ROP exhibited significant elevations in MMP9 (p=0.035), CFH (p=0.002), C3 (p=0.006), C4 (=0.0009), Prealbumin (p=0.012), SAP (p=0.026), APOA1 (p=0.002) and APOC3 (p=0.006) compared to the controls. The concentrations of the remaining proteins in the vitreous humor were not significantly different between the patients and controls (p>0.05).

Conclusions: The elevated levels of 8/21 proteins in the vitreous humor of patients indicated that abnormal immune environments and ECM components might play a role in the development of ROP. Commercial Relationships: None; Subhadra Jalali, None; Ramesh Kekunnaya, None; Inderjeet Kaur, None

Support: Department of Biotechnology, Government of India

Program Number: 588 Poster Board Number: D0110
Presentation Time: 10:30 AM - 12:15 PM
Vascular Stabilization with Adipose Stromal Cells in Retinopathy of Prematurity

Breedge Callaghan1, Chandrika Abburi1, Pamela I. Rogers1, Brian C. Samuels1, Keith L. March1,2, Gangaraju Rashashekhary3,4.

1Ophthalmology, Eugene and Marilyn Glick Eye Institute, Indiana Univ., Indianapolis, IN; 2Medicine, IU School of Medicine, Indianapolis, IN; 3Indian Center for Vascular Biology & Medicine, Indianapolis, IN.

Purpose: In USA, nearly 50% of low-birth weight infants develop Retinopathy of prematurity (ROP). Current strategies for the treatment of ROP including cryotherapy are not effective in all patients and there is unmet need for identification of new therapies. We have shown that cells derived from the stromal fraction of adipose tissue (ASC) are pluripotent stem cells, reside in perivascular niche, possess functional and phenotypic overlap with pericytes and improve ischemia reperfusion in-vivo. In this study, we hypothesized that ASC may stabilize vasculature and therapeutically rescue ROP features.

Methods: In this study, we hypothesized that ASC may stabilize vasculature and therapeutically rescue ROP features. We have shown that cells derived from the stromal fraction of adipose tissue (ASC) are pluripotent stem cells, reside in perivascular niche, possess functional and phenotypic overlap with pericytes and improve ischemia reperfusion in-vivo. In this study, we hypothesized that ASC may stabilize vasculature and therapeutically rescue ROP features.

Conclusions: The elevated levels of 8/21 proteins in the vitreous humor of patients indicated that abnormal immune environments and ECM components might play a role in the development of ROP. Commercial Relationships: None; Subhadra Chakrabarti, None; Ganeswara R. Musada, None; Subhadra Jalali, None; Ramesh Kekunnaya, None; Inderjeet Kaur, None

Support: Department of Biotechnology, Government of India

Program Number: 588 Poster Board Number: D0110
Presentation Time: 10:30 AM - 12:15 PM
Vascular Stabilization with Adipose Stromal Cells in Retinopathy of Prematurity

Breedge Callaghan1, Chandrika Abburi1, Pamela I. Rogers1, Brian C. Samuels1, Keith L. March1,2, Gangaraju Rashashekhary3,4.

1Ophthalmology, Eugene and Marilyn Glick Eye Institute, Indiana Univ., Indianapolis, IN; 2Medicine, IU School of Medicine, Indianapolis, IN; 3Indian Center for Vascular Biology & Medicine, Indianapolis, IN.

Purpose: In USA, nearly 50% of low-birth weight infants develop Retinopathy of prematurity (ROP). Current strategies for the treatment of ROP including cryotherapy are not effective in all patients and there is unmet need for identification of new therapies. We have shown that cells derived from the stromal fraction of adipose tissue (ASC) are pluripotent stem cells, reside in perivascular niche, possess functional and phenotypic overlap with pericytes and improve ischemia reperfusion in-vivo. In this study, we hypothesized that ASC may stabilize vasculature and therapeutically rescue ROP features.

Methods: In this study, we hypothesized that ASC may stabilize vasculature and therapeutically rescue ROP features. We have shown that cells derived from the stromal fraction of adipose tissue (ASC) are pluripotent stem cells, reside in perivascular niche, possess functional and phenotypic overlap with pericytes and improve ischemia reperfusion in-vivo. In this study, we hypothesized that ASC may stabilize vasculature and therapeutically rescue ROP features.

Conclusions: The elevated levels of 8/21 proteins in the vitreous humor of patients indicated that abnormal immune environments and ECM components might play a role in the development of ROP. Commercial Relationships: None; Subhadra Chakrabarti, None; Ganeswara R. Musada, None; Subhadra Jalali, None; Ramesh Kekunnaya, None; Inderjeet Kaur, None

Support: Department of Biotechnology, Government of India

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apoptosis was measured by Caspase-3 and viability by WST-1 assay. 

Results: Retinal wholemounts obtained from OIR mice, revealed a dramatic decrease in total tubulength (assessed by MetaMorph angiogenesis tube formation module) compared to age-matched control mice, was significantly increased in OIR mice that received ASC (25395±1600 v/s 34453±1919µm; p<0.001). In addition, OIR mice that received ASC demonstrated a 2-3 fold decrease in mouse specific ICAM-1, MCP-1 and an increase in VEGF and VEGFR2 compared to OIR mice that received saline. In-vitro, HREC formed capillary networks with ASC in direct contact co-culture, as evidenced by wVF staining. Immunostaining with aSMa suggested that HREC were able to direct differentiation of the ASC along a pericytic lineage potentially capable of stabilizing vasculature. Furthermore, HREC subjected to hypoxia demonstrated a significant decrease in cell viability and increased capase-3 staining, while those co-cultured with ASC alleviated apoptosis and improved cell viability.

Conclusions: Our findings suggest that, ASC impart vasculoprotection under hypoxic/inflammatory conditions and may have therapeutic potential in treating ischemic conditions and pathological angiogenesis. Further characterization of ASC will provide vital information about vasculoprotective nature of these cells.

Commercial Relationships: Breeedge Callaghan, None; Chandrika Abbur, None; Pamela I. Rogers, None; Brian C. Samuels, Merck & Co., Inc (F), Merck & Co., Inc (C), ICHE (C); Keith L. March, None (P); Ganganaru Rajashekar, IU Research & Technology Corporation (P)

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Gap Junctions and Retinal Angiogenesis
Jessica M. Ackert, Tamas Atlasz, MT Sinai Medical Center, New York, NY.

Purpose: To study the role of gap junctions in the development of proliferative retinal disease.

Methods: A well-established mouse model of oxygen-induced retinopathy (OIR) was used to induce proliferative retinal disease (Smith et al 1994). Briefly, litters were exposed to hyperoxic conditions (75% oxygen) from post-natal day (PD) 7 through PD 12 causing retinal vaso-oblation. The litters were returned to room air on PD 12. The right eye of the mouse pups received a 1 µl intravitreal injection of 500 micromolar of the global gap junctional blocker meclofenamic acid (MFA) on PD12 and 13. The left eye served as an untreated control. The relative hypoxia of room air induces a decrease in cell viability and increased caspase-3 staining, while those co-cultured with ASC demonstrated apoptosis and improved cell viability.

Conclusions: Our findings suggest that, ASC impart vasculoprotection under hypoxic/inflammatory conditions and may have therapeutic potential in treating ischemic conditions and pathological angiogenesis. Further characterization of ASC will provide vital information about vasculoprotective nature of these cells. Our findings suggest that, ASC impart vasculoprotection under hypoxic/inflammatory conditions and may have therapeutic potential in treating ischemic conditions and pathological angiogenesis. Further characterization of ASC will provide vital information about vasculoprotective nature of these cells.

Corinne, crystalline lens and whole ocular refractive power in premature infants with retinopathy of prematurity at one year of age
Takako Tachikawa1, 2, Ritsuko Ueno1, Daisuke Yuzurihara3, Tetsuko Mita1, Osamu Katsumi1, 3, Toru Noda2, 4, Kazuhiro Ohnuma1,1
ophthalmology, Tokyo Metropolitan Ohtsuka Hospital, Tokyo, Japan; 2ophthalmology, Tokyo Women's Medical University, Medical Center East, Tokyo, Japan; 3ophthalmology, Nishikasaki Inouye Eye Clinic, Tokyo, Japan; 4ophthalmology, National Hospital Organization Tokyo Medical Center, Tokyo, Japan; 5Medical System Engineering, Chiba University, Chiba, Japan.

Purpose: To investigate the corneal, crystalline lens, and whole ocular refractive powers in premature 1-year-old infants with retinopathy of prematurity (ROP) using a method we devised to determine the refractive power in infants.

Methods: We studied 50 eyes (50 infants with ROP; overall mean gestational age, 25.3±1.9 weeks; range, 22-29; mean birth weight, 763.±195 5 g; range, 438-1,230) at 1 year corrected age. The infants were divided into 3 primary groups: group 1, 29 untreated eyes; group 2, 9 treated eyes (zone I and aggressive posterior ROP (APROP)); and group 3, 12 treated eyes (zone II). The spherical equivalent (SE), anterior chamber depth (ACD), axial length (AL), corneal radius (CR), and lens thickness (LT) were measured by ultrasound A-scan biometry, autorefactometry, and keratometry under cycloplegia. The individual refractive index using the Gullstrand-Emsley model (except that of the lens, which was modified to 1.43) and anterior and posterior lens curvature ratio (1.29) were used to calculate the corneal power (CP), crystalline lens power (LP) and whole ocular refractive power (WP). The parameters were compared among groups by the Student’s t-test and Tukey HSD test.

Results: The average group 1 values were AL, 19.81±0.74 mm; CR, 7.44±0.32 mm; LT, 3.85±0.14 mm; ACD, 3.05±0.38 mm; SE, 0.56±0.10 diopters (D); CP, 45.20 D; LP, 39.01 D; and WP, 76.66 D. Group 2: AL, 18.79±0.57 mm; CR, 7.22±0.33 mm; LT, 4.32±0.22 mm; ACD, 2.23±0.35 mm; SE, -2.49±1.56 D; CP, 46.45 D; LP, 45.88 D; and WP, 84.06 D. Group 3: AL, 19.65±0.86 mm; CR, 6.88±0.24 mm; LT, 4.11±0.16 mm; ACD, 2.77±0.34 mm; SE, -0.75±2.32 D; CP, 45.12 D; LP, 41.52 D; and WP, 78.79 D. The SE differences between groups 1 and 2 were significant (p<0.041) but not between groups 1 and 3 (p=0.19). The CP differences among the 3 groups were not significant (p<0.2). The LPs differed significantly (p<0.05) among groups. The WPs differed significantly (p<0.0001) between groups 1 and 2 but not between groups 1 and 3 (p=0.11).

Conclusions: In premature 1-year-old infants with ROP, there was no significant difference between the group not treated with laser and zone II laser-treated group in SE and WP. Zone I and APROP laser-treated groups had higher myopia and greater WP than other groups.

Commercial Relationships: Takako Tachikawa, None; Ritsuko Ueno, None; Daisuke Yuzurihara, None; Tetsuko Mita, None; Osamu Katsumi, None; Toru Noda, None; Kazuhiro Ohnuma, None

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Presentation Time: 10:30 AM - 12:15 PM
Effects of Lower Dosage of Intravitreal Bevacizumab in Retinopathy of Prematurity

Yuta Saito, Isamu Ito, Toshihiko Ueda, Michiko Matsubara, Eiichi Nishimura, Haruo Takahashi. Ophthalmology, Showa University, Tokyo, Japan.

Purpose: To evaluate the effects of lower dosage of intravitreal injections of bevacizumab (IVB) in retinopathy of prematurity (ROP).

Methods: There were fourteen eyes of 7 patients receiving IVB (0.25mg/eye) for treatment of ROP from April 2011 to June 2012 at Showa University. This retrospective case series included the patients who were followed up at least 5 months after IVB.

Results: Ten eyes of 5 patients (4 male and 1 female) were included in this study. 2 patients were excluded from the study because of a follow-up time of less than 1 month. Mean gestational age and birth weight were 24.6 (range: 22-26) weeks and 770.2 grams (range: 505-1055). There were eight eyes of 4 patients with stage 3 ROP treated by conventional laser, and two eyes of 1 patient with aggressive posterior ROP (AP-ROP) without laser treatment. All of the eyes received only a single injection of IVB. The mean injection time was 37.2 (range: 34-39) weeks. No complications such as cataract or endophthalmitis occurred. Of eight eyes with stage 3 ROP, six eyes (4 patients) regressed after IVB. Two eyes (2 patients) were treated with vitrectomy after IVB because of progressive tractional retinal detachment. The retina of one eye failed to reattach after vitrectomy surgeries. AP-ROP was regressed after IVB and subsequent conventional laser treatment.

Conclusions: IVB was performed as a salvage therapy in this study. Lower dosage of IVB seems effective to regress ROP. However, it also increased fibrotic traction in some eyes. In the BEAT-ROP study, a dosage of 0.625 mg is recommended as a monotherapy. Whereas intravitreal injected bevacizumab can escape to systemic circulation. Thus, usage of lower dosage of IVB for ROP in combination with conventional laser therapy appears to be safe until the optimal dosage will be established.

Commercial Relationships: Yuta Saito, None; Isamu Ito, None; Toshihiko Ueda, None; Michiko Matsubara, None; Eiichi Nishimura, None; Haruo Takahashi, None

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Vitreoretinal interface changes in the fibrovascular demarcation line after intravitreal bevacizumab for type 1 retinopathy of prematurity

Rafael Romero Vera, Alay Banker, Rosa E. Martinez, Samantha Salinas Longoria, Guillermo Salcedo-Villanueva, Hugo E. Sepulveda-Vazquez, Maria A. Martinez-Castellanos. Retina, Asociación para Evitar la Ceguera, México, D.F., Mexico.

Purpose: To report the changes in the vitreoretinal interface of the fibrovascular demarcation line after intravitreal bevacizumab for stage 3, zone 1 or 2 with plus disease retinopathy of prematurity (ROP)

Methods: Non comparative, prospective, case series. We included ten eyes of five premature patients of 2 different centers one in Mexico and one in India who were treated for type 1 ROP with 0.03cc/(0.75 mg) intravitreal bevacizumab as monotherapy. Demographic data: gender, birth weight, gestational age at birth, age at treatment and severity of ROP were recorded. Weekly clinical photographs and fluorangiography (performed every 2 weeks) were obtained using the RETCAM system (Clarity medical systems) Additional information was obtained by spectral domain optical coherence tomography iVue (Optovue corporation)

Results: After the injection of bevacizumab in all 10 eyes pathological neovascularization regressed, the fibrovascular ridge persisted fibrotic for 3 to 5 weeks after the injection in the demarcation line, some retina traction without detachment was observed in the OCT scan in the ridge area. In the third week we could assessed by angiography that retinal normal vasculature was developing under the fibrotic ridge towards the periphery. Between the sixth and eight weeks after injection, the fibrovascular ridge completely detached in all ten eyes. Large vitreous condensations are visible in all the eyes

Conclusions: Vitreous adhesion in pediatric pathologies is poorly understood, there are some reports of tractional retinal detachment and retinal crunch after the use of antiangiogenic therapy for ROP treatment. As more babies are treated worldwide, we will be able to fill the gaps on the safety profile of these drugs that were not address in clinical trials or small series. As new clinical features of ROP after anti VEGF treatment emerge, such as the ones presented, pediatric retina specialists will be face with questions regarding appropriate follow up and possible complications such as retinal hole formation and retinal detachment on these patients

Commercial Relationships: Rafael Romero Vera, None; Alay Banker, None; Rosa E. Martinez, None; Samantha Salinas Longoria, None; Guillermo Salcedo-Villanueva, None; Hugo E. Sepulveda-Vazquez, None; Maria A. Martinez-Castellanos, None

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Refraction Changes After The Use of Bevacizumab in The Treatment Of Patients With Prethreshold Retinopathy Of Prematurity

Yihsing Chen1,2, Nan-Kai Wang1,2, Yen-Po Chen1,2, An-Ning Chao1,2, Kuan-Jen Chen1,2, Yi-Shiou Hwang1,2, Chi-Chun Lai1,2, Wei-Chi Wu1,2. 1Ophthalmology department, Chang Gung Memorial Hospital, Taoyuan county, Taiwan; 2College of Medicine, Chang Gung University, Taoyuan county, Taiwan.

Purpose: To evaluate the refractive status in patients with premature birth and variant stages of retinopathy of prematurity (ROP) at the age of 6, 18, 30, 36 months-old.

Methods: This longitudinal, prospective cohort study enrolled 41 preterm patients. Patients were divided into the following groups: ROP without the need of treatment; prethreshold ROP treated with intravitreal injection of 0.625mg/0.025ml bevacizumab (Avastin) (IVB); prethreshold ROP treated with combined bevacizumab and peripheral diode laser (LIO); and stage 4A ROP treated with lens sparing vitrectomy (VT). Cyclopegic refraction, axial length (AXL), anterior chamber depth (ACD), and lens thickness were measured at the age of 6, 18, 30 and 36 months’ corrected age.

Results: In total, 79 eyes from 41 patients were included in the study. 8 eyes (10.1%) received observation only; 35 eyes (44.4%) required IVB; 28 eyes (35.4%) received IVB and LIO treatment; and 8 eyes (10.1%) received VT. The average follow-up duration was 23.8 months (11 to 41 months). The mean spherical equivalence (SE) were -1.87 diopter (D) (range -13.50D to 7.13D, N = 41); -3.37D (range -15.63D to 2.88D, N=44); -1.93D (range -14.75D to 7.50D, N=33); and -2.91D (range -8.75D to 0.38D, N=8) at 6, 18, 30 and 36 months old. Most patients developed with the role (WTR) astigmatism. At age 15 months, 31 eyes (75%) had WTR astigmatism, and the trend continued to 24 months, whereas 36 eyes (45.6%) developed WTR astigmatism. The mean AXL were 20.60mm (range 19.50 to 21.76, N = 41); 20.65mm (range 19.14 to 21.75, N=21); 21.4mm (range 19.85 to 23.1, N=22); and 22.48mm (range 21.79 to 23.04, N=4) at 6, 18, 30 and 36 months old. The AXL did not differ significantly between different ages in the 4 groups but the vitrectomized group tend to have a longer AXL during follow-up. The ACD and average lens
thickness did not differ significantly between different ages in the 4 groups.  

Conclusions: ROP patients developed relatively minimal refractive errors after receiving IVB. The vitrectomized eyes tend to have higher chances of developing high refractive errors. Most of the patients developed WTR type astigmatism in the four groups. The vitrectomized eyes tend to develop longer AXL during follow-up, but no statistically difference was found.  

Commercial Relationships: Yi-Bing Chen, None; Nan-Kai Wang, None; Yan-Po Chen, None; An-Ning Chao, None; Kuan-Jen Chen, None; Yi-Shiou Huang, None; Chi-Chun Lai, None; Wei-Chi Wu, None

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Screening for Retinopathy of Prematurity in China   
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Purpose: The current screening criteria for retinopathy of prematurity (ROP) in China define a birth weight of less than 2000g or the gestational age of less than 34 weeks, which is different than what was used by the United States of America and United Kingdom. This study evaluated the incidence of ROP and the validity of current ROP screening criteria in China.  
Methods: A retrospective study of ROP indices was carried out in infants admitted to the neonatal intensive care unit in Xinhua Hospital and Children’s Hospital, Shanghai, China, from June 2011 to May 2012. All infants who met the above screening criteria were reviewed for ROP diagnosis and related indices. This study was performed in accordance to the tenets of the Declaration of Helsinki and approved by the Institutional Review Board (IRB) of Xinhua Hospital and the Children’s Hospital.  
Results: 2995 infants were screened and ROP was diagnosed in 537 infants (17.89%). 285 infants (9.51%) had type 1 or worse ROP and were treated with laser, cryocoagulation or vitrectomy. For patients having ROP, the mean GA was 29.9±2.3 weeks and mean BW was 1443.4±394.4 g. Infants who needed treatment for ROP had a mean GA of 29.5±2.1 weeks and mean BW of 1394.9±373.8 g. Only one infant greater than 2000 g BW and more than 34 weeks GA was required laser photocoagulation treatment within 72 hours of diagnosis. Among these treated infants, 16 (5.6%) infants exceeded UK screening criteria, and 38 (13.3%) exceeded the criteria used in the United States.  
Conclusions: Larger, older infants are at risk for ROP in China and screening criteria recommended by the American Academy of Pediatric Ophthalmology and Strabismus and the Royal College of Ophthalmologists, United Kingdom, may not be suitable for China. Current ROP screening criteria in China seems reasonable and we do not recommend lowering current criteria for ROP screening.  
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Presentation Time: 10:30 AM - 12:15 PM  
The Incidence of Retinopathy of Prematurity in Armenia   
Albert Hovhannisyan1,2, Cassandra Fink1, Anna S. Brown1, Susan Ostmo2, Robison V. Chan1, Tadevos Hovhannisyan3, 4, Ruzanna Harutyunyan5, 4, Inga Sargsyan1, 2, 5, Michael F. Chiang2, 6, Thomas C. Lee2, 6. 1The Vision Center, Children's Hospital Los Angeles, Los Angeles, CA; 2Department of Ophthalmology, Oregon Health and Science University., Portland, OR; 3Department of Ophthalmology, Weill Cornell Medical College; Cornell University, New York City, NY; 4Malayan Ophthalmological Centre, Yerevan, Armenia; 5Armenian EyeCare Project, Newport Beach, CA; 6Department of Medical Informatics and Clinical Epidemiology, Oregon Health and Science University., Portland, OR; 7Keck School of Medicine, University of Southern California, Los Angeles, CA.  
Purpose: Armenia opened their first Neonatal Intensive Care Units (NICUs) in 1995, leading to increased survival in premature infants (1,600 in 2010) and an epidemic of blindness due to Retinopathy of Prematurity (ROP). ROP affects premature and low birth-weight infants, and can lead to permanent blindness. Fortunately, serial screening examinations and timely treatment leads to complete regression of the disease in up to 90% of patients. Throughout the years Armenia had NICUs, no ROP screenings were performed. When the US ophthalmologists initially traveled to Armenia, 1 in 5 infants in one NICU was observed to be at risk of going blind. During a one year period in which Armenian ophthalmologists were trained to screen, diagnose and treat ROP through a telemedicine training program, data from the examinations were recorded. The objective of this study was to assess the incidence of ROP, treatment requiring ROP, and birth weight and gestational age (GA) cut offs for screening criteria in Armenia.  
Methods: This retrospective study utilized data from screenings between 06/30/2010 and 06/29/2011 in eight NICUs in Armenia. All babies in the NICUs were screened. The screening was performed by an ophthalmologist using indirect ophthalmoscopy and wide-field digital imaging device (RetCam). Interpretations of retinal images and establishment of diagnoses were performed by well trained Armenian ophthalmologists. The decision to treat with laser photocoagulation was based on the Early Treatment Retinopathy of Prematurity (ETROP) guidelines.  
Results: The incidence of ROP was 65% (102/157), while 16.6% (26/157) required laser photocoagulation treatment within 72 hours of high risk ROP diagnosis. The mean birth weight for infants without ROP, with ROP and with treatment requiring ROP were 1536grams (±274.1), 1378.9 g (±335.6) and 1240.4 g (±293.2), respectively. The mean GA corresponding to these infants were 32 weeks (±1.69), 30 weeks (±2.24) and 28.9 weeks (±2.3), respectively. Study results demonstrate that 2/26 treated infants (7.7%) did not meet the AAO/AAP/AAPOS screening criteria (birth weight ≤1500g or GA ≤30wks).  
Conclusions: The incidence of ROP in Armenia is high, and large birth-weight infants are at risk for severe disease. Implementation of AAO/AAP/AAPOS screening guidelines in Armenia would result in a considerable number of infants going blind. These data can serve as the basis for developing new screening guidelines for infants in Armenia.  
Commercial Relationships: Albert Hovhannisyan, None; Cassandra Fink, None; Anna S. Brown, None; Susan Ostmo, None; Robison V. Chan, None; Tadevos Hovhannisyan, None; Ruzanna Harutyunyan, None; Inga Sargsyan, None; Michael F. Chiang, Clarity Medical Systems (unpaid member of Scientific Advisory Board) (S); Thomas C. Lee, None  
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Treatment Of Type I Pre-Threshold and Threshold Retinopathy Of Prematurity in Northern Colombia- Efficacy of Laser Alone
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1 Cleveland Clinic, Cole Eye Institute, Cleveland, OH; ²Department of Ophthalmology, Universidad del Norte, Barranquilla, Colombia.

Purpose: Describe the clinical characteristics and outcomes of children with Retinopathy of Prematurity (ROP) who were screened and treated in 11 Neonatal Intensive Care Units in Colombia between January 2008 - June 2012.

Methods: 749 eyes were examined in 377 infants born with a gestational age (GA) of 32 weeks or less and a birth weight (BW) of 1750 g or less. All infants were screened at the fifth week of life or by 34 weeks post-conception.

Results: 152 of 377 patients (40%) had any type of ROP, affecting 299 eyes. 181 eyes of 97 patients required surgery (24%). 127 eyes of 69 patients required Laser Photocoagulation and 54 eyes of 28 patients required Rescue Therapy (Laser and intravitreal anti-VEGF). Follow-up was lost in 34 cases of 18 patients in the laser group and in 4 eyes of 2 patients in the Rescue Therapy Group. In addition, 4 eyes of 3 patients of this last group were also excluded because of progression to Stage 4 ROP. In this report we analyze the results of the Laser Group. There were 101 eyes of 51 patients with a mean GA of 28.3 weeks. More than 50% of infants were born between 27 and 29 weeks. 98% of the patients with ROP were born ≤ 32 weeks of gestation. The mean BW was 1057 g. 94% of the infants of this group weighed 1500 g or less at birth. 24/51 infants (47%) had a BW between 1001 and 1500 g and 24/51 (47%) had a BW of 1000 g or less. The types of ROP were Pre- threshold type 1 89 eyes of 45 patients (88%) and Threshold 12 eyes of 6 patients (12%). 16 eyes (16%) required rescue therapy to obtain regression of the ROP.

Conclusions: The development of ROP was related to low birth weight and gestational age, however not all babies followed this trend. In the United States it is standard to screen only those infants born weighing ≤ 1500 g at birth. Some institutions will routinely screen only those infants born with a birth weight of ≤ 1250 g. In our study, 6% of the infants that required Laser Photocoagulation weighed ≥ 1500 g, and 2% of patients were born after 32 weeks gestation. Thus, we advocate that each institution carefully monitor their trends and rates of ROP in order to develop screening criteria that will capture the greatest number of infants with ROP. Laser Photocoagulation seems effective and well tolerated in most patient and in our study less than 20% needed additional treatment to promote ROP regression.

Commercial Relationships: Paul J. Rychwalski, None; Jenny V. Lobo Lopez, None; Sarah K. Jordan, None; Carlos A. Abdala, None

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Computer-based image analysis for ROP: development of a quantitative index based on vascular tortuosity
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1Ophthalmology, Casey Eye Institute, Oregon Health & Sciences University, Portland, OR; 2Medical Informatics, Casey Eye Institute, Oregon Health & Sciences University, Portland, OR; 3Kaiser Permanente, Los Angeles Medical Center, Los Angeles, CA; 4Electrical and Computer Engineering, Northeastern University, Boston, MA; 5Radiology, Massachusetts General Hospital, Boston, MA.

Purpose: Plus disease is a critical marker of treatment-requiring retinopathy of prematurity (ROP), but clinical diagnosis has been shown to be subjective and qualitative. Computer-based image analysis of vascular tortuosity has potential to provide diagnostic assistance based on objective and quantitative principles. This pilot study proposes and evaluates a methodology for creating a quantitative “plus index” for diagnostic assistance.

Methods: A set of wide-angle retinal images (RetCam; Clarity Medical Systems, Pleasanton, CA) from infants with ROP was collected and diagnosed by experts as plus or not plus. 41 images were reviewed by 23 experts. 384 retinal vessels (both arterioles and venules) from all images were manually segmented by author consensus. Tortuosity, defined as vessel length from starting point to end point divided by the straight line distance between those points, was calculated using a computer-based image analysis system developed by the authors. Mean tortuosity of all vessels was calculated for each image at various distances from the optic disc. For each image, correlations between mean tortuosity and proportion of experts who diagnosed it as plus disease were calculated at each distance to determine which distance resulted in strongest correlation. The full range of tortuosity at that distance was divided into a scale from 1 to 7 to create a “plus index”. Sensitivity and specificity for detecting plus disease were calculated at each “plus index” value using the expert majority diagnosis as the reference standard.

Results: The strongest correlation between mean tortuosity and proportion of experts who diagnosed plus disease was found at 0-2 disc diameter (DD) from the optic disc (R^2=0.636). At 0-2 DD, the range of tortuosity was 1.04-1.45 and was divided into the 7 point scale to create the “plus index” values. Sensitivity/specificity for diagnosing plus disease was 0.929/0.556 (using “plus index” ≥3 as cutoff) and 0.571/1.00 (using “plus index” ≥4 as cutoff).

Conclusions: This study outlines a methodology for creating a quantitative plus disease index utilizing computer-generated retinal vessel tortuosity measurements from wide-angle retinal images. With a large cohort of retinal images from infants with ROP, this methodology could generate an index to aid in the identification of plus disease with potential applications in ROP telemedicine systems.

Commercial Relationships: Grant Aaker, None; Daniel Lattin, None; Esra Atea-Cansizoglu, None; Katie M. Keck, None; Deniz Erdogmus, None; Jayashree Kalpathy-Cramer, None; Michael F. Chiang, Clarity Medical Systems (unpaid member of Scientific Advisory Board) (S)

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Presentation Time: 10:30 AM - 12:15 PM

An Analysis of the Retinal Vascular Development in a Mouse Model of Bronchopulmonary Dysplasia
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Purpose: To study retinal vasculature development in an established mouse model of Bronchopulmonary Dysplasia (BPD).

Methods: A total of 24 eyes from 24 C57Bl6 mice were examined. Half the mice were exposed to 14 days of hyperoxia (75% O2) immediately following birth in order to induce BPD. The other half was reared under normoxic conditions. At day 14, the mice were sacrificed, and their eyes were fixed and subsequently flatmounted

Research to Prevent Blindness (New York, NY). Also supported by NIH grant EY19474 (MFC).
and the vasculature were thresholded using the NIH’s ImageJ software. The resulting vessel maps were then analyzed using the NCI’s AngioTool software to determine average vessel length, the number of vessel junctions and the lacunarity of each vessel map. The hyperoxia exposed BPD eyes were then compared to the normoxic controls using these measurements.

**Results:** The BPD pups exhibited severely reduced vascularization with only 30% of the average vascular area of the normoxic pups (p<.01). Average vessel length in the BPD pups was 12% of the normoxic groups (p<.01). The total number of junctions in the BPD vessels was 8.6% of normoxic controls (p<.01). Lacunarity, a measure of the average gap between the blood vessels was increased in the BPD mice was 490% higher compared to the normoxic pups (p<.01).

**Conclusions:** Retinal vascular development in the BPD mouse model is significantly impaired compared to control pups. Overall, the retina of BPD mice is less vascularized, less organized and coherent. The BPD model presents a challenge to retinal development both from hyperoxic exposure and decreased blood flow and oxygenation due to BPD. Further study may help elucidate the individual contribution of both challenges to retinal dysfunction that we have characterized in this study. Given the frequent concurrence of BPD and Retinopathy of Prematurity (30%), determining influence of BPD conditions on retinal vascular development may elucidate future therapeutic strategies for treating both diseases.
Analyses were performed for associations in supplemented infants at 7 and 28 days after birth (p < 0.03) but did not differ between groups at 36 weeks' PMA before any ROP treatment and ROP not requiring treatment. Results were adjusted with multivariate analyses to control for gestational age (GA), small for GA antenatal steroid use, race represented from eigenvector values generated from the sample population, and gender as covariables. P-values < 0.01 were considered significant.

Results: 871 infants had at least one eye exam. Of these, 814 were successfully genotyped for 1278 of the targeted SNPs. There were 601 infants with any ROP, and 128 infants with severe ROP. When comparing ROP vs. no ROP, there were 3 SNPs with p-values < 0.005 from LRP5. There were also SNPs with p values < 0.01 from BDNF, EPAS1, WDR43, and ABCA4. However, false discovery rates (FDRs) were 0.94 for all SNPs in this analysis. When comparing severe ROP requiring treatment vs. ROP not requiring treatment, the SNPs with p values < 0.01 included 3 from BDNF, 4 from IGF1, and 5 from the CFH pathway. For BDNF, FDRs were 0.095, whereas for the other SNPs, FDRs were > 0.37.

Conclusions: High FDRs limit certainty of associations with ROP compared to control. However, results support novel associations between BDNF SNPs and severe ROP. In addition, links between severe ROP and familial exudative vitreoretinopathy and macular degeneration should be replicated and validated.

Commercial Relationships: M Elizabeth Hartnett, National Eye Institute (F), Genentech (C), Axikin Pharmaceuticals (R); Grier Page, None; Michael Cotten, None; Jeff Murray, None; Margaret M. DeAngelis, None

Support: U510 HD040492-12 (NRN MC, GP); EY015130 (MEH PI); HD52593 (JM); RPB

Program Number: 602 Poster Board Number: D0124
Presentation Time: 10:30 AM - 12:15 PM

Luminance-response functions for light-adapted electroretinograms (ERGs) in preterm infants at risk of retinopathy of prematurity (ROP)

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Purpose: Scotopic retinal sensitivity in infants at risk of ROP is improved by early supplementation with high-dose vitamin A(1). Here we report the sensitivity and amplitude of light-adapted ERGs in this population.

Methods: In a double-blind, controlled trial, eligible infants born before 32 weeks’ gestation and/or < 1501 g birth-weight were randomised to receive additional intramuscular vitamin A 10,000IU three times weekly from birth for two weeks or until oral feeding was established. ERGs were measured at 36 weeks postmenstrual age (PMA) before any ROP treatment. Following dark-adapted ERGs(1), 46 infants were light-adapted (30 cd/m^2) for 10 minutes for a luminance-response (LR) series to white flashes from 0.01 to 500 cd/s/m^2. Parameters calculated using non-linear regression were saturated amplitude (sAMP) for a- and b-waves, and b-wave sensitivity (luminance at semi-saturation).

Results: All parameters for light-adapted LR series were immature (> 1.5 log units below adult values). The 90% CI were 5.0 to 19µV for a-wave sAMP, 19 to 73 µV for b-wave sAMP and 1.1 to 8.5 cd/s/m^2 for b-wave sensitivity. B-wave amplitudes were typically fit with simple logistic growth functions; only 4 cases showed reduced b-waves for strong stimuli (photopic hills). Plasma retinol was higher in supplemented infants at 7 and 28 days after birth (p < 0.03) but did not differ between groups at 36 weeks’ PMA. Supplementation did not reproduce any abstract, contact the ARVO Office at arvo@arvo.org.
not affect any of the light-adapted LR parameters. Low birth weight and short gestation were strong risk factors for ROP as was postnatal illness based on duration of oxygen requirement and length of hospital stay (p<0.01). LR functions from the 36 infants without ROP did not differ from those of the 8 who developed stage 1 or 2 disease. In two infants who developed stage 3+ ROP requiring treatment, b-wave LR functions were markedly reduced (ANOVA p<0.01). Five of seven infants who developed severe ROP could not undergo ERG testing because of ongoing respiratory support.

**Conclusions:** We present normative ranges for light-adapted ERGs at 36 weeks’ PMA for infants without ROP. Parameters for infants who developed mild disease did not differ from normals. Two infants who developed severe ROP showed reduction in light-adapted b-wave sensitivity and sAMP in advance of treatment.

2. **Commercial Relationships:** Daphne L. McCulloch, None; Helen Mactier, None; Lesley Farrell, None; Gen Hanazono, None; Ruth Hamilton, None
3. **Support:** Chief Scientist Office, Scottish Government, grant CZB/4/316
4. **Clinical Trial:** EudraCT number 2005-003402-29

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**Program Number:** 603 **Poster Board Number:** D0125

**Presentation Time:** 10:30 AM - 12:15 PM

**Wnt Signaling Mutations can Compromise Peripheral Retinal Vascular Development and Confuse the Diagnosis in Prematurely Born Infants**

**Purpose:** To determine if Wnt signaling mutations as known in familial exudative vitreoretinopathy (FEVR) may play a role in the lack of peripheral retinal vascular development in older premature infants (52 weeks postmenstrual age and older) and to develop a treatment paradigm for this clinical problem

**Methods:** 20 premature infants (24 to 32 weeks gestational age) were followed for retinopathy of prematurity (ROP) who did not develop retinal vessels to within two disc diameters of the ora serrata by 52 weeks or more postmenstrual age were studied by wide-angle fluorescein angiography (WAFA), exam under anesthesia, and genetic testing to determine if they might actually have familial exudative vitreoretinopathy (FEVR). Those with fluorescein findings of FEVR and leakage, or positive genetic testing, were treated with peripheral laser ablation. Children with positive fluorescein angiography or positive genetic testing also had their parents tested with WAFA looking for asymptomatic peripheral retinal vascular changes of FEVR.

**Results:** Four children were found to have Wnt signaling mutations and 10 additional children had fluorescein angiographic changes consistent with FEVR and leakage, but without identifiable mutations. 20 percent of parents showed findings on WAFA consistent with Wnt signaling mutations of FEVR

**Conclusions:** We have previously reported that Wnt signaling mutations can result in more severe aggressive posterior ROP, but it also appears that there may be Wnt signaling mutations that also play a role in modulating peripheral retinal vascular development as is seen in FEVR. These mutations may be an explanation for these premature infants who show a lack of peripheral retinal vascular development when being followed for ROP. This type of mutation may also explain the larger infants seen in some parts of the world with the diagnosis of ROP.

**Commercial Relationships:** Michael T. Trese, Nu-Vue Technologies (P), Synergistic (C), Thrombogenics (I), Genentech (R), Focus ROP (I), Retinal Solutions LLC (I); Joshua Robinson, None; Antonio Capone, Retinal Solutions (P); Kimberly A. Drenser, None

**Program Number:** 604 **Poster Board Number:** D0126

**Presentation Time:** 10:30 AM - 12:15 PM

**Iridocorneal angle characteristics of infants with retinopathy of prematurity (ROP) compared to full-term infants using spectral domain optical coherence tomography**

**Purpose:** To compare measurements and morphologic characteristics of the iridocorneal angle in preterm infants with retinopathy of prematurity (ROP) vs full-term infants of the same group of age using spectral domain optical coherence tomography (SD-OCT)

**Methods:** Children aged under 1 year old were recruited at an ophthalmologic center. SD-OCT was used to obtain one scan per eye, images were analyzed with custom software. Angle recess area (ARA) was located 750 μm anterior to the scleral spur. Angle width was represented by the angle opening distance (AOD) at 500 μm anterior to scleral spur. Angle opening in grades (AOG) was measured at the iridocorneal junction. ROP staging was recorded from previous diagnosis made by a pediatric retinal specialist

**Results:** Forty-six infant’s eyes (27 with ROP and 21 without ROP) were studied. The mean gestational age and birth weight of the ROP group participants was 30 weeks and 1,500 g. The non-ROP patients were 35 weeks and 2,100 g. Mean age at the moment of the study was 18.1 weeks vs 25.7 wk (ROP vs non-ROP). AOP, AOG, ARA on the ROP group were 477 μm (CI 95% 358 to 597 μm), 37.3 grades (CI 95% 30.4 to 44.3 grades) and 231 mm² (CI 95% 171 to 291 mm²) respectively. The same parameters on the non-ROP group were 400 μm (CI 95% 333 to 468 μm), 34.7 grades (CI 95% 30.4 to 39 grades) and 203 mm² (CI 95% 171 to 236 mm²). Mean values for AOD, AOG and ARA by ROP stage were as follows; Stage 1: 780 μm, 49 degrees, 568 mm²; Stage 1+: 701 μm, 51 degrees, 359 mm²; Stage 2: 439 μm, 36 degrees, 224 mm²; Stage 2+: 276 μm, 25 degrees, 132 mm²; Stage 3: 1029 μm, 60 degrees, 510 mm²; Stage 3+: 311 μm, 26 degrees, 138 mm²; Stage 4: 182 μm, 43 degrees, 67 mm²; Stage 5: 440 μm, 31 degrees, 201 mm². The main descriptive difference was the configuration of the iris, showing a more convex pattern on eyes with ROP than without the disease (56% vs 23%).

**Conclusions:** Children without ROP showed a smaller AOP, AOG and ARA than children with ROP. It may be due to differences of iris configuration or to different patterns of development in children with ROP. Further studies should be performed to assess our findings.

**Commercial Relationships:** Linda A. Cernichiaro-Espinosa, None; Veronica E. Giordano, None; Magdalena Garcia-Huerta, None; Samantha Salinas Longoria, None; Rafael Romero Vera, None; Gerardo Garcia-Aguirre, None; Guillermo Salcedo-Villanueva, None; Hugo Quiroz-Mercado, None; Maria A. Martinez-Castellanos, None; Linda A. Cernichiaro-Espinosa, None

**Program Number:** 605 **Poster Board Number:** D0127

**Presentation Time:** 10:30 AM - 12:15 PM

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Role of the Krebs Cycle metabolite α-ketoglutarate and its receptor, GPR99, in retinal angiogenesis

François Duhamel, Karine Zaniolo, Houda Tahir, Sylvain Chemtob. Pharmacology, Ste-Justine Hospital Research Center, Montreal, QC, Canada.

**Purpose:** Retinopathy of prematurity (ROP), a major cause of blindness in developed countries, occurs in two phases: the cessation of normal eye development after birth and a subsequent abnormal and exaggerated vessel growth. Peripheral hypoxia occurs after the first phase in premature eye and induces production of many growth factors implicated in this second destructive neovascularization phase. Our laboratory has previously demonstrated the role of succinate/GPR91 in the modulation of retinal vessel growth. Here, we investigated the role of α-ketoglutarate and its cognate receptor GPR99 in retinal angiogenesis.

**Methods:** Effects of α-ketoglutarate on developmental retinal vascularess were assessed following intravitreal injection of Sprague-Dawley rat pups in development. Moreover, the effects of a siGPR99 knockdown following intravitreal injection were investigated in the neovascular phase of ROP. Endogenous expression of retinal GPR99 was assessed by immunohistochemistry on retina cuts and Western blots analysis of different cell lines while expression of pro-angiogenic factors was assessed by PCR analysis.

**Results:** α-ketoglutarate significantly enhanced developmental vascular densities at different time points. Neovascularization was blocked by a siGPR99 and allowed normal vessel growth in ROP. Moreover, GPR99 was robustly expressed in RGCs as confirmed by co-labeling with neuron markers and, in vitro, mainly in neuronal cells. Conditioned media from α-ketoglutarate stimulated-neurons induced aortic rings sprouting, in correlation with an up-regulation of pro-angiogenic factors expression.

**Conclusions:** Our results disclose a pro-angiogenic role for α-ketoglutarate and its receptor, GPR99, providing increasing supports for the involvement of metabolite signalling in ischemic conditions.

**Commercial Relationships:** François Duhamel, None; Karine Zaniolo, None; Houda Tahir, None; Sylvain Chemtob, None

**Support:** Canadian Institutes of Health Research (CIHR) - Banting & Best PhD Scholarship

Program Number: 606 Poster Board Number: D0128

Presentation Time: 10:30 AM - 12:15 PM

Circadian Clock Gene Regulation of Retinal Neovascularization

Lili Xu1, John S. Penn2, Douglas McMahon1. 1Biological Science, Vanderbilt University, Nashville, TN; 2Vanderbilt Eye Institute, Vanderbilt University, Nashville, TN.

**Purpose:** Abnormal neovascularization of the retina is a fundamental cause of blindness in a number of eye diseases including retinopathy of prematurity (ROP). Expression and secretion of VEGF by Müller glial cells is a critical element in the development of aberrant neovascularization. We have shown previously that mouse and human retinal Müller cells exhibit self-sustained clock gene and these rhythms were suppressed by treated with siRNA knockdown of Per1. Here we demonstrated that genetic knockout of the specific circadian clock genes Period1 (Per1) and Period2 (Per2) results in increased hypoxia-induced VEGF in Müller cells and an increased neovascularization phenotype in the mouse oxygen-induced retinopathy (OIR) model.

**Methods:** Purified primary Müller cells from KO and WT were cultured in low-glucose DMEM medium containing 10% FBS at 37°C in a 5% CO2 incubator. The cells were serum starved for 12 hours and then were grown at 37°C for 24 hours in growth medium under both normoxic and hypoxic (O2 < 5%) conditions; P7 KO and WT pups with nursing mothers were subjected to hyperoxia (75% oxygen) or room air for 5 days and then oxygen-exposed mice were returned to room air. Gene expression, vascular development and neovascularization were measured in mouse Müller cells and retinas by quantitative RT-PCR and whole-mount retina staining on vary time points, respectively.

**Results:** The baseline VEGF expression in WT and KO Müller cells did not differ, but was significantly increased in KO cells in hypoxia. There was a day/night difference in VEGF expression levels in WT cells in hypoxia. In vivo, consistent with in vitro, WT and KO mice had similar baseline levels of VEGF expression and angiogenic development, but KO mice in OIR protocol exhibited higher retinal VEGF levels and blunted VEGF rhythms. Vascular development of WT and KO retinas did not differ in OIR or control mice at P13, but OIR-induced neovascularization was significantly increased in KO mice at P18 when measured as proportion of vascular retinal area or whole retinal area.

**Conclusions:** These data suggest that the Period clock genes act to negatively regulate VEGF are protective against neovascularization, and may constitute novel targets for intervention in the neovascularization process. We will determine that precise clock genes are critical in regulating VEGF, and determine if Müller cell clocks are the key locus of clock gene regulation of neovascularization.

**Commercial Relationships:** Lili Xu, None; John S. Penn, PanOptica (C), PanOptica (F), Alcon Laboratories (C), Alcon Laboratories (F), Centocor/Janssen (F); Douglas McMahon, None

**Support:** NIH R01EY015815, P30EY008126

Program Number: 607 Poster Board Number: D0129

Presentation Time: 10:30 AM - 12:15 PM

Defective Wnt-signaling is associated with progressive retinopathy in Incontinentia pigmenti (IP)

Cagri G. Besirli1, Joshua Robinson2, Ekia Lakhani3, Michael T. Tresse3. 1Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, MI; 2Associated Retinal Consultants, William Beaumont Hospital, Royal Oak, MI; 3School of Medicine, Wayne State University, Detroit, MI.

**Purpose:** To describe the association of a Wnt-signaling mutation with accelerated and progressive proliferative retinopathy in Incontinentia pigmenti (IP).

**Methods:** DNA sequence evaluation of Wnt-signaling pathway genes for mutations in a family with IP and 3-D protein structure prediction analysis of H69Y Frizzled-4 (FZD4) mutation identified in this family.

**Results:** A 3-day old full-term female infant with a family history of IP was diagnosed with IP after punch biopsy for vesicular skin lesions. Ophthalmic examination and fluorescein angiography showed largely avascular retinal periphery in both eyes with abnormal shunt vessels and dye leakage. Peripheral laser ablation therapy was performed. Repeat ophthalmic examinations demonstrated progressive capillary dropout and retinopathy, requiring additional laser treatments and prompting mutation analysis for Wnt pathway genes. Direct sequencing of exons and exon-intron boundaries revealed a single-nucleotide change in exon 1 of the FZD4 gene, resulting in Histidine to Tyrosine change on amino acid 69. Protein sequence analysis demonstrated that this amino acid is highly conserved across species and among other members of the Frizzled receptor family. 3-D protein structure prediction revealed that His69 residue resides at a critical location in the ligand-binding domain of FZD4.

**Conclusions:** Progressive retinopathy in IP may indicate a second
AN IMPACT OF SEQUENCING WNT-PATHWAY GENES ON RETINAL VASCULAR DEVELOPMENT.
Exome sequencing of Wnt-pathway genes may be a useful clinical adjunct in determining the frequency of ophthalmic examinations and guiding the decision-making for retinal laser treatment in patients with IP.

The finding of a second genetic mutation in a patient with IP indicates that genome sequencing for Wnt signaling mutations may improve the diagnosis and treatment of other acquired and inherited pediatric retinal vascular diseases.

Commercial Relationships: Cagri G. Besirli, None; Joshua Robinson, None; Ektza Lakhani, None; Michael T. Trese, Nu-Vue Technologies (P), Synergetics (C), Thrombogenics (I), Genentech (R), Focus ROP (I), Retinal Solutions LLC (I)

Program Number: 608 Poster Board Number: D0130
Presentation Time: 10:30 AM - 12:15 PM

Quantifying vascular tortuosity in retinopathy of prematurity: impact of segmentation method and vascular length
Daniel Lattin1, Grant Aaker2, Esra Ater-Cansizoglu3, Dongseok Choi4, Katie M. Keck2, Rony Gelman5, Jayashree Kalpathy-Cramer3, Deniz Erdogmus4, Michael F. Chiang5. 1Kaiser Permanente, Los Angeles Medical Center, Los Angeles, CA; 2Ophthalmology, Casey Eye Institute, Oregon Health & Science University, Portland, OR; 3Electrical and Computer Engineering, Northeastern University, Boston, MA; 4Biostatistics, Public Hlth & Prevent Med, Oregon Health & Science University, Portland, OR; 5Ophthalmology, Doheny Eye Institute, University of Southern California, Los Angeles, CA; 6Radiology, Massachusetts General Hospital, Boston, MA; 7Ophthalmology and Medical Informatics, Casey Eye Institute, Oregon Health & Science University, Portland, OR.

Purpose: Plus disease is defined by vascular tortuosity and dilation, and is a critical marker for treatment-requiring retinopathy of prematurity (ROP). Various computational systems for quantifying retinal vascular tortuosity have been developed, which rely on different algorithms for segmenting vessels and calculating tortuosity. The variability in tortuosity values calculated by these systems is not known. This is important to understand the extent to which quantitative vascular tortuosity in ROP is dependent on the specific computer system used. The purpose of this study is to compare the mean tortuosity calculated by two different systems, which used different methods of vascular segmentation but similar algorithms for tortuosity.

Methods: 34 wide-angle retinal images from infants with ROP were analyzed using two different systems: (1) System A performed semi-automated segmentation and calculated tortuosity over the entire vessel length, and (2) System B relied on manual segmentation and calculated tortuosity as a function of distance from the optic disc center. Both systems calculated tortuosity using the same algorithm: vessel length from start point to end point divided by the straight line distance between the same points. Overall tortuosity of each image was used for comparison, and was defined as mean tortuosity of all individual arteries and veins segmented by each system. Correlation between the two systems was measured by Pearson’s r coefficient, and correlation coefficients were calculated for varying distances from the optic disc.

Results: Systems A and B showed strong correlation when computing tortuosity over the entire vessel length. System A (analyzing the entire vessel length) had strong correlation with System B (analyzing over a range of vessel lengths): for 1 disc diameter (DD) distance (r<0.688, p <0.0001), 2 DD (r=0.801, p <0.0001), 3 DD (r=0.811, p <0.0001), and 4 DD (r=0.819, p <0.0001) from the optic disc margin. There was not a statistical difference between the correlations calculated (p >0.22).

Conclusions: There is strong correlation between vascular tortuosity computations in ROP when performed using similar methods by different systems, even when using a range of vascular lengths and segmentation methods. This may have implications for development and implementation of computer-based image analysis systems for ROP.

Commercial Relationships: Daniel Lattin, None; Grant Aaker, None; Esra Ater-Cansizoglu, None; Dongseok Choi, None; Katie M. Keck, None; Rony Gelman, None; Jayashree Kalpathy-Cramer, None; Deniz Erdogmus, None; Michael F. Chiang, None; Clarify Medical Systems (unpaid member of Scientific Advisory Board) (S)

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Program Number: 609 Poster Board Number: D0131
Presentation Time: 10:30 AM - 12:15 PM

Progression of Myopia and Anisometropia in Individual Children with Regressed Retinopathy of Prematurity
Jingyun Wang1, Xiaowei Ren2, Li Shen3, Susan E. Yanni4, Joel Leffler5, Eileen E. Birch6,7,3. 1Glick Eye Institute, Department of Ophthalmology, Indiana University School of Medicine, Indianapolis, IN; 2Department of Biostatistics, Indiana University School of Medicine, Indianapolis, IN; 3Department of Radiology and Imaging Sciences, Indiana University School of Medicine, Indianapolis, IN; 4Retina Foundation of the Southwest, Dallas, TX; 5Department of Ophthalmology, University of Texas Southwest Medical Center, Dallas, TX.

Purpose: The prevalence of myopia increases from 58% (6-MO-old) to 68% (9-MO-old) in children with severe retinopathy of prematurity (ROP) following peripheral retinal laser ablation (Quinn et al 2008). However, individual patterns of myopia progression are not well documented. Here we compare the long-term individual refractive error (particularly myopia and anisometropia) development of preterm children with or without a history of laser treatment.

Methods: Longitudinal (0-7 years) cycloplegic refraction data was obtained from medical records of preterm children with normal-appearing posterior poles. Group 1: regressed ROP following bilateral panretinal laser (n=38; gestational age (GA)=25.4±2.7 wk); Group 2: no or spontaneously regressed ROP (n=35; GA=26.8±3.0 wk). Children with eye or brain malformations, or cortical visual impairment were excluded. Analyses were based on right eye spherical equivalent (SEQ), anisometropia (SEQ difference), and age (corrected for gestation).

Results: Groups 1 and 2 showed a significant difference in development of refractive error (Fig 1). Group 1 SEQ was best fit with a bi-linear spline model: y1=0.09-4.47*Age when Age≤13 years; y2=-5.61-0.17*(Age-1.3) when Age>1.3 years. Before the age of 1.3 years, the rate of myopic shift was -4.5D/year; after 1.3 years, the rate slowing to -0.2D/year. Group 2 SEQ was best fit with a linear model: y=1.66+0.007*Age; i.e., there was little change in refraction with age. In Group 1, by 12 months of age, most children (73%) were myopic and 36% had high myopia (≤-5D). In Group 2, most had low hyperopia and 87% maintained hyperopia at the final visit. Anisometropia was significantly larger in Group 1 than in Group 2 (p=0.029) initially and increased about two times faster than in Group 2 (0.27 vs 0.12 D/year) (Fig 2).

Conclusions: Unlike preterm children who had no ROP or whose ROP underwent spontaneous regression, laser-treated children showed rapid progression of myopia during the first 1.3 years and increasing anisometropia during the first 7 years. Therefore, infants treated with panretinal photocoagulation for severe ROP can develop
early and rapidly progressive myopia; they should be monitored closely with periodic cycloplegic refractions and early optical correction.

Results: 152 of 377 patients (40%) had any type of ROP, affecting 299 eyes. 181 eyes of 97 patients required surgery (24%). 127 eyes of 69 patients required Laser Photocoagulation and 54 eyes of 28 patients required Primary Rescue Therapy (Laser and intravitreal injection of anti-VEGF). 34 eyes of 18 patients in the laser group were lost to follow-up and 4 eyes of 2 infants in the Primary Rescue Therapy group were similarly lost to follow-up. In addition, 4 eyes of 3 patients of this last group were excluded due to progression to Stage 4 ROP before treatment.

In this report we analyze the results of the Primary Rescue Therapy Group. 46 eyes of 23 patients had a mean GA of 27.6 weeks. More than 50% of infants were born between 27 and 29 weeks. 100% of the patients with ROP were born < 32 weeks of gestation. The mean BW was 1008.4 g. 87% of the infants of this group weighed 1500 g or less at birth. 6/23 (26%) had a BW of between 1001 and 1500 g and 14/23 (61%) had a BW of 1000 g or less. All infants of this group had Threshold ROP. Eight eyes (17.39%) required a second rescue therapy treatment (fifteen days after the initial therapy) in order to obtain regression of ROP.

Conclusions: The development of ROP is related to low birth weight and gestational age. In our series, the infants had a mean BW of 1008 g with 87% of infants having a BW of 1500 g or less. 61% had a BW of 1000 g or less. In our group of patients, this was a significant risk factor in the development of threshold ROP. The combination of Laser and Anti-VEGF proved to be effective in treating Threshold ROP and halting the progression of the ROP in 93.5% of infants. Finally, 8/46 eyes (17.3%) required a second treatment in order to obtain the complete regression of the disease.

Commercial Relationships: Carlos A. Abdala, None; Jenny V. Lobo Lopez, None; Sarah K. Jordan, None; Paul J. Rychwalski, None

Program Number: 611 Poster Board Number: D0133
Presentation Time: 10:30 AM - 12:15 PM

Angiographic Features of FEVR versus ROP
Audina M. Berrocal, Vishak J. John. Retina Department, Bascom Palmer Eye Institute, Miami, FL.

Purpose: to examine clinical and angiographic features of children diagnosed with familial exudative vitreoretinopathy [FEVR] but were born prematurely

Methods: A retrospective review of charts and angiograms of patients seen through the Pediatric Retina Service at Jackson Memorial Hospital and Bascom Palmer Eye Institute. IRB approval was obtained.

Results: Participants: We included 16 eyes of 8 infants that had progressive vascular disease clinically consistent with FEVR but were born prematurely. Then we compared them to a control set of 16 eyes of 8 infants with a diagnosis of FEVR who were born at full term.

Baseline data including gestational age, birth weight were analyzed between the groups. Through angiography, we compared zones of disease, disk areas of non-perfusion, distance from the ora-serrata, features of the vascular-vascular junction, presence of arteriovenous shunts, vascular dilatation, degree of leakage, and foveal avascularity. In eyes of children with FEVR, regardless of prematurity of birth, FA clearly shows extreme variability in both retinal and choroidal filling patterns and in the clinical course of the disease despite adequate laser treatment.

Conclusions: The clinical similarities in ROP and FEVR have long been recognized. As fluorescein angiography becomes more widely available for pediatrics through the RETCAM system, it may provide valuable information in understanding the pathophysiologic
similarities and differences between the diseases. In the future, genetic studies and improved imaging technologies will further increase our knowledge.

**Commercial Relationships:** Audina M. Berrocal, thrombogenics (C), genentech (C); Vishal J. John, None

**Program Number:** 612 Poster Board Number: D0134

**Presentation Time:** 10:30 AM - 12:15 PM

New onset macular edema after laser photoacoagulation for retinopathy of prematurity

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**Purpose:** Cystoid macular edema (CME) is a known complication of panretinal laser treatment in patients with diabetic retinopathy. We aim to explore the relationship between CME in infancy and visual outcome and its effect on visual development is unknown. Future studies could increase our knowledge.

**Methods:** Retrospective analyses of spectral domain optical coherence tomography (SDOCT) images obtained as part of an Institutional Review Board approved study on infants having standard-of-care ROP screening sessions at Duke University Medical Center from January 2009 to January 2012. Thirteen of 97 enrolled infants had SDOCT imaging sessions both 1-2 weeks before as well as after laser treatment, and were included. SDOCT images were evaluated for the presence of CME.

**Results:** Only one of the 13 infants had no CME preoperatively or postoperatively. Six of the 13 infants (48%) had CME in both eyes 1-2 weeks before laser treatment. One and two weeks after laser treatment all of these subjects continued to have CME in both eyes. Six infants had no CME preoperatively but developed CME in both eyes within 1-2 weeks after laser treatment. In three of the infants who had longer follow-up, it was observed that the edema resolved within two weeks after laser treatment.

**Conclusions:** There appears to be a relationship between laser treatment for severe ROP and CME. The CME seems to be transient, and its effect on visual development is unknown. Future studies could explore the relationship between CME in infancy and visual outcome in infants with severe ROP.

**Commercial Relationships:** Dordi Austeng, None; Ramiro S. Maldonado, None; Sharon F. Freedman, Pfizer, Inc. (C); David Wallace, Allergan (C), Genentech (C), NEI (F), RPB (F); Cynthia A. Toth, Genentech (F), Biopigen (F), Physical Sciences Inc. (F), Unlicensed (P)

**Support:** The Hartwell Foundation

**Program Number:** 613 Poster Board Number: D0135

**Presentation Time:** 10:30 AM - 12:15 PM

**NADPH oxidase, NOX1, is a key source of oxidative stress in retinopathy and neovascularization**

Jennifer L. Wilkinson-Berka, 1-2, Devy Deliayanti, 1 Indrajeeet Singh Rana, 1 Alex Agrotis, 1 Roskana Armani, 1 Kirstin Wingler, 1 Rhian Touyz, 1 Mark E. Cooper, 1 Karin Jandelet-Dahm, 2 Harald H. Schmidt, 1

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**Purpose:** Neovascularization is a hallmark feature of retinal vasculopathies such as retinopathy of prematurity (ROP) and diabetic retinopathy and plays a critical role in vision impairment. Its pathomechanism is, however, not fully understood and no specific therapeutic intervention is available. Reactive oxygen species (ROS) have been suggested to play a role in physiological and pathological vascularization. Several potential enzymatic sources of ROS are known but NADPH oxidases (NOX) stand out as they are the only enzyme family whose only known function is to produce ROS. Here we evaluated the cellular source of NOX isoforms involved in retinal neovascularization and whether a deficiency in these isoforms influenced ROP.

**Methods:** Primary cultures of retinal microglia, glia, ganglion cells, endothelial cells and pericytes were evaluated for the expression of NOX1, NOX2 and NOX4. Microglial cultures were exposed to normoxia, hypoxia and blockers of the renin-angiotensin system, a known stimulator of ROP and NOX. ROP was induced in NOX1, NOX2 and NOX4 knockout mice and their wildtype controls. Comparisons were made to room air controls.

**Results:** Microglia were found to express NOX1, NOX2, and NOX4. However, only mice with a deletion of the NOX1, but not the NOX2 or NOX4 genes, showed reduced levels of ROS and microglial density as well as pro-angiogenic and pro-inflammatory factors and vascular leakage. This coincided with less leukostasis and vaso-obliteration with a striking protection against ROP. In retinal microglial cultures, angiotensin II and aldosterone induced microglial NOX expression, ROS generation and vascular endothelial growth factor and cytokine production in a manner that was pharmacologically reversible by angiotensin II and aldosterone blockade.

**Conclusions:** NOX1 is a key mediator of retinal neovascularization, opening up the possibility for mechanism-based therapy for this otherwise vision-impairing condition.

**Commercial Relationships:** Jennifer L. Wilkinson-Berka, National Health and Medical Research Council of Australia (F), JDRF (F); Devy Deliayanti, None; Indrajeeet Singh Rana, None; Alex Agrotis, None; Roskana Armani, None; Kirstin Wingler, None; Rhian Touyz, None; Mark E. Cooper, None; Karin Jandelet-Dahm, JDRF Project grant (F), NHMRC SRF Fellowship (F); Harald H. Schmidt, None

**Support:** NHMRC and JDRF

**Program Number:** 614 Poster Board Number: D0136

**Presentation Time:** 10:30 AM - 12:15 PM

**Risk Factors for Treatment-Relieving Retinopathy of Prematurity and Implications for Screening Guidelines**

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**Purpose:** Develop novel screening criteria through evaluation of potential risk factors for treatment-reaching retinopathy of prematurity (ROP), including threshold or type 1, in infants who were screened in 11 Neonatal Intensive Care Units in Colombia, South America between January 2008 and June 2012.

**Methods:** Retrospective study of 380 infants with a birth weight (BW) of ≤ 1750 g and/or a gestational age (GA) of ≤ 32 weeks that were screened by one physician. Univariate and multivariate logistic regression models were fit to determine the odds ratio (OR) and 95% confidence intervals (CI) for treatment-reaching ROP, in association with putative risk factors (year of exam, gestational age, birth weight, sepsis, oxygen, hyaline membrane disease (HMD), transfusion and intraventricular hemorrhage).

**Results:** The mean GA and BW for the 92 cases (24%) of treatment-reaching ROP were 28.2±2.00 weeks and 1049±281 grams
Results: APN and its receptor adipoR1 were examined for serum adiponectin levels in two mouse models of oxygen deprivation. A group of neonatal rats fed a linoleic acid-enriched diet showed decreased APN levels in ROP compared to controls. In contrast, a group of neonatal rats fed a docosahexaenoic acid-enriched diet showed increased APN levels in ROP compared to controls. These findings suggest that APN and its receptor adipoR1 may mediate the protective effect of omega-3 LCPUFA in ROP.

Conclusions: APN and its receptor adipoR1 may mediate the protective effect of omega-3 LCPUFA in ROP.

Commercial Relationships: Zhongjie Fu, None; Chatarina Lofqvist, None; Aimee Juan, None; Zhenghao Cui, None; Dorothy T. Pei, None; Christian G. Hurst, None; Lucy Evans, None; Jing Chen, None; Ann Hellström, Premature AC (B), Premature AC (I); Lois E. Smith, None

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Presentation Time: 10:30 AM - 12:15 PM

Expression of eNOS and VEGF in Normoxia Mediated Vasculopathy in Rat Retinopathy of Prematurity Model

Alireza Hosseini, 1 Frank A. Lattanzio, 2 Nazita Youssefi, 1 Ryan R. Wade, 4 Jorge L. Jacot, 4 1Physiological Sciences, Eastern Virginia Medical School, Norfolk, VA; 2Anatomy and Pathology, Eastern Virginia Medical School, Norfolk, VA; 3CONRAD IPR Lab, Eastern Virginia Medical School, Norfolk, VA; 4Angeiocutics International, Virginia Beach, VA.

Purpose: Retinopathy of prematurity (ROP) causes neonatal vision loss that accounts globally for 50,000 annual cases. The eNOS enzyme plays a prominent role in regulation of the retinal vasculature and in modulating vascular tone in response to changes in oxygen tension. This study aimed to establish a correlation between the extent of retinal vascularity, VEGF and eNOS expression, and post-translationally modified Serine-1177 phosphorylated eNOS (P-eNOS), in an oxygen-induced rat model of ROP.

Methods: Sprague-Dawley pups were placed in an oxygen chamber (cycling every 24 hours at 50% and 10% FiO2) for post-natal (P) days P1-P14. On P15 pups were exposed to normoxia (21% oxygen). Littermate non-oxygen treated naïve pups were used as controls. Rats were euthanized on P15, P18 & P20. One retina of each rat was flat-mounted and ADPase stained for evaluation of the vasculature. Contralateral retinas were homogenized and evaluated using real time RT PCR for VEGF and eNOS mRNA levels or using Western Blots (WB) for eNOS and P-eNOS. A subset of the samples were fixed and cross-sectioned for eNOS or P-eNOS immunohistochemistry.

Results: RT PCR data demonstrates a relative increase of VEGF mRNA at P15, 18 and P20. The eNOS mRNA levels, in conjunction with immunohistochemistry (IHC) for eNOS immunoreactivity in retinal vessels demonstrated an appreciable progressive reduction at P15, 18 and 20 relative to controls. No apparent reduction of P-eNOS was observed. WB evaluations for eNOS and P-eNOS protein expressions are pending.

Conclusions: During the normoxic phase of the ROP model, progressive increases in VEGF mRNA expression are consistent and temporally correlate with the extent of neovascularization. However, despite eNOS maintaining its phosphorylation state both eNOS mRNA and protein expressions (IHC) decline during the normoxia period. This reduction in eNOS expression could lead to exacerbation of tissue hypoxia resulting in an augmentation of the neovascular response in this ROP model.
Commercial Relationships: Aline Hasen, None; Frank A. Lattanzio, None; Nazita Yousefieh, None; Ryan R. Wade, None; Jorge L. Jaoet. None
Support: Commonwealth Health Research Board

Program Number: 617 Poster Board Number: D0139
Presentation Time: 10:30 AM - 12:15 PM

Validation and Characterization of Murine Oxygen-induced Retinopathy of Prematurity Model


Purpose: The mouse oxygen-induced retinopathy model is widely used to investigate the mechanism and treatment of proliferative ocular angiogenesis. The purpose of this study is to characterize the growth of retinal neovascularization (RNV) in response to oxygen treatment, to establish a positive control for the inhibition of RNV for future compound testing and to explore the mechanism of ocular angiogenesis.

Methods: C57Bl/6 mice were exposed to 70% oxygen from postnatal day 7 to 12. Eyes were harvested at fixed at P17. To identify vasculature, retinas were stained with Isocetin B4-594. Fluorescent images of the tissue were captured and RNV areas were quantified with AxioVision software. In addition, eyes were freshly frozen in OCT for IHC.

Fluorescein angiography was performed in P17 pups. Pups were anesthetized, and images were acquired after intraperitoneal (IP) injection of sodium fluorescein with a MicronIII lens and StreamPix5 single Camera Program from Phoenix Research Laboratories, Inc. In the efficacy studies, pups were treated at P12 and P14 via IP injection with an anti-VEGF antibody (12 pups) or negative control (12 pups). Inter-group differences were compared by one-way analysis of variance (ANOVA) with a Neuman-keuls post hoc analysis.

For the characterization study, retinas were collected at P5, P8, P12, P13, P15, P17 and P19. Retinas from each mouse were pooled as one sample and 6 samples per condition were assessed for mRNA expression. At P17, 4 retinas were pooled for VEGF protein analysis using Elisa. The mRNA expression profile was evaluated with microarray analysis and genes with altered expression were confirmed with a TaqMan assay.

Results: Hyperoxia results in retinal vessel loss and subsequent RNV, vessel tortuosity, and leakage. RNV growth was dose dependent inhibited by 44% and 89% with anti-VEGF antibody treatment at 3 mg/kg and 10 mg/kg, respectively. In this model, VEGF protein levels are elevated ~ 4 fold at P17; the expression profiles of many known genes, such as VEGFα, VEGFβ, PDGFB, Ang2 and EPO, as well as genes without annotation were significantly up-regulated.

Conclusions: RNV was induced under hypoxia conditions. Anti-VEGF antibody can inhibit RNV growth in a dose dependent manner and therefore can be used as a positive control in this model. Genes expression profile changes may be used as biomarkers to study the mechanism of retinal angiogenesis.

Commercial Relationships: Yubin Qiu, Novartis (E); Amber Woolfenden, Novartis Institutes for Biomedical Research (E); Wei Zheng, Novartis (E); Karen Anderson, Novartis (E); Melinda Hubbard, Novartis Institutes of Biomedical Research (E); John Demirs, Novartis Institutes for Biomedical Research, Inc. (E); Joseph Loureiro, novartis (E); Joy Ghosh, Novartis (E); Stephen H. Poor, Novartis Institute of Biomedical Research (E); Bruce D. Jaffee, Novartis (E)

Program Number: 618 Poster Board Number: D0140
Presentation Time: 10:30 AM - 12:15 PM

Induction Of The VEGF-related Proteins Prokineticin 1 and 2 In The Ischemic Retina

Frances Fan', Folami Lamoke1,2, Sean Shaw', Babak Baban', Manuela Bartoli1,2, 1Ophthalmology, Georgia Health Sciences Univ, Augusta, GA; 2Department of Pharmacology and Toxicology, Georgia Health Sciences University, Augusta, GA.

Purpose: VEGF-A is a pivotal regulator of retinal neovascularization and a key pharmacological target for its prevention and cure. However, patients resistant to anti-VEGF therapies reveal the potential role of other contributing factors. The purpose of the present study was to determine the expression levels and immunolocalization of two VEGF-related growth factors: Prokatinetic 1 (PKCN1), also known as eg-VEGF, and prokineticin 2 (PKCN2), also known as Bv8, which have been implicated in tumor angiogenesis and in induction of inflammatory processes.

Methods: We assessed PKCN1 and 2 expression and localization in retinas of mice subjected to oxygen-induced retinopathy (OIR). Mice were exposed from postnatal day 7 to 12 (P7 and OIR12 respectively) to 73% oxygen tension. At OIR12 the mice were returned to normoxic conditions and analyzed at postnatal day 14 and 17 (OIR14 and OIR17, respectively). Western blotting, qRT-PCR and immunohistochemistry were employed to assess PKCN1 and 2 production and localization in the ischemic retinas and in age-matched control mice retinas (P12, P14 and P17).

Results: Western blotting and immunochemistry analyses revealed that PKCN1 and 2 were up-regulated in the ischemic retina (OIR14 and OIR17). Both of these factors appeared to be strongly colocalized with retinal and choroidal blood vessels. PKCN1- and 2-specific immunoreactivity was also evidenced in much less extent in the inner retina and around the retinal pigmented epithelium.

Conclusions: Our data demonstrates the presence of PKCN1 and 2 in the developing retina and shows an induction in the expression of these VEGF-related proteins in the ischemic retina. The results of the present study, thus, suggest a potential role for these growth factors in the pathological processes associated with the induction and progression of ischemic retinopathy and retinal neovascularization.

Commercial Relationships: Frances Fan, None; Folami Lamoke, None; Sean Shaw, None; Babak Baban, None; Manuela Bartoli, None

Program Number: 619 Poster Board Number: D0141
Presentation Time: 10:30 AM - 12:15 PM

Foveal Fine Structure in Retinopathy of Prematurity (ROP) Subjects: an Adaptive Optics Spectral Domain Optical Coherence Tomographic Study

Emily A. Swanson1, James D. Akula1,2, Tara L. Favazzo1, Daniel X. Hammer2, R. D. Ferguson2, Anne Moskovitz1,2, Ronald M. Hansen1

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Evaluation of a portable, non-contact digital fundus camera (Pictor) in premature infants

Sasapin G. Prakalapakorn, David Wallace, Sharon F. Freedman.
Duke Eye Center, Durham, NC.

Purpose: To evaluate the feasibility of using a new portable, non-contact digital fundus camera, Pictor (Volk Optical Inc., Mentor, OH), to obtain high-quality images of the retina of premature infants.

Methods: We retrospectively reviewed digital Pictor images taken of infants during routine examinations for Retinopathy of Prematurity (ROP) in the Duke Hospital Intensive Care Nursery over a 6-month period. Infants were included if they had at least one color and one red-free photograph taken of each eye that included an image of the optic nerve. The color and red-free images were obtained simultaneously. Up to 3 images were included for each eye. For each eye, the image with the greatest field of view was quantified in disc diameters (DD), using the average DD measured from the same image. Two ROP experts reviewed the color and red-free images independently and evaluated them for (1) quality (good, fair or poor) based on the ability to determine the dilation and/or tortuosity of the vessels in the image and (2) number of gradable quadrants (0 to 4), based on the adequate visibility of ≥1 DD length of a major vessel in a given quadrant.

Results: There were 96 eyes of 48 infants [mean gestational age 27 weeks (range 23–34), birth weight 872 grams (420–1480), post-menstrual age at examination 38 weeks (31–47)]. The mean field of view for all eyes was 5.0 DD x 6.1 DD. Grader 1 and Grader 2 found image quality to be good or fair in 96% and 97% of images, respectively. Grader 1 and Grader 2 judged images as having at least 3gradable quadrants in 80% and 86% of images, respectively.

Conclusions: The Pictor camera is able to capture digital retinal images of premature infants that are of good quality and that usually have at least 3 gradable quadrants. The Pictor camera may be a valuable tool for ROP screening. Future studies will evaluate the accuracy of grading pre-plus and plus disease using Pictor fundus images.
Knockdown of Mueller cell specific VEGF reduces retinal neovascularization in a rat model of retinopathy of prematurity (ROP)

Manabu McCloskey1, Yanchao Jiang1, Haibo Wang1, zhihong yang1, Jeremy Strange1, Tal Kafri2, John G. Flannery1, M Elizabeth Hartnett1. 1University of Utah, Salt Lake City, UT; 2University of North Carolina, Chapel Hill, UT; 3University of California, Berkeley, Berkeley, CA.

Purpose: Increased VEGF causes intravitreal neovascularization (IVNV) in a rat ROP model, but inhibition of VEGF may have adverse effects on the developing retina in preterm infants. We hypothesized that inhibition of cell-specific expression of VEGF may be a safe way to inhibit IVNV.

Methods: Newborn rat pups were exposed to repeated fluctuations in oxygen between 50% and 10% inspired oxygen in a controlled environment (Oxyoyclic, Biospherix) every 24 hours for 14 days (rat OIR model). Short hairpin RNAs to VEGF or control luciferase fashioned as microRNAs with green fluorescent protein tags were cloned into a lentiviral transfer vector with a CD44 promoter to specifically target Mueller cells. At postnatal day (p) 8, the pups received subretinal injections of 1ul of shRNA-VEGF or shRNA-luc. At p18, pups were weighed and eyes were processed for analysis of in situ hybridization for mRNA localization, protein for ELISA, percent avascular area (AVA) and intravitreal neovascularization (IVNV) of total retinal areas from lecint stained flat mounts, and sections for immunohistochemistry.

Results: At p14, VEGF localized to retinal layers corresponding to retinaldehyde-binding protein-stained Mueller cells. Increased VEGF protein was detected in pups from the rat OIR model compared to room air raised pups (p < 0.001). IVNV was reduced 75% by VEGFA-shRNA (p < 0.001) compared to Lucif-sh. AVA and body weights were unaffected compared to control. Retinal VEGF protein was reduced in shRNA-VEGF (p <0.05) compared to Lucif-sh (p < 0.01), and shRNA-VEGF reduced VEGF level to room air.

Conclusions: In the rat model of ROP, knockdown of Mueller cell-derived VEGF significantly reduced IVNV compared to Luci-sh control and PBS injected. shRNA-VEGF was able to reduce retinal VEGF protein level to that of p18 room air raised pups. Mueller cell derived VEGF is a significant factor leading to IVNV in the rat model of ROP. Further study into cell and molecular mechanisms driving pathological IVNV and AVA is warranted.

Commercial Relationships: Manabu McCloskey, None; Yanchao Jiang, None; Haibo Wang, None; zhihong yang, None; Jeremy Strange, None; Tal Kafri, None; John G. Flannery, None; M Elizabeth Hartnett, National Eye Institute (F), Genentech (C), Akxin Pharmaceuticals (R)

Support: NIH Grant R01EY015130 Research to Prevent Blindness

Program Number: 623 Poster Board Number: D0145

Antagonizing IL-1β effectively prevents inner and outer retinal degenerative changes associated with retinopathy of prematurity

Thanev (Ellen) Zhou1, 2, Jose Carlos Rivera2, Isabelle Laharie2, Zhou Shao1, 2, Anna Polosa1, Allison L. Dorfman1, Pierre Lachapelle1, Sylvain Chemtob1, 2, 3, 4. 1Pharmacology and Therapeutics, McGill University, Montreal, QC, Canada; 2Ophthalmology, Université de Montréal, Montréal, QC, Canada; 3Neurosciences, Ophthalmology, McGill University, Montreal Children's Hospital, Montréal, QC, Canada.

Purpose: Retinopathy of prematurity (ROP) is a serious complication in premature infants. Besides inner retina damages reported in ROP subjects, photoreceptor malfunction is also observed and appears to result from a sustained inflammation of the choroid - the exclusive energy source to the photoreceptors. However, mechanisms for this choroidal inflammation remain unexplained. Since oxidant stress associated with the pathogenesis of ROP is intertwined with inflammation, we explored the role of major pro-inflammatory cytokine, notably IL-1β, in rats subjected to Oxygen-induced retinopathy (model for ROP).

Methods: Oxygen-induced retinopathy (OIR) model was induced by exposing rat pups for the first 2 weeks of life to cycled O2 levels. Retinal and choroidal histology was performed to study thickness and integrity of microvasculature. Expression of factors of interest was studied by immunohistology, PCR, and Western blots. Finally, electroretinogram (ERG) was performed to evaluate retinal functions.

Results: OIR caused retinal vasculature damage, inner nuclear layer gestation) who arrived to the Retina department of our hospital with clinical diagnosis of ROP. SD-OCT scan, Fluorescein angiography with RetCam imaging was performed at patient arrival and post-administration of a single dose of Bevacizumab (Avastin, 0.625 mg).

Program Number: 623 Poster Board Number: D0145

Presentation Time: 10:30 AM - 12:15 PM

Knockdown of Mueller cell specific VEGF reduces retinal neovascularization in a rat model of retinopathy of prematurity (ROP)

Manabu McCloskey, Yanchao Jiang, Haibo Wang, zhihong yang, Jeremy Strange, Tal Kafri, John G. Flannery, M Elizabeth Hartnett. 1University of Utah, Salt Lake City, UT; 2University of North Carolina, Chapel Hill, UT; 3University of California, Berkeley, Berkeley, CA.

Purpose: Increased VEGF causes intravitreal neovascularization (IVNV) in a rat ROP model, but inhibition of VEGF may have adverse effects on the developing retina in preterm infants. We hypothesized that inhibition of cell-specific expression of VEGF may be a safe way to inhibit IVNV.

Methods: Newborn rat pups were exposed to repeated fluctuations in oxygen between 50% and 10% inspired oxygen in a controlled environment (Oxyoyclic, Biospherix) every 24 hours for 14 days (rat OIR model). Short hairpin RNAs to VEGF or control luciferase fashioned as microRNAs with green fluorescent protein tags were cloned into a lentiviral transfer vector with a CD44 promoter to specifically target Mueller cells. At postnatal day (p) 8, the pups received subretinal injections of 1ul of shRNA-VEGF or shRNA-luc. At p18, pups were weighed and eyes were processed for analysis of in situ hybridization for mRNA localization, protein for ELISA, percent avascular area (AVA) and intravitreal neovascularization (IVNV) of total retinal areas from lecint stained flat mounts, and sections for immunohistochemistry.

Results: At p14, VEGF localized to retinal layers corresponding to retinaldehyde-binding protein-stained Mueller cells. Increased VEGF protein was detected in pups from the rat OIR model compared to room air raised pups (p < 0.001). IVNV was reduced 75% by VEGFA-shRNA (p < 0.001) compared to Lucif-sh. AVA and body weights were unaffected compared to control. Retinal VEGF protein was reduced in shRNA-VEGF (p <0.05) compared to Lucif-sh (p < 0.01), and shRNA-VEGF reduced VEGF level to room air.

Conclusions: In the rat model of ROP, knockdown of Mueller cell-derived VEGF significantly reduced IVNV compared to Luci-sh control and PBS injected. shRNA-VEGF was able to reduce retinal VEGF protein level to that of p18 room air raised pups. Mueller cell derived VEGF is a significant factor leading to IVNV in the rat model of ROP. Further study into cell and molecular mechanisms driving pathological IVNV and AVA is warranted.

Commercial Relationships: Manabu McCloskey, None; Yanchao Jiang, None; Haibo Wang, None; zhihong yang, None; Jeremy Strange, None; Tal Kafri, None; John G. Flannery, None; M Elizabeth Hartnett, National Eye Institute (F), Genentech (C), Akxin Pharmaceuticals (R)

Support: NIH Grant R01EY015130 Research to Prevent Blindness

Program Number: 623 Poster Board Number: D0145

Presentation Time: 10:30 AM - 12:15 PM

Macular Morphology Before and After Intravitreal Bevacizumab in Patients with Retinopathy of Prematurity: A Spectral Domain Ocular Coherence Tomography Comparative Case Series

Martin Guzman-Sanchez, Veronica E. Giordano, Samantha Salinas Longoria, Rafael Romero Vera, Guillermo Salcedo-Villanueva, Virgilio Morales-Cantón, Hugo Quiroz-Mercado, Maria A. Martinez-Castellanos. Asociacion para evitar la ceguera en Mexico "Hospital Luis Sanchez Bulnes", Coyoacan, Mexico.

Purpose: The purpose of this study is to describe macular changes with spectral domain ocular coherence tomography (SD-OCT) in preterm patients with retinopathy of prematurity before and after administration of intravitreal Bevacizumab (Avastin).

Methods: We evaluated 6 preterm infants (mean 28 weeks of gestation) who arrived to the Retina department of our hospital with clinical diagnosis of ROP. SD-OCT scan, Fluorescein angiography with RetCam imaging was performed at patient arrival and post-administration of a single dose of Bevacizumab (Avastin, 0.625 mg). In each eye, we studied by SD-OCT sc

Commercial Relationships: Martin Guzman-Sanchez, None; Veronica E. Giordano, None; Samantha Salinas Longoria, None; Rafael Romero Vera, None; Guillermo Salcedo-Villanueva, None; Virgilio Morales-Cantón, None; Hugo Quiroz-Mercado, None; Maria A. Martinez-Castellanos, None

Program Number: 623 Poster Board Number: D0145

Presentation Time: 10:30 AM - 12:15 PM

Antagonizing IL-1β effectively prevents inner and outer retinal degenerative changes associated with retinopathy of prematurity

Thanev (Ellen) Zhou1, 2, Jose Carlos Rivera2, Isabelle Laharie2, Zhou Shao1, 2, Anna Polosa1, Allison L. Dorfman1, Pierre Lachapelle1, Sylvain Chemtob1, 2, 3, 4. 1Pharmacology and Therapeutics, McGill University, Montreal, QC, Canada; 2Ophthalmology, Université de Montréal, Montréal, QC, Canada; 3Neurosciences, Ophthalmology, McGill University, Montreal Children's Hospital, Montréal, QC, Canada.

Purpose: Retinopathy of prematurity (ROP) is a serious complication in premature infants. Besides inner retina damages reported in ROP subjects, photoreceptor malfunction is also observed and appears to result from a sustained inflammation of the choroid - the exclusive energy source to the photoreceptors. However, mechanisms for this choroidal inflammation remain unexplained. Since oxidant stress associated with the pathogenesis of ROP is intertwined with inflammation, we explored the role of major pro-inflammatory cytokine, notably IL-1β, in rats subjected to Oxygen-induced retinopathy (model for ROP).

Methods: Oxygen-induced retinopathy (OIR) model was induced by exposing rat pups for the first 2 weeks of life to cycled O2 levels. Retinal and choroidal histology was performed to study thickness and integrity of microvasculature. Expression of factors of interest was studied by immunohistology, PCR, and Western blots. Finally, electroretinogram (ERG) was performed to evaluate retinal functions.

Results: OIR caused retinal vasculature damage, inner nuclear layer...
(INL) degeneration, and choroidal atrophy. These changes were associated with a marked increase in pro-inflammatory IL-1β, and drastic reductions in ERG responses. Early neonatal treatment with IL-1 receptor antagonist (IL-1ra [Kineret]) significantly decreased IL-1β levels attenuated INL degeneration, retinal vasooobliteration and choroidal involution. IL-1ra also curtailed expression of the anti-angiogenic factor Sema3F while promoting the expression of pro-angiogenic factor PDGF and photoreceptor protective factor PEDF. The protective effects of IL-1ra on retinal and choroidal integrity were associated with improved retinal function measured by ERG. To confirm a role for IL-1β in retinal injury associated with OIR/ROP, we injected healthy rat pups with IL-1β intravitreally; the latter reproduced salient features of OIR/ROP, including retinal vascular abnormality, INL degeneration and choroidal involution, all of which were prevented by co-administration with IL-1ra.

Conclusions: Our observations reveal a dominant role for IL-1β in inner and outer retinal damage associated with the ROP model of OIR. The findings set forth new concepts and mechanistic notions for ROP and outcome; IL-1 receptor blockers may protect the retina and sub-retina and possibly limit a progressive retinopathy that ensues from ROP.

Commercial Relationships: Tianwei (Ellen) Zhou, None; Jose Carlos Rivera, None; Isabelle Lahaie, None; Zhuo Shao, None; Anna Polosa, None; Allison L. Dorfman, None; Pierre Lachapelle, None; Sylvain Chemtob, None

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Program Number: 624 Poster Board Number: D0146
Presentation Time: 10:30 AM - 12:15 PM
Handheld Spectral Domain Optical Coherence Tomography as a Tool to Assess Retinopathy of Prematurity Zone and Stage in Premature Infants
Ronald W. Milam, Jan N. Ulrich, Michelle T. Cabrera. Department of Ophthalmology, University of North Carolina School of Medicine, Chapel Hill, NC.

Purpose: This study used the wide angle Envisu R2300-II (Bioptigen, Inc, Morrisville, NC) handheld spectral domain optical coherence tomography (SDOCT) to diagnose ROP zone and stage.

Methods: Nine premature infants receiving routine ROP screening in the North Carolina Children’s Hospital Neonatal Critical Care Center underwent imaging with the Envisu R2300-II. Attempts were made to image the ROP ridge and the border between zones 1 and 2. Images were analyzed using the InViviVue 2.0 (Bioptigen, Inc, Morrisville, NC) software, using calipers to identify the zone 1-2 border (twice the distance from the optic nerve to the foveal depression). SDOCT results were compared to the clinical ROP examination and RetCam (Clarity Medical Systems, Inc, Pleasanton, CA) images when available.

Results: Nine premature infants (median gestational age 27 weeks, range 23-30 weeks; median birth weight 760g, range 615-1196g; median postmenstrual age at imaging 37 weeks, range 32-52 weeks) were imaged with handheld SDOCT. Of the 13 imaging sessions, 4 sessions (3 infants, 3 eyes) captured the zone 1-2 border and 3 sessions (1 infant, 1 eye) captured the ROP ridge, confirmed with RetCam. The ROP ridge consisted of preretinal hyperreflective structures located in zone 1 and measured 0.19x0.30mm and 0.21x0.60mm at the time of the zone 2 stage 3 clinical diagnosis. The infant then received bilateral intravitreal bevacizumab injections. At 1 week post-treatment these structures measured 0.14x0.15mm and 0.16x0.33mm, respectively. At 2 weeks post-treatment, they measured 0.11x0.10mm and 0.11x0.25mm, respectively.

Conclusions: The Envisu R2300-II identified ROP zone and stage in some infants, in one case contradicting the clinical zone diagnosis. Images also demonstrated progressively decreasing size of the ridge’s neovascular structures following bevacizumab. The Envisu R2300-II could potentially enhance objectivity in assessing zone and stage of ROP, to help determine need for treatment as well as treatment response. Larger studies are necessary to fully evaluate the ability of handheld SDOCT to accurately diagnose zone and stage of ROP.

Handheld SDOCT B-scan revealing hyperreflective preretinal structures (asterisks) consistent with the neovascular ridge.

Volume intensity projection displaying the zone 1-2 border. Asterisks indicate the corresponding location of the preretinal structures.

Commercial Relationships: Ronald W. Milam, None; Jan N. Ulrich, None; Michelle T. Cabrera, None
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Program Number: 625 Poster Board Number: D0147
Presentation Time: 10:30 AM - 12:15 PM
Correlation of clinically undetected macular features by spectral domain OCT and angiography in early stages of retinopathy of prematurity
Cynthia Villalobos-Ojeda1, Veronica E. Giordano1, Samantha Salinas Longoria1, Rafael Romero Vera1, Guillermo Salcedo-Villanueva1, Gerardo Garcia-Aguirre1, Virgilio Morales-Cantón1, Hugo Quiroz-Mercado2, Maria A. Martinez-Castellanos2.
1Asociacion para evitar la ceguera, Mexico, Mexico; 2Denver health medical center, denver, CO.

Purpose: To describe and correlate the fluorescein angiography (FA) and hand held spectral domain optical coherence tomography (HH-SD OCT) macular findings in eyes with stage 1 and 2 ROP with a clinically normal appearing macula.

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Methods: Observational, retrospective case series of infants who underwent routine screening with indirect ophthalmoscopy and imaging under topical anesthesia. Imaging included retinal FA using the Retcam II (Clarity Medical Systems, Pleasanton, CA) and hand held spectral domain OCT imaging with iVue (Optovue, Inc, Freemont, CA).

Results: We included 12 eyes of 7 infants that were diagnosed with ROP stage 1 or 2 in zones II and III with clinically normal macula, but by angiography presented an abnormal diffuse capillary leakage pattern in the parfoveal area. Mean gestational age at birth was 29.5 weeks (range 26-33 weeks). Mean postmenstrual age (PMA) was 39.8 weeks (range 34-44 weeks). Retinal FA of the 12 eyes (100%) showed an angiographic diffuse capillary leakage pattern. OCT studies of 3 eyes (25%) showed no macular abnormalities. 9 eyes (75%) presented intraretinal cystoid spaces with preservation of the foveal depression. This findings regressed once the retinal vasculature reached the ora serrata. 3 eyes (25%) presented a probable epiretinal membrane formation.

Conclusions: Macular abnormalities of premature infant eyes with ROP seen on angiographic or tomographic evaluation might reflect variability in remodeling of foveal architecture during development either neural, vascular or both. The vascular changes could be explained due to parietal leakage because of vascular immaturity, related to the formation and the maturation of the mural cells (pericytes). The abnormalities seen by OCT may explain the deficits in acuity, color and visual sensitivity in adulthood. This pilot study provides valuable information of macular findings of patients with mild ROP. A larger series with longer follow up is needed, in order to know if these subtle changes can influence the final macular morphology and visual acuity in adulthood.

Commercial Relationships: Cynthia Villalobos-Ojeda, None; Veronica E. Giordano, None; Samantha Salinas Longoria, None; Rafael Romero Vera, None; Guillermo Salcedo-Villanueva, None; Gerardo Garcia-Aguirre, None; Virgilio Morales-Canton, Clearside Biomedical (F); Hugo Quiroz-Mercado, Allegro Pharmaceutical (C); Maria A. Martinez-Castellanos, None

Program Number: 626 Poster Board Number: D0148
Presentation Time: 10:30 AM - 12:15 PM

McCready findings in preterm Non-Retinopathy Of Prematurity infants using Spectral Domain Optical Coherence Tomography Samantha Salinas Longoria1, Veronica E. Giordano1, Rafael Romero Vera1, Gerardo Garcia-Aguirre1, Guillermo Salcedo-Villanueva1, Virgilio Morales-Canton1, Hugo Quiroz-Mercado3, Maria A. Martinez-Castellanos2. 1 Asociacion para Evitar la Ceguera en Mexico I.A.P., Mexico, Mexico; 2 Retina, Denver Health Medical Center, Denver, CO.

Purpose: To evaluate macular thickness in eight eyes of six preterm infants without history of retinopathy of prematurity (ROP) using SD-OCT and describe morphological findings and parameters in this population.

Methods: A total of six preterm infants, eight eyes, without retinopathy of prematurity confirmed by previous funduscopic examination by a retina specialist were enrolled. Four female infants (66.67%) and two male infants (33.33%), between 34 weeks and 11 months of postmenstrual age (PMA) were evaluated using iVue Spectral-Domain OCT (Optovue, Incorporated). The SD-OCT images were obtained under pupil dilation with phenylephrine and tropicamide. The Central foveal thickness (CFT) and parafoveal thickness were analyzed and interpretation of each OCT was performed.

Results: Of the eight eyes, four presented hyporeflective areas in internal retinal layers (between ganglion cell layer and nuclear internal layer) that could correspond to “B” pattern of retinoschisis. One eye showed probable lack of differentiation of external retinal layers. In three eyes a highly reflective internal layer was appreciated, observation that could correspond to an epiretinal membrane or a high reflective never fiber layer. Three eyes had normal architecture, with no abnormalities in internal and external retinal layers. The central foveal thickness was measured adequately in two of the patients reporting 177 microns and 199 microns.

Conclusions: Optical coherence tomography has become an invaluable tool in the evaluation of macular architecture. With the advent of new devices, we can expand our field of research and make new discoveries in poorly understood diseases. Although SD-OCT can achieve high quality images, in preterm patients without sedation is of great difficulty leaving a lot of questions in diagnosis. Continuous practice is needed to achieve best results.

Commercial Relationships: Samantha Salinas Longoria, None; Veronica E. Giordano, None; Rafael Romero Vera, None; Gerardo Garcia-Aguirre, None; Virgilio Morales-Canton, Clearside Biomedical (F); Hugo Quiroz-Mercado, Allegro Pharmaceutical (C); Maria A. Martinez-Castellanos, None

Program Number: 627 Poster Board Number: D0149
Presentation Time: 10:30 AM - 12:15 PM

Net Weight Gain from Birth to Time of First Retinopathy of Prematurity (ROP) Examination as Sole Inclusion Criteria for Screening Examinations for ROP Jennifer L. Hsu, Christopher Shelvock, Stefan Sillau, Robert Enzenauer, Rebecca S. Braverman. Department of Ophthalmology, University of Colorado, Denver, CO.

Purpose: Poor postnatal weight gain in premature infants has previously been associated with increased incidence of complications associated with prematurity and ROP. The purpose of this study was to determine the utility of net weight gain (NWG) between birth and time of first ROP screening examination as a predictor for developing ROP.

Methods: An Institutional Review Board (IRB) approved retrospective chart review was performed on all premature infants who underwent ROP screening examinations between June 2008 and December 2011 at a tertiary referral system’s neonatal intensive care units. Infants who did not complete the entirety of their ROP examinations within our healthcare system were excluded. Birthweight, weight at date of first ROP screening examination, and findings at each ROP examination until retinal maturation were recorded.

Results: 428 infants met the inclusion criteria. 29 infants developed Type 1 ROP, and 100 infants developed Type 2 ROP. Excluding any infants with greater than 700g NWG at first ROP examination did not result in any missed cases of Type 1 ROP (Sensitivity = 1.0, 99% CI 0.84-1.0). 1 infant with Type 2 ROP was missed. There was no statistical difference in the sensitivity in detecting Type 2 ROP between standard criteria (1.0, 99% CI 0.95-1.0) and the 700g NWG criteria (0.99, 99% CI 0.96-1.00) while improving the relative specificity (0.15, 99% CI 0.10-0.21) of ROP examination compared to standard criteria (0.0, 99% CI 0.0-0.018).

Conclusions: Our findings suggest that it may be feasible to use 700g NWG as a sole criteria for identifying premature infants for ROP screening examinations. Using the 700g NWG criteria at our institution would have eliminated 11% of normal exams without missing any cases of Type 1 ROP. By extrapolating the proportional reduction in examinations using the 700g NWG criteria to national estimates on the number of infants examined for ROP and estimating the cost equivalent using the 2012 Colorado Medicaid fee schedule,
this would incur a cost savings of approximately $6 million dollars annually in the United States.

Distribution of infants by highest grade of ROP on any screening examination by gestational age (GA) and net weight gain at the time of first ROP Exam. No infants with type 1 ROP were missed using 700g NWG or less as screening criteria. A) Type 1 ROP. B) Type 2 ROP. C) No ROP.

Commercial Relationships: Jennifer L. Hsu, None; Christopher Shelvock, None; Stefan Sillau, None; Robert Enzenauer, None; Rebecca S. Braverman, None

Program Number: 629 Poster Board Number: D0151
Presentation Time: 10:30 AM - 12:15 PM
Variations in Retinal Nuclear Areas in a Neonatal Mouse Model of Retinopathy of Prematurity by Histopathology
Olachi J. Mezu-Ndubuisi1, Norman P. Blair2, Amy Lin1, Justin Wanek2, Narsa M. Reddy3, Usha Raj1, Sekhar P. Reddy3, Mahnaz Shahidi2. Pediatrics, University of Illinois at Chicago, Chicago, IL; 2Ophthalmology and Visual Sciences, University of Illinois, Chicago, IL; 3Pathology, University of Illinois, Chicago, IL.

Purpose: Premature infants requiring supplemental oxygen are at risk of developing retinopathy of prematurity (ROP) and retinal structural and vascular abnormalities. The purpose of the current study is to investigate changes in retinal cell density in an oxygen-induced retinopathy (OIR) mouse model of ROP by quantitative analysis of ex-vivo histological slides.

Methods: Histological slides of the retina were obtained from enucleated eyes of OIR C57BL/6j mice (N = 6 eyes) and control mice (N = 6). OIR mice were exposed to 75% oxygen from post-natal day 7 (P7) to P12 before returning to room air, while control mice were exposed to room air continuously. Mice were sacrificed at P17-P19, the eyes enucleated, and histological slides stained with hematoxylin and eosin. The areas of the cell nuclei in the retinal inner nuclear and ganglion cell layers (inner retinal area) and in the retinal outer nuclear (outer retinal area) were quantified using a semi-automated morphometric image analysis software (Motic). These areas were divided by the total area of a selected region of the retina.

Results: The relative inner retinal area in OIR mice (14 ± 1%) and control mice (15 ± 1%) were similar (p = 0.2). Likewise, there was not a statistically significant difference in the outer retinal area in OIR mice (26 ± 2%) and control mice (23 ± 4%) (p = 0.2). In both control and OIR mice, the outer retinal area was significantly greater than the inner retinal area (p < 0.001). The sum of the inner and outer retinal areas in OIR mice (40 ± 2%) and control mice (38 ± 5%) was similar (p = 0.4). The ratio of the outer to inner retinal areas was significantly higher in OIR mice (1.9 ± 0.1) than control mice (1.6 ± 0.3) (p = 0.04).

Conclusions: In OIR mice, there was an increased proportion of outer to inner retinal nuclei, as compared to control mice. This may reflect variations in vascular supply and metabolic needs. Study of retinal structural changes may aid the understanding of ROP pathogenesis.

Commercial Relationships: Olachi J. Mezu-Ndubuisi, None; Norman P. Blair, None; Amy Lin, None; Justin Wanek, None; Narsa M. Reddy, None; Usha Raj, None; Sekhar P. Reddy, None; Mahnaz Shahidi, Patent (P)
Support: R01 EY17918, R01 HL66109, and Research to Prevent Blindness

Program Number: 630 Poster Board Number: D0152
Presentation Time: 10:30 AM - 12:15 PM
Influence of the difference of Breastfeeding volume on a Rat Model of Oxygen-induced Retinopathy
Michiko Matsubara1, Yuta Saito1, Takako Nakaniishi-Ueda2, Toshihiko Ueda1, Tadashi Hisamitsu1, Haruo Takahashi1, 1Ophthalmology, Showa University, Tokyo, Japan; 2Physiology, Showa University, Tokyo, Japan.

Purpose: To investigate the effects of abundant breast milk nutrition on body weight gains, retinopathy, concentration of vascular endothelial growth factor (VEGF) in retina and insulin-like growth factor-1 (IGF-1) in serum and retina in oxygen-induced retinopathy (OIR) rat model.

Methods: Neonatal Sprague-Dawley rats were divided into seven rat
pups (7-rats group) or fourteen rat pups (14-rats group) after birth. Each group was put in cage with a dam. Some group were exposed to 80% oxygen (20.5 h) from postnatal day 0 (P0) to P12, and then placed in ambient air until P18. The groups in room air (RA) were used as a control. Body weight was measured every day. At P8, 13 or 18, rat pups were sacrificed and blood samples were collected. Retinas in left eyes were collected for ELISA, and retinas in right eyes were fixed, flatmounted and stained with adenosine diphosphatase. Retinal neovascularization in flatmounted retinas was scored (NV score), and total retinal areas (TRA) and avascular areas (AVA) were measured. From them a percent of avascular areas (%AVA) were calculated. Concentrations of VEGF and IGF-1 were measured with ELISA. Statistical analyses were performed with Mann-Whitney’s U test. P value <0.05 was considered significantly.

Results: Body weight gains in 7-rats group were significantly greater than in 14-rats group from P3 through P18. Retinal VEGF levels in OIR were significantly lower at P8 and higher at P13 than in RA. In OIR, NV score and %AVA of smaller litters was higher than that of 7-rats group at P18. TRA of 7-rats group was significantly bigger than that of 14-rats group at P18 in both OIR and RA. In addition, TRA in OIR groups tended to be larger than in RA groups. IGF-1 levels in serum of 14-rats group were significantly higher than that of 7-rats group at P13 and 18 in both OIR and RA, however, retinal IGF-1 levels had no significant difference between 7-rats group and 14-rats group at any time points in neither OIR nor RA.

Conclusions: In OIR model, the eye ball development appeared to be promoted by serum IGF-1 and oxygen exposure, whereas normal retinal vascular development was delayed by oxygen exposure. Consequently, AVA was relatively increased in 7-rats group OIR, more than in 14-rats group. These results suggest that overnutrition intake may worsen the severity of OIR.

Commercial Relationships: Michiko Matsubara, None; Yuta Saito, None; Takako Nakanishi-Ueda, None; Toshihiko Ueda, None; Tadashi Hisamitsu, None; Haruo Takahashi, None

Program Number: 631 Poster Board Number: D0153
Presentation Time: 10:30 AM - 12:15 PM

Anterior Chamber Angle Evaluation with Spectral-Domain Optical Coherence Tomography in preterm patients with and without retinopathy of prematurity

Purpose: To describe optical coherence tomography (OCT) findings of the anterior chamber angle in preterm infants with less than 37 weeks gestational age.

Methods: Retrospective case series of premature infants who underwent imaging of the anterior chamber angle under topical anesthesia with Handheld ivVue OCT device (OptoVue, Fremont, CA).

Results: We included 37 eyes of 21 premature infants with mean gestational age 30.41 ± 2.42 weeks (27-33) with mean birthweight 1339 ± 365.26 gr (898-2500). By the time of examination mean age was 14.09 ± 13.85 (1-35) weeks corrected gestational age, average oxygen therapy was 34.55 ± 20.67 days (10-60). Amongst our sample, there were 8 patients with retinopathy of prematurity (ROP) stage 1 zone II (1 patient), stage 1 zone II (2 patients), stage 1 zone 1 with plus disease (1 patient), stage 2 zone II (2 patients), stage 3 zone II (1 patient), stage 5 (1 patient).

We measured the anterior chamber angle in 11 eyes with a mean opening of 28.54 degrees ± 10.97 (15.29-44.16). Trabecular-iris space area distances at 500μ from scleral spur (TISAS500) were measured in 13 eyes with a mean of 0.179 mm2 ± 0.077 (0.093-0.327).

Twenty six eyes were not analyzed due to inability to identify the scleral spur (15 eyes) angle vertex (2 eyes) and/or an oblique measurement in relation to the limbus (14).

Conclusions: Using OCT we were able to measure the anterior chamber angle and TISAS500 of premature infants. We found that the visualization of the scleral spur was challenging with this method. Despite the difficulty in the obtention of high-quality images, OCT is a useful tool for evaluation and measurements of some the anterior chamber angle structures. Obtaining these images helps our understanding of the mechanisms of development of ocular structures in vivo and may be used in the future for additional evaluation in paediatric population.

Commercial Relationships: Andrea Portilla Demichelis, None; Magdalena García-Huerta, None; Veronica E. Giordano, None; Samantha Salinas Longoria, None; Rafael Romero Vera, None; Armando Castillo-Josè-Chevez, None; Guillermo Salcedo-Villanueva, None; Virgilio Morales-Cantón, Clearside Biomedical (F); Hugo Quiroz-Mercado, Allegro Pharmaceutical (C); Maria A. Martinez-Castellanos, None

Program Number: 632 Poster Board Number: D0154
Presentation Time: 10:30 AM - 12:15 PM
Review of retinopathy of prematurity in Asahikawa Medical University Hospital, Japan
Ichiro Tanano, Eiichi Sato, Hiroyuki Hirokawa, Akitoshi Yoshida, Ophthalmology, Asahikawa Medical University, Asahikawa, Japan.

Purpose: To report the current status about the incidence and treatment rate of retinopathy of prematurity (ROP) in Asahikawa medical university.

Methods: This retrospective study was made on 130 newborn infants with birth weights below 2500 g from 2005 to 2011. The series comprised 63 male and 67 female babies. They were born as single birth in 99 cases, as twins in 14 cases, and as triplets in 1.

Results: The mean birth weight was 1400±453 g, and the mean gestational age was 30.1±2.9 weeks. ROP was present in 34.6% in whole series. Treatment was performed on 13.8% of cases. In 31 babies with birth weights of 1000 g or less, ROP was present in 80.6% and treatment was performed on 35.5%. There were significant differences in birth weight and gestational age between cases with and without ROP. There were no significant differences in the incidence and treatment rate of ROP between years.

Conclusions: Incidence and severity of ROP in our hospital were about the same as those reported from other institutions in Japan.

Commercial Relationships: Ichiro Tanano, None; Eiichi Sato, None; Hiroyuki Hirokawa, None; Akitoshi Yoshida, None

Program Number: 633 Poster Board Number: D0155
Presentation Time: 10:30 AM - 12:15 PM
Choroidal Thickness in Patients with a History of Retinopathy of Prematurity
Wei-Chi Wu, Chia-Pang Shih, Nan-Kai Wang, Rey-In Lin, Yen-Po Chen, An-Ning Chao, Kuan-Jen Chen, Yih-Shiou Hwang, Chi-Chun Lai, Shawn Tsai. Ophthalmology, Chang Gung Memorial Hosp, Taoyuan, Taiwan; Health Care Management, Chang Gung University, Taoyuan, Taiwan; Department of Pediatrics, Chang Gung Memorial Hospital, Taoyuan, Taiwan; Ophthalmology, Mackay Memorial Hospital, Taipei, Taiwan.

Purpose: To examine choroidal thickness by spectral-domain optical coherence tomography (SD-OCT) in children with a history of

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retinopathy of prematurity (ROP) and to access the impact of choroidal thickness on patients’ visual acuity.

Methods: This was designed as a prospective case-controlled study. Children aged 6 to 14 years were classified into the following 4 groups: patients with a history of threshold ROP and the treatment of laser or cryo-therapy (group 1); those with regressed ROP who had not received any treatment (group 2); those born prematurely but without ROP (group 3); and normal full-term children (group 4). All of the patients had normal-appearing posterior pole. Main outcome measures included best-corrected visual acuity (BCVA), optical components, and OCT findings.

Results: In total, 138 patients were enrolled in the study. Patients in group 1 had a significantly thinner choroidal thickness than the patients in group 2. Choroidal thickness was found to be positively associated with spherical power and spherical equivalent and negatively associated with foveal thickness, axial length, and vitreous depth. When only patients with choroidal thickness less than 237.4 \( \mu \text{m} \) were analyzed, macular choroidal thickness was negatively associated with BCVA of the patients. Choroidal thickness had less predictive power on patients’ vision than gestation age and birth weight.

Conclusions: Choroidal thickness is thinner in patients with threshold ROP. Only when choroidal thickness is less than a certain level, 237.4 \( \mu \text{m} \) in the current study, that it is significantly associated with worse vision of the patients. Above this level, there is no significant impact on the patient’s vision.

Commercial Relationships: Wei-Chi Wu, None; Chia-Pang Shih, None; Nan-Kai Wang, None; Rey-In Lin, None; Yen-Po Chen, None; An-Ning Chao, None; Kuan-Jen Chen, None; Yih-Shiou Hwang, None; Chi-Chun Lai, None; Shawn Tsai, None
Support: This study was partially supported by a Chang Gung Memorial Hospital Research Grant (CMRPG3A0391) and a National Science Council Research Grant (NSC98-231-B-182A-001-MY2).

Program Number: 634 Poster Board Number: D0156
Presentation Time: 10:30 AM - 12:15 PM
FA findings in regressed mild ROP

Purpose: To study the characteristic of retinal and choroidal circulation in the retina of former premature with regressed mild ROP.

Methods: Eight preterm babies (mean GA 28.88 and mean BW 1973.7 grams), with a mild ROP diagnosed in the Catholic University NICU in Rome. Underwent fundus photographs and fluorescein angiography (FA) using RetCam (Clarity, Clarity, Pleasanton, CA) at a mean age of 33.6 months of chronological age. ROP expertly reviewed and classified FA. Periaxial and central retinal and choroidal abnormalities were observed and classified.

Results: Avascular areas are observed in the extreme retinal periphery in all but one baby. Retinal and choroidal capillary obliteration and artero-venous shunts are frequent. Abnormal vessels branching and leakage are rare. Choroidal circulation seems to remain immature only in three eyes.

Conclusions: Using FA, we have assessed the persistence of peripheral retinal avascularity, with rare abnormal vessels branching and leakage. Loss of capillary beds inside the vascularized retina and retino-choroidal hypo perfusion areas affects only the periphery. Further studies are needed to classify these long-lasting vascular abnormalities and better understand their implications for visual function of the child.

Commercial Relationships: Domenico Lepore, None; Pierdavide Perrini, None; Fernando Molle, None; Lorenzo D’Aizzi, None; Antonio Baldascino, None; Rachele Desantis, None

Program Number: 635 Poster Board Number: D0157
Presentation Time: 10:30 AM - 12:15 PM
Sequential vascular changes followed by angiography in spontaneously regressed retinopathy of prematurity in infants born greater than 32 weeks gestation and birthweight greater than 1250g with high oxygen dependance
ARCELIA DEL ROCIO VILLAÑEÑOR GARCIA, Hugo E. Sepulveda-Vazquez, Guillermo Salcedo-Villanueva, Samantha Salinas Longoria, Rafael Romero Vera, Gerardo Garcia-Aguirre, Hugo Quiroz-Mercado, Maria A. Martinez-Castellanos. Retina, Asociacion Para Evitar la Ceguera en Mexico, Mexico, Mexico.

Purpose: To describe retinal abnormalities assessed by fluorescein angiography (FA) in eyes of bigger and mature preterm infants exposed to high oxygen saturation and developed retinopathy of prematurity (ROP).

Methods: A retrospective, nonrandomized, case series. We included three patients (6 eyes) diagnosed with retinopathy of prematurity and oxygen saturation rate over 95% measured with a pulse oximeter. Fundus photographs and FA were obtained every two weeks using a wide-field digital pediatric imaging system until the resolution from the disease. (RetCam II Clarity)

Results: Fluorescein angiography showed incomplete vascularization of peripheral retina with a tortuous demarcation line with a ridge in some areas, all eyes showed capillary free areas in all ready vascularized retina, vessels in the posterior pole showed parietal hyperfluorescence near the foveal avascular zone. Some vessels showed microaneurism-like lesions. Once the oxygen was regulated the disease showed involution with growth of a normal capillary pattern all the way to the ora serrata.

Conclusions: The high oxygenation in preterm infants is a factor for the generation of oxygen toxicity retinopathy, decreased oxygenation parameters can cause regression of retinopathy and subsequent vascularization of the peripheral retina. Further studies are needed to confirm this hypothesis.

Commercial Relationships: ARCELIA DEL ROCIO VILLAÑEÑOR GARCIA, None; Hugo E. Sepulveda-Vazquez, None; Guillermo Salcedo-Villanueva, None; Samantha Salinas Longoria, None; Rafael Romero Vera, None; Gerardo Garcia-Aguirre, None; Hugo Quiroz-Mercado, Allegro Pharmaceutical (C); Maria A. Martinez-Castellanos, None

Program Number: 636 Poster Board Number: D0158
Presentation Time: 10:30 AM - 12:15 PM
Next Generation Sequencing Analysis of Gene and Pathway Regulation in the Rat Model of Retinopathy of Prematurity
Tara L. Favazza, Rachel M. Griffith, Hu Li, Nan Zhang, Ronald M. Hansen, Anne B. Fulton, James D. Akula

1Ophthalmology, Boston Children’s Hospital, Boston, MA; 2Ophthalmology, Harvard Medical School, Boston, MA; 3Biomedical Engineering, Boston University, Boston, MA; 4Wyss Institute for Biologically Inspired Engineering, Harvard Medical School, Boston, MA.

Purpose: To identify the genes, biochemical signaling pathways, and biological themes involved in the pathogenesis of retinopathy of prematurity (ROP).

Methods: Next-generation sequencing was performed on the RNA transcriptome of rats with the Penn et al. (1994) oxygen-induced retinopathy model of ROP at the height of vascular abnormality, postnatal day 19, and normalized to age-matched, littermate controls.
Custom developed pathways with potential relevance to known ROP sequellae were developed and evaluated for significant regulation in ROP. Regulation of other biological pathways and themes was detected by comparison with the online Kyoto Encyclopedia of Genes and Genomes (KEGG) and the Database for Annotation, Visualization and Integrated Discovery (DAVID) genomic databases. Results: In the custom pathway analyses, canonical Wnt signaling was found to be regulated, but the non-canonical PCP and Wnt/Ca$^{2+}$ pathways were not. Nitric oxide (NO) signaling, as measured by the activation of nitric oxide synthase (NOS), neuronal (nNOS) and endothelial (eNOS), was also regulated, as was retinoic acid (RA) signaling. Biological themes related to protein translation (ribosomes), neural signaling, inflammation and immunity, cell cycle and cell death, were (among others) detected by KEGG and DAVID to be highly regulated in ROP rats.

Conclusions: ROP alters expression in many genes and pathways that may provide novel targets for intervention.

Commercial Relationships: Tara L. Favaaza, None; Rachel M. Griffith, None; Hu Li, None; Nan Zhang, None; Ronald M. Hansen, None; Anne B. Fulton, None; James D. Akula, None

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Program Number: 637 Poster Board Number: D0159

Presentation Time: 10:30 AM - 12:15 PM

OCT findings in mild ROP

Rachele DeSantis¹, Antonio Trabacca¹, Domenico Lepore², Fernando Molle², Pierdavide Perrini², Lorenzo Orazi³. ¹Scientific Institute “Eugenio Medea”; Brindisi, Italy; ²Ophthalmology, Catholic University of the Sacred Heart, Rome, Italy.

Purpose: To study the morphology of the central retina in a population of ex-preterm babies with an history of regressed mild ROP and to compare these findings with visual acuity

Methods: Six babies (12 eyes) with a mean age of 1267 days (range 1071-1460 days) underwent OCT macular examination with Spectralis (Heidelberg Engineering). All babies had a documented history of mild ROP, fully regressed. Their mean GA was 28 weeks (ranging from 24 to 30 weeks) and mean BW was 1144 grams (ranging from 660 to 1500 grams). ROP experts retrospectively examined OCT scans. Visual acuity was also tested using Teller Acuity card.

Results: The median thickness of the fovea was 249.0 microns, ranging from 224 to 302 microns. The foveal pit appears shallow and photoreceptors layer thin compare to adults. Visual acuity was 6.8 cycles/degree in all 12 eyes.

Conclusions: Our findings demonstrate that some signs already described in the acute phase of ROP, persist over the years in the ex premature retina. This is likely to have long lasting implications for visual function of the child.

Commercial Relationships: Rachele DeSantis, None; Antonio Trabacca, None; Domenico Lepore, None; Fernando Molle, None; Pierdavide Perrini, None; Lorenzo Orazi, None

Program Number: 635 Poster Board Number: D0160

Presentation Time: 10:30 AM - 12:15 PM

Wide field fluorescein angiography vs indirect ophthalmoscopy in the screening of retinopathy of prematurity (ROP); Does understanding better the vascular pathology became essential in diagnosis and management of ROP?

Fernando Cisneros-Luna¹, Guillermo Salcedo-Villanueva¹, Samantha Salinas Longoria¹, Rafael Romero Vera¹, Fernando Schoonewolff², Hugo Quiroz-Mercado², Maria A. Martinez-Castellanos².

¹Asociación para evitar la ceguera en México, Distrito Federal, Mexico; ²Retina, Denver Health Medical Center, Denver, CO.

Purpose: To explore the possible benefits of wide field fluorescein angiography (WFFA) over conventional indirect ophthalmoscopy in the screening, management and understanding of ROP

Methods: Ninety six consecutive patients were recruited for a nonrandomized, investigational trial. At least three sessions for each patient of fundus fluorescein angiography were performed as part of ROP screening utilizing the Retcam II (Clarity Medical Systems, Pleasanton, CA) imaging under topical anesthesia and injecting fluorescein 10% solution at a doses of 0.1ml/kg to evaluate the disease and guide the treatment.

Results: Wide field fluorescein angiography enabled visualization of the retinal vasculature and helped to identify early flat neovascularization, capillary free zones, non perfusion areas, vascular shunts, detect previously missed areas of active retinopathy of prematurity in the peripheral retina. There were no side effects related to sodium fluorescein or the procedure. The vascular abnormalities were not noted during the clinical exploration with indirect ophthalmoscope.

Conclusions: Wide field fluorescein angiography is crucial in the evaluation of vascular abnormalities missed in the clinical exam, facilitates diagnosis of multiple vascular abnormalities in the periphery of the retina, allows a more objective assessment of the disease stage and zone. WFFA in ROP is essential not only for diagnosis and management, but to further our understanding of the pathology and new emerging treatments.

Commercial Relationships: Fernando Cisneros-Luna, None; Guillermo Salcedo-Villanueva, None; Samantha Salinas Longoria, None; Rafael Romero Vera, None; Fernando Schoonewolff, None; Hugo Quiroz-Mercado, Allegro Pharmaceutical (C); Maria A. Martinez-Castellanos, None

30 Retinitis Pigmentosa I

Sunday, May 05, 2013 10:30 AM-12:15 PM

Exhibit Hall Poster Session

Program #/Board # Range: 639-690/D0161-D0212

Organizing Section: Retina

Contributing Section(s): Retinal Cell Biology

Program Number: 639 Poster Board Number: D0161

Presentation Time: 10:30 AM - 12:15 PM

Photoreceptors in whirler mice show defective transducin translocation and are susceptible to light-induced degeneration

Dominic E. Cosgrove, Mei Tian, Wei-Min Wang, Marissa L. Zalloccchi, You-Wei Peng, Sensory Neuroscience, Boys Town Natl Research Hosp, Omaha, NE.

Purpose: Usher syndrome combines congenital hearing loss and retinitis pigmentosa (RP). Mutations in the whirler gene (DFNB31/WHRN) cause a subtype of Usher syndrome (USH2D). Whirler mice have inner ear defects but do not develop retinal degeneration. Here we investigate abnormalities in whirler mouse photoreceptors.

Methods: Immunohistochemistry, serial tangential section immunoblotting and hydroethidine-based detection of intracellular superoxide production were used. Photoreceptor cell densities under various conditions of light/dark exposures were evaluated.

Results: In whirler mouse photoreceptors, the light-activated rod transducin translocation is delayed and its activation threshold is shifted to a higher level. Rhodopsin is observed in the connecting cilia of rods. Continuous moderate light exposure induced significant rod photoreceptor degeneration and superoxide accumulation.
Whirler mice reared under a 1500 lux light/dark cycle also resulted in significant photoreceptor degeneration. Previously, we reported that shaker1 mice, a USH1B model, also showed moderate light-induced photoreceptor degeneration with delayed transducin translocation.

**Conclusions:** The results from shaker1 and whirler mice suggest that defective transducin translocation is linked to light-induced degeneration, and these two symptoms may reflect defects in rod photoreceptors. These results also indicate that both Usher syndrome mouse models may share a closely related pathobiological mechanism for retinal degeneration.

**Commercial Relationships:** Dominic E. Cosgrove, None; Mei Tian, None; Wei-Min Wang, None; Marisa L. Zallocchi, None; You-Wei Peng, None

**Support:** This work was supported by NIH Grant P20 RR018788, R01 DC04844, and the tobacco settlement fund from the State of Nebraska.

**Program Number:** 640 **Poster Board Number:** D0162 **Presentation Time:** 10:30 AM - 12:15 PM

Long-term follow-up of patients with retinitis pigmentosa (RP) receiving sustained-release CNTF through intracocular encapsulated cell technology implants

David G. Birch1, 2, Kirsten G. Locke1, Travis Porco1, Martin Klein1, Austin Roorda1, Weng Tao1, Jacque L. Duncan2.1 Retina Fndn of the Southwest, Dallas, TX; 2Ophthalmology, UT Southwestern Medical school, Dallas, TX; 3Optometry, UC Berkeley, Berkeley, CA; 2Neurotech, USA, Lincoln, RI.

**Purpose:** In a multicenter Phase 2 study, ciliary neurotrophic factor (CNTF) was delivered to one eye via encapsulated cell technology implants (NT-501, Neurotech Pharmaceuticals, Inc.) in 68 patients with RP. Patients had the option of having the implant removed at 24 months. Here we report cone photoreceptor density and visual field sensitivity (VFS) changes from a subset of patients with or without implant for up to 54 months.

**Methods:** For 3 patients, high-resolution images of regions of interest (ROIs) with unambiguous cones were obtained with Adaptive Optics Scanning Laser Ophthalmoscopy (AOSLO) in CNTF-treated and control eyes at baseline, 3, 6, 12, 18, and 24 months post-implant. Patients 1 and 3 elected to have the devices removed after 24 months and patient 2 retained the implant. They were subsequently imaged at 36 and 48 months. For 16 patients who consented to post-30 month visual field testing, VFS was measured twice per eye at baseline and every 6 months through month 30. Of these, 10 chose to retain the implant and 6 chose to have the device explanted. They were subsequently evaluated at 42 and 54 months.

**Results:** Cone density was measured within selected ROIs at baseline and at least one subsequent imaging session 12 to 35 months later. Overall, cone density decreased by 9% to 24% in 8 of 9 locations (89%) in sham-treated eyes but remained stable in 12 of 12 (100%) locations in the CNTF treated eyes, changing less than the range of estimated measurement error (6.3%). VFS showed greater loss in eyes treated with CNTF than sham treated eyes starting at 6 months. At 42 months, loss in the eyes with the high-dose implant (compared to baseline) was 370 ± 43 dB, which was significantly greater (p<0.05) than 266 ± 29 dB loss in sham-treated eyes. Implant removal slowed the rate of VFS loss. Consequently, explanted eyes showed comparable sensitivity loss (p = 0.23) to sham-treated eyes at 42 months and less total sensitivity loss than the sham-treated eyes at 54 months.

**Conclusions:** CNTF treatment preserved cone photoreceptors from degeneration in the RP patients but concurrently reduced VFS. The loss of VFS was reversible upon implant removal. Further follow-up will be necessary to determine whether CNTF exposure preserves photoreceptors and slows long-term field loss relative to sham-treated eyes.

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**Commercial Relationships:** David G. Birch, Acucela (C), QLT (C), Neurotech, USA (C); Kirsten G. Locke, None; Travis Porco, NIH NEI (F); Martin Klein, None; Austin Roorda, US Patent #6890076 (P), US Patent #7118216 (P), UC Berkeley (P); Weng Tao, Neurotech (E); Jacque L. Duncan, None

**Support:** EY014375, Foundation Fighting Blindness, Research to Prevent Blindness, That Man May See, NEI Core grant EY002162

**Clinical Trial:** NCT00447980

**Program Number:** 641 **Poster Board Number:** D0163 **Presentation Time:** 10:30 AM - 12:15 PM

Light-Induced Rod Death in RHO P23H Swine Triggers Microglial Invasion, TNF-α Release and Rapid Blue Cone Loss

Sang-Joon Lee1, 2, Wei Wang1, Henry J. Kaplan1, Douglas C. Dean1.1Ophthalmology, Univ of Louisville, Louisville, KY; 2Ophthalmology, Kosin University, Busan, Republic of Korea.

**Purpose:** The aim of this study is to identify factors leading to loss of rod and cone photoreceptors in RHO P23H transgenic swine

**Methods:** Wild-type and P23H transgenic swine eyes were collected at different embryonic and postnatal stages. Eyes from at least three pigs were used for each time point. Retinas were immunostained for markers (Calnexin, Iba1, TNF-α, MCP-1, and Endoplasmic reticulum (ER) makers (Calnexin, and caltrectulin). Cone number was determined by counting successive 100 μm squares along the length of the retina.

**Results:** RHO became trapped in the ER at birth in P23H swine, and apoptosis initiated in rods at postnatal day (P1). This rod apoptosis coincided with expression of the microglial chemotactic cytokine MCP-1, microglial invasion into the ONL and release of TNF-α. By P3, most blue cones were apoptotic, and by P14 these cones were largely lost. By contrast, red/green cones remained viable until at least P90.

**Conclusions:** Light-induced retention of P23H RHO in the ER at birth initiates rod apoptosis in P23H swine. This apoptosis triggers invasion of microglia and release of TNF-α leading to rapid death of blue cones.

**Commercial Relationships:** Sang-Joon Lee, None; Wei Wang, None; Henry J. Kaplan, None; Douglas C. Dean, None

**Support:** Research to Prevent Blindness, American Health Assistance Foundation, NIH Grants (P20 RR018733 and EY015636) and The Commonwealth of Kentucky Research Challenge.
Correlation of retinal sensitivity with the area of normal autofluorescence in choroideremia patients

Markus Groppe1,2, Charles Cottriall1, Susan M. Downes1, Robert E. MacLaren1,2, 1Nuffield Laboratory of Ophthalmology, Oxford Eye Hospital and NIHR Oxford Biomedical Research Centre, NDCC University of Oxford, Oxford, United Kingdom; 2Ophthalmology, Columbia University, New York, NY.

Purpose: To investigate whether patients with choroideremia have defects in retinal sensitivity prior to the onset of degeneration and how function correlates to fundus autofluorescence (FAF).

Methods: Thirty-eight patients (72 eyes) with choroideremia underwent a complete ophthalmologic examination, including best-corrected visual acuity, microperimetry (Maia system), FAF and spectral-domain optical coherence tomography (Heidelberg Spectralis). The residual area of functioning retina was determined using FAF. The mean retinal sensitivities within the central 2 degrees of visual field were examined.

Results: The area of autofluorescent retina ranged from 0.13 mm² to 62 mm² and correlated highly with the central retinal sensitivity (range 1-30 dB) and age of the patient (13-63 years) (P<0.01). Central retinal sensitivity was reduced in all patients compared to controls, including those with normal visual acuity.

Conclusions: Choroideremia is a progressive retinal and choroidal degeneration. The size of the area of surviving retinal tissue determined by FAF is a biomarker for disease progression. There is a functional deficit in retinal sensitivity in these patients which exists prior to the onset of degeneration and might therefore be partly reversible following successful gene replacement therapy.

Commercial Relationships: Markus Groppe. None; Charles Cottriall. None; Susan M. Downes. Novartis (F); Robert E. MacLaren. None

Support: Wellcome Trust

Program Number: 642 Poster Board Number: D0164
Presentation Time: 10:30 AM - 12:15 PM

Intravitreal Autologous Bone-Marrow Stem Cells in Retinitis Pigmentosa Patients: One-Year Results

Rafael S. Arcieri, Katharina Messias, Vinicius M. Castro, Rubens C. Siqueira, Rodrigo Jorge, Andre Messias, Ophthalmology, School of Medicine of Ribeirão Preto, University of São Paulo / USP, Ribeirão Preto, Brazil.

Purpose: To evaluate the effects of a single intravitreal injection of autologous bone-marrow stem cells (ABMSC) in Retinitis Pigmentosa (RP) patients.

Methods: A prospective, single blind, phase II, nonrandomized clinical trial, including 20 RP patients showing good fixation during visual field examination. Intravitreal ABMSC injection was performed in the study eye, while the contralateral eye served as control, and underwent sham procedure. Evaluations included best-corrected visual acuity (BCVA), static 30-2 visual field (Octopus 900), microperimetry (MAIA - CenterVue) for fixation stability (BCEA), and macular sensitivity (AVT) determination. Full-field and multifocal electroretinograms (ERG) were performed according to the ISCEV standards using Espion E2 (Diagnosys LLC). Examinations were performed at baseline, 4, 16, 32 and 48 weeks after injection.

Results: No significant intra-individual (48 weeks - baseline) BCVA change was observed, with a slight improvement of -0.04 ± 0.02, and -0.03 ± 0.01 logMAR in treated and control eyes, respectively (P=0.3898), whereas AVT improved by 1.0 ± 0.5 dB on treated eyes, with a trend towards significance for the comparison with the smaller AVT improvement observed on control eyes: 0.2 ± 0.5 dB (P=0.0569). No significant difference was found between changes of BCEA 95% in treated (-1.8 ± 1.0), and control (-2.0 ± 1.8) eyes (P=0.557). Corroborating to the microperimetry findings, 30-2 visual field mean deviations exhibited smaller worsening in treated (0.33 ± 0.70 dB) than in control (1.12 ± 0.58 dB) eyes after 48 weeks (P=0.0761). No significant changes were observed for any ERG parameters, or OCT during follow-up, and no side effects due to the injections were observed.

Conclusions: These data indicates that intravitreal injection of ABMSC is associated to a small improvement of macular thresholds on microperimetry, concomitant to a slight hindering of the 30-2 visual field sensitivity deterioration, one year after injection in RP. Further studies are needed to clarify possible mechanisms related to the potential use of ABMSC in RP.

Commercial Relationships: Rafael S. Arcieri. None; Katharina Messias. None; Vinicius M. Castro. None; Rubens C. Siqueira. None; Rodrigo Jorge. None; Andre Messias. None

Clinical Trial: NCT01560715

Program Number: 644 Poster Board Number: D0166
Presentation Time: 10:30 AM - 12:15 PM

Evaluation of Inner Retinal Layers in Patients with Retinitis Pigmentosa Using Optical Coherence Tomography

Kenzo Hokazono1,2, Rithambhar Ramachandran3, Lisa Zhou2, Kirsten G. Locke4, David G. Birch5, Donald C. Hood6.
1Ophthalmology, Sao Paulo Ramachandran, New York, NY; 2Departments of Psychology and Ophthalmology, Columbia University, New York, NY; 3Retina Foundation of the Southwest, Dallas, TX.

Purpose: Preservation of the inner retina in patients with retinitis pigmentosa (RP) is an important prerequisite for restoration therapy. However, the degree of preservation is not fully understood. Using frequency-domain optical coherence tomography (FD-OCT), we evaluated changes of the thickness of the inner retinal layers in patients with x-linked (X) RP and tracked the thickness over a 2-year period.

Methods: FD-OCT 9mm X 6mm (30°X20°) volume scans (Spectralis, Heidelberg) were obtained from one eye of 26 patients with X-linked (15.0 ± 7.0 yrs) and compared with those of 41 controls (22.0 ± 7.4 yrs). Three layers, the retinal nerve fiber layer (RNFL), the combined retinal ganglion cell and inner plexiform layers (RGCL+), and the inner nuclear layer (INL), were segmented using an automated algorithm[1] and then manually hand-corrected[2]. Average thickness values were obtained for 3 areas centered on the fovea: 2X2 mm, 4X4 mm, and 6X6 mm of the scan. The measurements were evaluated and compared at the initial point and final time points spaced by approximately 2 years.

Results: For all 3 areas analyzed, RNFL thickness was greater than controls and the average RNFL thickness for the entire (6X6mm) scan showed the largest absolute (30.1um) and relative (1.67%) increase (table 1). The increased thickness of the other 2 layers (INL & RGCL+) was smaller and reached statistically significant in the center of the macula (2x2 and 4x4mm; table 1), but not for the entire scan. For all layers and areas, the change in thickness over the 2 year period was extremely small (<1 um) and not statistically significant (p>0.39 to p>0.95).

Conclusions: There is disagreement over which inner retinal layers in RP are increased in thickness.[2-6] Here patients with XRP showed increased thickness of all 3 inner retinal layers compared to controls, although the major thickening was observed for the RNFL.

<table>
<thead>
<tr>
<th>Inner Retinal Layer</th>
<th>Area Analyzed</th>
<th>Controls (n=4) (SD)</th>
<th>Patients (n=4) (SD)</th>
<th>Relative Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNFL</td>
<td>2X2</td>
<td>23.3 (1.9)</td>
<td>26.1 (6.0)*</td>
<td>1.11</td>
</tr>
<tr>
<td></td>
<td>4X4</td>
<td>35.7 (2.4)</td>
<td>44.8 (7.2)**</td>
<td>1.22</td>
</tr>
<tr>
<td>RGCL*</td>
<td>6X05</td>
<td>44.6 (4.8)</td>
<td>74.7 (11.4)**</td>
<td>1.67</td>
</tr>
<tr>
<td></td>
<td>8X2</td>
<td>86.7 (7.1)</td>
<td>100.2 (11.5)**</td>
<td>1.16</td>
</tr>
<tr>
<td></td>
<td>4X4</td>
<td>81.8 (5.3)</td>
<td>90.9 (9.5)**</td>
<td>1.10</td>
</tr>
<tr>
<td></td>
<td>6X05</td>
<td>57.7 (6.5)</td>
<td>64.6 (6.5)</td>
<td>0.95</td>
</tr>
<tr>
<td>BRL</td>
<td>2X2</td>
<td>34.5 (3.6)</td>
<td>37.8 (7.4)*</td>
<td>1.09</td>
</tr>
<tr>
<td></td>
<td>4X4</td>
<td>34.7 (2.2)</td>
<td>37.9 (6.6)**</td>
<td>1.10</td>
</tr>
<tr>
<td></td>
<td>6X05</td>
<td>30.2 (2.3)</td>
<td>32.2 (5.4)</td>
<td>1.07</td>
</tr>
</tbody>
</table>

Table 1. Average thickness in um for 3 retinal layers and 3 areas of analysis. * p < 0.05, ** p <0.01

Commercial Relationships: Kenzo Hakozono, None; Rithambhar Ramachandran, None; Lisa Zhou, None; Kirsten G. Locke, None; David G. Birch, Acucela (C), QLT (C), Neurotech, USA (C); Donald C. Hood, Topcon, In (F)

Program Number: 645 Poster Board Number: D0167
Presentation Time: 10:30 AM - 12:15 PM
Transmission Electron Microscopic Study of P23H Retinopathy in a Swine Model of Retinitis Pigmentosa
Patrice A. Scott, Henry J. Kaplan. Ophthalmology & Visual Sciences, University of Louisville, Louisville, KY.

Purpose: Characterize ultrastructural changes that occur during retinogenesis and postnatal development in transgenic (tg) swine expressing the Proline-23-Histidine (P23H) rhodopsin mutation, the most common form autosomal dominant Retinitis Pigmentosa (adRP) in man, which are not detectable with standard histology and immunohistochemistry.

Methods: P23H and wild type (Wt) swine were euthanized during gestation at embryonic (E) day 85, 105, and after birth at postnatal (P) days 3, 14, 30, 60, 90, 120, and 180. Each group contained 1 Wt and 1 tg eye (N = 18 eyes). Eyes were fixed in a mixture of 2% paraformaldehyde/2% glutaraldehyde. Posterior eyecups containing the retina were bisected along the vertical meridian and retinal tissue was retrieved 5-7 mm above the optic disc and processed for transmission electron microscopy (TEM).

Results: Wt: E85 retinae exhibit photoreceptor (PR) inner segments (IS) in the subretinal space (SRS) and no PR synaptic terminals in the OPL. E105 retinae show PR outer segments (OS) in the SRS, and development of PR synaptic terminals is incomplete. P3-P180 Wt retinae appear mature and normal. P23H: E85 retinae look similar to Wt. E105 retinae exhibit abnormal rod OS that are disorganized, vacuolated, and truncated; PR synaptic terminals appear similar to Wt. P3 retinae exhibit rod inner segments (IS) with malformed OS, rod spherules have abnormal triad configuration, or no triads at all, and most cones appear normal. P14-P60 retinae show no rod IS/OS, abnormal rod spherules, progressive loss of PR nuclei from the ONL, infrequent pyknotic nuclei in the ONL, Müller cell hypertrophy, cone PRs with and without OS, and flattening of cone pedicles. P90 -P120 retinae show few cone OS, blob-like structures and vacuoles in the cone myoid, and vacuoles in the ONL, INL, and OPL. P180 show abnormal and normal cone somata with retracted abnormal pedicles surrounded by Müller cell cytoplasm, cone IS are largely absent, and the retinal pigment epithelium abuts the external limiting membrane.

Conclusions: P23H tg swine exhibit progressive retinopathy that begins before birth and has a primary effect on rod PRs, followed by a secondary protracted phase of cone PR degeneration. This may be a useful model for studying the protracted phase of cone PR degeneration, and for development of intervention therapies intended to preserve vision in humans with RP.

Commercial Relationships: Patrick A. Scott, None; Henry J. Kaplan, None
Support: NEI R21 EY020647 (HK); Research to Prevent Blindness, Inc. NYC, NY; KY Challenge Research Trust Fund (HK); KY Science and Engineering Foundation (HK); University of Louisville Basic Science Research Grant (PAS); Fight for Sight Grant-in-Aid (PAS); The American Optometric Foundation and Beta Sigma Kappa Optometric Honor Society Fellowship (PAS)

Program Number: 646 Poster Board Number: D0168
Presentation Time: 10:30 AM - 12:15 PM
Evaluation of fundus autofluorescence in retinitis pigmentosa using ultra-wide-field scanning laser ophthalmoscope
Yukitoshi Shimoda, Shoji Kishi. Department of Ophthalmology, Gunma Univ School of Med, Maebashi City, Japan.

Purpose: We evaluated fundus autofluorescence images in retinitis pigmentosa using ultra-wide-field scanning laser ophthalmoscope.

Methods: Fundus autofluorescence (FAF), spectral-domain optical coherence tomography (OCT) and full-field electroretinogram (full-field ERG) were prospectively examined in 20 eyes of 10 cases who were clinically diagnosed with a retinitis pigmentosa.

Results: In 8 eyes (40%) of 20 eyes, a ring-like hyper FAF at macula (ring FAF) or a hypo FAF around vascular arcade area were observed. A diffuse hypo FAF at peripheral retina was demonstrated in 4 eyes (20%) and a diffuse hypo FAF at whole retina was showed in 9 eyes (45%). In 8 eyes with the ring FAF, the mean best-corrected visual acuity (BCVA) was good (from 1.0 to 1.2) and photoreceptor inner and an outer segment (IS/OS) lines were remained inside a ring FAF area, while these IS/OS lines were defected at the surrounding area of the ring FAF. In 5 eyes with a diffuse hypo FAF at whole retina and no ring FAF, the mean BCVA was poor (from light sense to 0.06) and these IS/OS lines were defected at macular area. In 2 eyes with both a ring FAF and a diffuse hypo FAF at peripheral retina, and in 9 eyes with a diffuse hypo FAF at whole retina, cone and rod components in full-field ERG were completely disappeared.

Conclusions: Using ultra-wide-field scanning laser ophthalmoscope, fundus autofluorescence of wide range could observe in retinitis pigmentosa. The finding of a ring-like hyper FAF indicated remaining of a foveal IS/OS line and good visual acuity. The existence of a diffuse hypo FAF in whole retina was thought to be a serious damage of retinal function.

Commercial Relationships: Yukitoshi Shimoda, None; Shoji Kishi, None
Support: do not use n/a

Program Number: 647 Poster Board Number: D0169
Presentation Time: 10:30 AM - 12:15 PM
Test-Retest Variability for Semi-Automated Kinetic Perimetry and GATE Static Perimetry in Retinitis Pigmentosa
Dawn Peters1,2, Elvira N. Chegarnov3, Laura Erker4, Mark E. Pennesi2,3, Richard G. Weleber2,3,1. Public Health and Preventive Medicine, Oregon Health and Science University, Portland, OR; 2Ophthalmology, Oregon Health and Science University, Portland, OR; 3Casey Eye Institute, Oregon Retinal Degeneration Center, Portland, OR.

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**Purpose:** Visual fields provide information essential for clinical evaluation of patients with inherited retinal degenerations and serve as endpoints for clinical trials. We present test-retest variability data for static and kinetic perimetry in patients with retinitis pigmentosa (RP).

**Methods:** Semi-automated Kinetic Perimetry (SKP) and German Adaptive Thresholding Estimation (GATE) static perimetry (GSP) were performed on 32 patients with RP on 3 sessions using Octopus 900 perimeter (Haag-Streit, Köniz, Switzerland). The solid angles (degrees) subtended by three isopters (V4e, III4e, I4e) were measured. Full-field static perimetry used the GATE strategy, Goldmann stimulus size V, and a centrally condensed grid of 164 points extending from 56° nasally to 80° temporally. Visual Field Modeling and Analysis software fit the sensitivity data to a thin spline to create 3-dimensional models of the Hill of Vision (HOV), from which the sensitivity volume (dB-sr) for the total field (HOVT) and the central 30° field (HOV30°) were independently measured for test and re-test sessions using the 1st pair of sessions for each subject. The average age at first session was 52.8 yrs (SD=9.4, range 36.9 to 70.9 years).

**Results:** Differences between sessions for both kinetic and static variables tended to be greater for larger session values. As seen in the table, the coefficients of variation for within subject differences were fairly similar for SKP and GSP, ranging from 0.06 to 0.13 for SKP and 0.10 to 0.14 for GSP. The findings appear comparable to other reports.

**Conclusions:** The test-retest variability for SKP and GSP support their use as endpoints for clinical trials.

<table>
<thead>
<tr>
<th>Semi-automated Kinetic Perimetry (degree)</th>
<th>Left n=30; Right n=32</th>
<th>CV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Isopter</strong> V4e</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>5943</td>
<td>0.06</td>
</tr>
<tr>
<td>Right</td>
<td>5464</td>
<td>0.11</td>
</tr>
<tr>
<td><strong>Isopter</strong> III4e</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>3900</td>
<td>0.07</td>
</tr>
<tr>
<td>Right</td>
<td>3619</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>Isopter</strong> I4e</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>1314</td>
<td>0.12</td>
</tr>
<tr>
<td>Right</td>
<td>1188</td>
<td>0.13</td>
</tr>
</tbody>
</table>

CV is coefficient of variation of within subject differences obtained as within subject SD divided by mean.

**Commercial Relationships:** Dawn Peters, None; Elvira N. Chegarnov, None; Laura Erker, None; Mark E. Pennesi, Pfizer (F); Richard G. Weleber, AGTC (C), VFMA patent application (P), Pfizer (C), Oxford Biomedica (F)

**Support:** Foundation Fighting Blindness (Weleber, C-CL-0711-0534-OHSU01), Research to Prevent Blindness (Unrestricted, CEI)

**Clinical Trial:** NCT01233609

**Program Number:** 649 Poster Board Number: D0170

**Presentation Time:** 10:30 AM - 12:15 PM

**Pupillometry in Patients with Leber Congenital Amaurosis:** Feasibility, Residual Retinal Cell Function, and Paradoxical Response

**Response**


Pupillometry testing is feasible in children with LCA with a wide variety of disease severities and genotypes. It is a promising method for testing different retinal cell types objectively in a noninvasive way using preferential light stimulation while bypassing cortical processing. Our data also describes the retinal cells and layers mostly affected in the different genotypes, as well as providing evidence of residual viable cells previously thought to be lost.

**Commercial Relationships:** Radwan Ajjain, None; Leah M. Wood, None; Jamie Koenekoop, None; Sorathnoorani Siddiqui, None; Irma Lopez, None; Vafa Kesen, None; Ayesha Khan, QLT (C); Huanan Ren, None; Rui Chen, None; Robert K. Koenekoop, QLT Inc (C)

**Support:** FFB Canada, CIHR, NIH

**Program Number:** 649 Poster Board Number: D0171

**Presentation Time:** 10:30 AM - 12:15 PM

**Is solute carrier protein (SC1) a novel gene for autosomal recessive retinitis pigmentosa?**

Alice Y. Zhang, Shen Li, Huanan Ren, Irma Lopez, Sorathnoorani Siddiqui, Dror Sharon, Ayesha Khan, Paul R. Gooddy, Rui Chen, Robert K. Koenekoop.

Ophthamology, McGill University, Montreal, QC, Canada; Ocular genetics laboratory, McGill University, Montreal, QC, Canada; Molecular Ophthalmology Laboratory, Hadassah-Hebrew University Medical Center, Jerusalem, Israel; Pediatrics, McGill University, Montreal, QC, Canada; Molecular and Human Genetics, Baylor College of Medicine, Houston, TX.

**Purpose:** Autosomal recessive retinitis pigmentosa (arRP) is a severe, clinically and genetically heterogeneous, retinal disease that
leads to blindness. Approximately 50% of RP patients have mutations in known genes. Our goal is to identify the remaining RP genes. We have identified nine unrelated patients with a clinical phenotype of arRP who are genetically unsettled. In this study we aim to identify their causal gene.

**Methods:** In one arRP proband, we used a RetNet chip to exclude mutations in known genes and subsequently subjected her DNA to whole exome sequencing by next generation sequencing. We identified two deleterious mutations in a novel solute carrier (SC1). We then tested a second RP cohort with the same cultural background and found mutations in five more families. In a Quebec RP cohort, we identified mutations in another three families. In affected patients with one mutation, we tested the digenic, trigenic, and quadrigenic hypotheses by sequencing related solute carrier proteins (SC2, SC3 and SC4). We are revisiting the ocular and subclinical systemic phenotypes. All mutations are characterized in silico by using SIFT, polyphen, and Blosum.

**Results:** We have found novel mutations in all four genes (SC1, SC2, SC3, SC4). Mutations in SC1 are found in all 9 patients, those in SC2 are found in 7 patients, and those in SC3 and SC4 are found in 1 patient. One patient has mutations in 1 out of 4 genes, three patients have mutations in 2 genes, two patients have mutations in 3 genes, and three patients have mutations in 4 genes. Multiple mutations demonstrate residues conserved down to zebrafish and drosophila.

**Conclusions:** We believe that we have identified a new gene and a novel pathway for retinitis pigmentosa. We are currently investigating the full extent of the mutation spectrum and severity and will conduct mutagenesis studies and functional testing. Our findings are crucial in expanding the current understanding of hereditary retinal degenerations and in developing new potential therapeutics.

**Commercial Relationships:** Alice Y. Zhang, None; Shen Li, None; Huanan Ren, None; Irma Lopez, None; Sorathnoorni Siddiqui, None; Dror Sharon, None; Ayeshia Khan, QLT (C); Paul R. Goodyer, None; Rui Chen, None; Robert K. Koenekoop, QLT Inc (C)

**Support:** FFB Canada, CHRI, NIH

**Program Number:** 650 Poster Board Number: D0172

**Presentation Time:** 10:30 AM - 12:15 PM

**Role of ER Stress-Induced Caspase12 in Retinal Degeneration of T17M RHO mice**

Yogesh Bhootada1, Shreyasi Choudhury2, Marina S. Gorbatyuk1, 1Vision Sciences, University of Alabama at Birmingham, Birmingham, AL; 2Vision Sciences, University of North Texas HSC, Fort Worth, TX.

**Purpose:** The T17M mutation within the rhodopsin gene (RHO) causes protein misfolding, endoplasmic reticulum (ER) stress, and activation of the unfolded protein response leading to autosomal dominant retinitis pigmentosa (adRP). The adRP photoreceptor cell death is known to occur through apoptosis and activation of caspases. Previous studies have shown that Casp-7 is activated under ER stress conditions in ADRP animal models. Therefore, the goal of this study is to validate the UPR downstream marker, Casp-12 as a new therapeutic target for T17M RHO retina. This therapeutic approach aimed to reduce ER stress-associated apoptosis could be used in the advanced stages of the ADRP alone or in combination with the therapy designed to reduce misfolded rhodopsin.

**Methods:** T17M RHO Casp-12-/-, T17M RHO Casp-12+/+ mice were used in the study. All groups were subjected to electroretinogram (ERG) and spectral domain optical coherence tomography (SD-OCT) analysis at postnatal (P) day 30 and P90 of retinal degeneration. RNA was extracted from C57BL6 and T17M RHO retina at P12, P18, P21, and P25 to perform qRT-PCR analysis of the Casp-12 gene expression

**Results:** Analysis of qRT-PCR demonstrated that the Casp-12 is significantly up regulated in T17M RHO retina at P18, P21 and P25 by 3-4 fold compared to C57BL/6. Analysis of the scotopic ERG response demonstrated that a- and b-wave amplitudes were significantly increased in T17M RHO retina deficient in Casp-12 by 222%, 669% and 154%, 232%, correspondingly at P30 and P90 compared to T17M RHO Casp-12+/+. The thickness of the Outer Nuclear Layer in superior and inferior regions of T17M RHO Casp12-/- mice measured by SD-OCT was dramatically increased by 132%,135% and 278%,317%, respectively at P30 and P90 as compared to T17M RHO Casp12+/+ mice

**Conclusions:** Casp-12 deficiency leads to functional and structural preservation of T17M RHO retina suggesting that the Casp-12 gene could be a viable therapeutic target for the treatment of ADRP.

**Commercial Relationships:** Yogesh Bhootada, None; Shreyasi Choudhury, None; Marina S. Gorbatyuk, None

**Support:** R01EY020905, Foundation Fighting Blindness

**Program Number:** 651 Poster Board Number: D0173

**Presentation Time:** 10:30 AM - 12:15 PM

**Phase I Trial of Subretinal Injection of a Recombinant Adeno-Associated Virus (rAAV2-VMD2-hMERTK) Gene Vector to Patients with MERTK RP**

Nicola G. Ghazi1, Fowzan S. Alkutayya2, Abdulrahman Al-Maghamst1, Fahad Al Saikhhan, Emad B. Abboud1. 1Vitreo/Retinal (KKESH), King Khaled Eye Specialist Hosp, Riyadh, Saudi Arabia; 2Developmental Genetics, King Faisal Specialist Hospital and research center, Riyadh, Saudi Arabia.

**Purpose:** To report short-term safety results of the phase I trial of subretinal injection of rAAV2-VMD2-hMERTK gene vector for retinitis pigmentosa (RP) secondary to the MERTK Mutation

**Methods:** Except in one patient, the worst seeing eye of patients with MERTK mutation proven RP was injected with rAAV2-VMD2-hMERTK gene vector into the subretinal space. Patients underwent a full ophthalmic evaluation including early treatment diabetic retinopathy (ETDRS) visual acuity testing, slit-lamp and funduscope evaluation, fundus photography, spectral-domain optical coherence tomography (SD-OCT), and full-field threshold stimulation test (FST). In addition, quality of life recordings, systemic evaluation and a battery of laboratory testing including AAV antibody and antigen specific reactivity as well as peripheral blood polymerase chain reaction (PCR) were performed at baseline and specific subsequent protocol visits. The vector injection was performed following a complete vitrectomy using a 39-gauge subretinal cannula.

**Results:** Six eyes of 6 enrolled patients have been injected so far. The age ranged from 15-50 years and the baseline visual acuity ranged from 20/40 Snellen equivalent to hand motion. The follow-up at the time of this writing ranged from 3-12 months. No intraoperative complications occurred. Postoperatively, one eye developed filamentary keratitis that resolved with lubrication, and another developed persistent submacular fluid that resolved spontaneously within 1 month with return of vision to baseline and subsequent improvement. Only one patient developed a rise in AAV antibodies but with a negative PCR. Three patients reported improved vision that was also documented on exam. In one of these, improvement in visual field was also reported and documented by field-testing compared to the fellow eye.

**Conclusions:** Subretinal injection of rAAV2-VMD2-hMERTK gene vector for patients with MERTK RP appears to be safe with no ocular or systemic side effects related to the vector itself. The treatment also appears to be beneficial in some cases.

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Commercial Relationships: Nicola G. Ghazi, None; Fowzan S. Afkuryaya, None; Abdurahman Al-Maghamdi, None; Fahad Al Saikhan, None; Emad B. Abboud, None
Clinical Trial: NCT01482195

Program Number: 652 Poster Board Number: D0174
Presentation Time: 10:30 AM - 12:15 PM
Integrated in silico and in vitro characterization of Rhodopsin mutations causing RP4
Valeria Marigo, Petra Behnen, Angelo Felliine, Francesca Fanelli.
Purpose: Retinitis pigmentosa (RP) is a genetic degenerative disease causing blindness in later life. Despite the high genetic heterogeneity of RP, ~140 point mutations were discovered in the rhodopsin gene (RHO). RHO belongs to the G protein Coupled Receptor superfamily of seven-transmembrane proteins. The vast majority of the rhodopsin mutations cause the Autosomal Dominant form (ADRP) of the disease. A recent analysis indicates that 89% of the biochemically characterized RHO mutants are misfolded, supporting the protein misfolding hypothesis of RP. The primary aim of this work was to develop a scoring that would be able to predict the misfolding tendency of RHO mutants, which can be used to identify mutants that may be therapeutic targets for treatment of RP.

Methods: In silico experiments on wild type RHO and 36 different mutations consisted in thermal unfolding simulations combined with the graph-based Protein Structure Network analysis. In parallel, the same mutants were cloned in expression vectors and in vitro expressed in COS-7 cells. The subcellular localization was performed with two monoclonal antibodies recognizing either the extracellular N-terminal or the intracellular C-terminal of RHO. In order to define levels of expression and differences in post-translational modifications of the mutants compared to the wild type, the proteins were analyzed by Western blotting.

Results: In silico studies revealed that ADRP RHO mutations share marked abilities to impair selected highly connected nodes in the protein structure network, i.e. hubs, essentially located in the retinal binding site, which participates in the stability core of the protein. We could define a number of computational indices whose combination led to a structural classification of the mutants. The in vitro level of analysis revealed reduction in expression levels and plasma membrane localization of some of the mutants compared to wild type RHO. We also defined different abilities of the mutated proteins to be affected by 9-cis retinal.

Conclusions: These two levels of analysis allowed a novel characterization of the different mutants to generate the first classification of ADRP RHO mutants based on a multiscale approach, i.e. at the cellular and atomic levels of detail. This knowledge will be our starting point for the choice of a number of mutations to be used to reveal therapeutic effect of chaperone molecules.

Commercial Relationships: Valeria Marigo, None; Petra Behnen, None; Angelo Felliine, None; Francesca Fanelli, None
Support: Fondazione Telethon #GGP11201A

Program Number: 653 Poster Board Number: D0175
Presentation Time: 10:30 AM - 12:15 PM
Identification and Characterization of Mouse Antisense Oligonucleotides (ASOs) Directed at Rhodopsin
Purpose: Antisense technology is a drug discovery platform that uses the availability of genetic information and sequences to treat diseases where small molecules and antibodies may have limited success. The use of antisense technology for the treatment of ocular diseases is an ideal drug development approach that combines specificity, simple formulations (saline) and a long duration of action. The following experiments highlight the discovery and characterization of antisense oligonucleotides (ASOs) targeting the mouse rhodopsin gene.

Methods: In-vitro ASO identification: ASOs were screened for reduct of rhodopsin expression in M-3 cells after electroporation. Rhodopsin mRNA levels were measured by RT-PCR and normalized to GAPDH. In vivo: Age matched Balb/C or C57BL/6 mice were IVT (intravitreal) injected with 1 ul of various concentrations of ASOs or PBS and sacrificed at various time-points. Eyes were encuclated for histology and retinas wrinkled for RT-PCR RNA analysis.

Results: In-vitro screening identified a number of potent ASOs targeting rhodopsin. Twelve of the most active ASOs were tested in-vivo by IVT delivery to demonstrate RNA reduction in C57BL/6 mice. Oligo Staining of treated mouse retinas revealed ASO distribution in all the cellular layers of the eyes, including the photoreceptor layer, inner and outer nuclear layers and the RPE. The in vivo screen identified several active ASOs, with ISIS 563334 producing the best rhodopsin mRNA reduction, approximately 60 ± 7% as compared to age matched saline injected eyes 7 days after the 50ug injection. Rhodopsin protein levels measured by IHC showed reductions within the photoreceptor layer and in the outer nuclear layer. Also western blot analysis showed similar reductions to those measured by RNA. Duration of action studies were performed using two ASOs targeting different regions of the mouse rhodopsin gene, demonstrated a long half-life of approximately 2 months following a single IVT injection in C57BLK6 mice.

Conclusions: Antisense technology represents an ideal ocular drug discovery platform. Here we describe the identification of murine ASO targeting rhodopsin gene, the cellular uptake in the rod photoreceptor cells and the long duration of action after a single injection. Our results support the use of ASOs for the treatment of retinal disorders.

Commercial Relationships: Ali Jazayeri, ISIS PHARMACEUTICALS (E); Raechel Peralta, Isis Pharmaceuticals, Inc. (E); Andy Watt, Isis Pharmaceuticals (E); Susan Freier, Isis Pharmaceuticals (E); Gene Hung, None; Bea DeBrosse-Serra, None; Shuling Guo, Isis Pharmaceuticals (E); Sue F. Murray, Isis Pharmaceuticals (E); Michael L. McCabe, Isis Pharmaceuticals (E); Brett P. Monia, Isis Pharmaceuticals, Inc. (E)

Program Number: 654 Poster Board Number: D0176
Presentation Time: 10:30 AM - 12:15 PM
Photoreceptor Vision and Structure in LCA1 caused by Mutations in GUCY2D
Purpose: The GUCY2D gene encodes retinal membrane guanylyl cyclase (RetGC1), a key component of the phototransduction machinery in photoreceptors. Mutations in GUCY2D cause Leber congenital amaurosis type 1 (LCA1), an autosomal recessive human retinal blinding disease. The effects of RetGC1 deficiency on human rod and cone photoreceptor structure and function are currently

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unknown.

**Methods:** We characterized a cohort of patients (ages 6 mos - 37 yrs) with GUCY2D mutations using spectral-domain OCT, full-field electroretinogram (ERG), full-field stimulus testing (FST), dark- and light-adapted chromatic static threshold perimeter, and direct transient pupillary light reflex (TPLR). Adaptation of rod- and cone-mediated vision to increasing levels of background lights was quantified with FST. A mobility performance task was used to quantify the ability of the patients to move through an indoor obstacle course under different ambient illuminations.

**Results:** Analyses of retinal architecture by SD-OCT indicated intact rod photoreceptors in all patients; foveal cones showed abnormalities. By functional phenotype, there were patients with and without detectable cone vision. Rod vision could be unexpectedly retained but the extent of rod vision did not correlate with that of cone vision or age. In patients without detectable cone vision, rod vision continued to function unsaturated under bright ambient illumination. The differences in cone function, but not rod function, were explained by the in vitro biochemical activity of the mutants.

**Conclusions:** We postulate a relationship between the level of RetGC1 activity and the degree of cone vision, and argue for cone function being the efficacy outcome measure in clinical trials of gene augmentation therapy in LCA1.

**Commercial Relationships:** Artur V. Cideciyan, None; Samuel G. Jacobson, None; Igor V. Peshenko, None; Alexander M. Sumaroka, None; Elena V. Olshevskaya, None; Alejandro J. Roman, None; Sam Sadigh, None; Elise Heon, None; Edwin M. Stone, None; Alexander M. Dizhoor, None

**Support:** FFB-CRI; NEI grant EY11522; Hope for Vision; Macula Vision Research Foundation; The Chatlos Foundation; RPB; and Pennsylvania Department of Health.

**Program Number:** 655 Poster Board Number: D0177
**Presentation Time:** 10:30 AM - 12:15 PM

**High-resolution Imaging of Retinal Structure in Retinitis Pigmentosa and Usher Syndrome**

**Christopher Langlo 1, Derek Denney 1, Robert F. Cooper 2, Dennis P. Han 3, David V. Weinberg 4, Judy E. Kim 4, Alfredo Dubra 4, Kimberly E. Stepien 1, Thomas B. Connor 2, Joseph Carroll 1, 3, 6**

1Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin, Milwaukee, WI; 2Biomedical Engineering, Marquette University, Milwaukee, WI; 3ophthalmology, Medical College of Wisconsin, Milwaukee, WI; 4Biophysics, Medical College of Wisconsin, Milwaukee, WI.

**Purpose:** Retinitis Pigmentosa (RP) and Usher Syndrome (USH) are progressive retinal degenerations that are clinically and genetically heterogeneous. This study aims to use reflectance Adaptive Optics Scanning Light Ophthalmoscopy (AOSLO) to examine the photoreceptor mosaic in RP and USH.

**Methods:** Eighteen subjects were recruited (4 USH, 14 RP), with 11 subjects having clinically detectable Cystoid Macular Edema (CME). In 6 subjects, total, Outer Nuclear + Henle’s Fiber layer (ONL+HFL), and inner retinal thickness were measured using SD-OCT images acquired through the fovea. Subjects were imaged using an AOSLO, and inner retinal thickness were measured using semi-automated cone counting software. DNA samples were acquired for 15 subjects.

**Results:** DNA testing identified mutations in 6 of the RP subjects. Consistent with previous findings, subjects with RP and USH had near-normal retinal thickness centrally with significant thinning in the perifovea. The ONL+HFL width was diminished with normal inner retinal thickness. On average, the subjects with USH had a greater reduction in retinal thickness than did the subjects with RP. In images of the parafoveal cone mosaic, subjects with USH had many presumed non-waveguiding cones, while subjects with RP had contiguous cone mosaics. Average cone density in the subjects with RP at 0.65 degrees from the fovea was 63.865 cones/mm² (n=3), comparable to previously reported normative values (72,528 cones/mm²). In contrast, the average cone density in the subjects with USH was 45,475 cones/mm² (n=4). All subjects imaged had areas devoid of visible photoreceptors where the RPE mosaic could be visualized in reflectance. The mean spacing of the RPE cells was 17.6μm, which agrees with previous findings in AOSLO and histologic estimates. Follow-up images in a subject with RP revealed no change in parafoveal cone density over a period of 16 months.

**Conclusions:** AOSLO imaging reveals different photoreceptor phenotypes in USH and RP. Though cone density varied, no differences in acuity or visual sensitivity were seen. While issues like CME and cataract remain barriers to imaging many individuals with RP and USH, the ability to repeatedly image single locations with AO will allow longitudinal tracking necessary for clinical trials of treatments for RP and USH.

**Commercial Relationships:** Christopher Langlo, None; Derek Denney, None; Robert F. Cooper, None; Dennis P. Han, None; David V. Weinberg, Regeneron (F); Judy E. Kim, None; Alfredo Dubra, US Patent No: 8,226,236 (P); Kimberly E. Stepien, None; Thomas B. Connor, None; Joseph Carroll. Imagine Eyes, Inc. (S)

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**Program Number:** 656 Poster Board Number: D0178
**Presentation Time:** 10:30 AM - 12:15 PM

**Identification of a novel mutation in the PRCD gene causing autosomal recessive retinitis pigmentosa in a Turkish family Ditta Zobor 1, Johanna Pacht 2, Florian Gekeler 2, Susanne Kohl 2**

1Institute for Ophthalmic Research, Centre for Ophthalmology, Tuebingen, Germany; 2Institute for Ophthalmic Research, Moleculat Genetics Laboboratory, Tübingen, Germany.

**Purpose:** Progressive rod-cone degeneration (PRCD) is a canine form of autosomal recessive photoreceptor degeneration and serves as an animal model for human retinitis pigmentosa (RP). To date only two RP-causing mutations of the PRCD gene have been reported in humans. We found a novel homozygous nonsense mutation in PRCD (c.52C>T, p.R18X) in three siblings affected by RP and present detailed morphologic and functional parameters.

**Methods:** Complete ophthalmological examination was performed including psychophysical tests (ETDRS visual acuity, Lanthony Panel D-15 color vision test and visual field) and electrophysiology (Ganzfeld and multifocal ERG). Additionally, color and infrared fundus photography, autofluorescence and spectral domain optical coherence tomography (OCT) recordings were performed.

**Results:** We identified a novel homozygous mutation in PRCD (c.52C>T, p.R18X) by diagnostic high-throughput panel sequencing. All three patients showed an advanced stage of disease with reduced visual acuity (mean VA: 20/80), small residual visual fields (mean VF for target III: 1143.34 deg2) and no recordable electrophysiological responses. Myopia, posterior subcapsular cataract, bone-spicule-like pigmentation and attenuated arterioles were typical findings. Interestingly, bulls eye maculopathy (BEM) due to patchy retinal pigment epithelium (RPE) atrophy was also present in all patients. The mean central retinal thickness (CRT) observed in OCT was 148μm.

**Conclusions:** The identification of a third mutation in PRCD confirms its role in the pathogenesis of RP. Clinical findings were in...
line with the morphological changes observed in previous studies. BEM seems to be a hallmark for RP due to mutations in PRCD.

**Commercial Relationships:** Ditta Zobor. None; Johanna Pach. None; Florian Gekeler. Retina Implant AG (F), OkuVision GmbH (F). Retina Implant AG (C), Retina Implant AG (P); Susanne Kohl. None

**Support:** The genetic analysis was funded by a BBMF grant (01GM1108 A) for SK.

**Program Number:** 657 Poster Board Number: D0179
**Presentation Time:** 10:30 AM - 12:15 PM
**Comparison of spectral domain optical coherence tomography images in cone rod dystrophy and rod cone dystrophy**

**Purpose:** To compare the pathologic changes in eyes with cone rod dystrophy (CRD) and rod cone dystrophy using spectral domain optical coherence tomography (SDOCT).

**Methods:** We investigated 35 eyes of 35 patients with CRD. As a control, we included visual acuity-matched patients with rod cone dystrophy. Visual acuity, mean deviation measured with Humphrey perimeter, amplitude of rod-, combined-, cone-, and flicker- ERG, and central retinal thickness was compared between the groups. The SDOCT findings including the presence or the absence of external limiting membrane (ELM), inner segment / outer segment junction (IS/OS), or cone outer segment tips (COST) was judged and compared.

**Results:** Patients with CRD were younger than visual acuity-matched patients with rod cone dystrophy (51.7 ± 14.6 vs 60.2 ± 10.7 year old, P = 0.01) and showed preserved amplitude in ERG (P < 0.001 in all components). COST was less frequently observed in CRD compared to rod cone dystrophy (0 cases (0 %) vs 7 cases (20 %), P=0.011). In addition, SDOCT revealed subretinal hyporeflective space more frequently in CRD (9 cases (25.7 %) vs 2 cases (5.7 %) P = 0.045).

**Conclusions:** The difference of SDOCT findings between CRD and rod cone dystrophy was most prominent in the presence or absence of COST. In addition, subretinal hyporeflective space was more frequently observed in eyes with CRD. The findings should reflect the pathologic process of cone dominant degeneration in the disease.

**Commercial Relationships:** Akio Oishi. None; Ken Ogino. None; Yukiko Makiyama. None; Masafumi Kurimoto. None; Maho Oishi. None; Norimoto Gotoh. None; Nagahisa Yoshimura. Canon (C), Canon (F), Nidek (C), Topcon (F), PCT/JP2011/073160 (P)

**Program Number:** 659 Poster Board Number: D0181
**Presentation Time:** 10:30 AM - 12:15 PM
**Screening of PRPH2/ RDS in patients with autosomal dominant retinitis pigmentosa reveals novel disease-causing mutations and 8.6% prevalence in French population**

**Purpose:** To determine the prevalence of mutations in peripherin-2/retinal degeneration slow (PRPH2/RDS) gene in a cohort of 245 French families with autosomal dominant retinitis pigmentosa (adRP).

**Methods:** Clinical investigations included visual field testing, fundus examination, OCT, autofluorescence testing and ERG recording. The 3 coding exons and adjacent intronic sequences of PRPH2/RDS were screened by Sanger sequencing. Genotyping was performed using microsatellite markers between D6S1575 and D6S1650 spanning approximately 3 Mb around PRPH2/RDS gene.

**Results:** Twelve - 5 novel and 7 previously described - mutations were found for 21 families (8.6%), including 3 missense (p.Asp194Glu, p.Trp246Cys and p.Leu254Gln), 1 frameshift (p.Val69CysfsX30) and 1 splice site (c.829-4C>G) novel mutations. They all co-segregated with the disease phenotype, and the novel mutations were not identified in ethnically matched controls. The severity of the disease was moderate with penetration variations. Some patients showed vitelliform deposits or macular involvement. The novel p.Leu254Gln was found in 4 families originating from the same geographic origin. Affected patients shared the same haplotype suggesting a founder effect. One affected subject was homozygous. A novel splice-site mutation, c.829-4C>G, found in 3 families, was predicted to create a new acceptor splice site 3 bp upstream the
natural splice site, leading to the in-frame insertion of a glutamine, p.Glu276_Val277insGln. The haplotypes of the 3 families were different.

**Conclusions:** The mutations in PRPH2/RDS account for 8.6% of adRP in the French population, making this gene a major cause of adRP in France after rhodopsin. This prevalence is higher than previously reported (1.3 to 2.9%), possibly because of underdiagnosed family members with mild disease, leading to erroneously classify them as simplex cases.

**Commercial Relationships:** Gael Manes, None; Claire-Marie Dhaenne, None; Werner L. Vos, None; Isabelle S. Audo, None; Xavier Zanlonghi, None; Sylvie Odent, None; Helene Dollus, None; Beatrice Bocquet, None; Isabelle Meunier, None; Christian P. Hamel, None

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**Program Number:** 660 Poster Board Number: D0182
**Presentation Time:** 10:30 AM - 12:15 PM
**Correlation of morphology and function in a mouse model of X-linked retinitis pigmentosa**
Dorothee Roell, Jutta U. Schlegel, Christoph Friedburg, Birgit Lorenz, Knut Stieger. Department of Ophthalmology, Justus-Liebig-University, Giessen, Germany.

**Purpose:** Retinitis pigmentosa (RP) is a heterogeneous group of hereditary disorders. In humans, over 80% of X-linked retinitis pigmentosa (XLRP) cases are caused by point mutations in the ORF15 as a first step towards the development of therapeutic interventions.

**Methods:** Animals were investigated at different time points between 1 to 21 months of age. Morphological analysis was performed using immunohistochemistry with specific antibodies for rhodopsin, S- and LM-opsin on cryosections of the retinae. In addition fundus appearance and vascular structure of the retinae were investigated using fundus photography with additional fundus angiography using the Micron III camera (Phoenix Research Laboratories). To assess function, electroretinography (ERG) examinations were performed under scotopic and photopic conditions using the Espion e3 desktop system (Diagnosys LLC).

**Results:** Morphological analysis revealed diffuse, widespread white dots in the fundus of affected animals, appearing from the age of 6 months on. Immunohistochemical analysis showed delocalization of S-opsin as early as 3 months of age, increasing with age. ERG a- and b-wave amplitudes under both dark- and light-adapted conditions were moderately reduced starting at 6 months of age. This reduction continued progressively up to 21 months of age, when a-wave amplitudes were reduced to 20% of normal. Oscillatory potentials were present even at late stage of the disease.

**Conclusions:** This mouse model with a humanized point mutation in ORF15 of rpgr exhibits morphological alterations like opsin delocalization and fundus changes, and functional alterations in ERG recordings, both starting around the same age. Interestingly, the kinetics of the pathology appear to be milder compared to the human XLRP phenotype. This mouse model will make a substantial contribution to the development of a new therapeutic strategy for further retinal gene therapy trials.

**Commercial Relationships:** Dorothee Roell, None; Jutta U. Schlegel, None; Christoph Friedburg, None; Birgit Lorenz, Optos (F); Knut Stieger, None

**Support:** University Medical Center Giessen and Marburg

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**Program Number:** 661 Poster Board Number: D0183
**Presentation Time:** 10:30 AM - 12:15 PM
**Video Head Impulse Test in Retinitis Pigmentosa patients**
Carmela Carnevale1, Nicola Iozzo2, Mario Gagliardi2, Giuseppe Magliulo3, Roberto Grenga2. 1Ophthalmology, University of Rome “La Sapienza”, Rome, Italy; 2Otorhinolaryngology, Audiology and Phoniatrics, University of Rome “La Sapienza”, Rome, Italy.

**Purpose:** To evaluate peripheral vestibular deficits of the anterior, lateral or posterior semicircular canals in patients with Retinitis Pigmentosa (RP) and Usher Syndrome (USH) using the Video Head Impulse Test (VHIT) with Ulmer technique.

**Methods:** 12 patients, 4 male and 8 female (mean age 54 ± 14.7 years) were enrolled. We examined 24 eyes: 16 typical RP, 4 Usher Syndrome, 2 rod-cone dystrophy and 2 cone dystrophy. All patients underwent a complete ophthalmologic, audiologic and vestibular assessment. The ophthalmologic examination included measurement of best corrected visual acuity (BCVA) with Snellen visual acuity chart and conventional perimetry with the Humphrey Field Analyzer (SITA Standard, program 30-2 or 10-2, Goldmann size III stimuli).

The audiologic and vestibular protocols included audiology, caloric test, cervical vestibular evoked myogenic potential (cVEMPs), ocular vestibular evoked myogenic potential (oVEMPs) and VHIT.

**Results:** Mean BCVA was 0.6 ± 0.5 logMAR. Humphrey visual field showed a mean defect (MD) of -19.81 ± 11.25 dB for OD and -19.4 ± 11.65 dB for OS.

At audiometry five patients showed bilateral hypacusia (38.5%), one had age-related hearing loss (7.7%) and six presented (53.8%) normal audiometric curves.

Caloric test was abnormal in four participants (30.8%): three showed hypo-excitability on both sides and one on one side only. In ten patients there were bilateral preservation of cVEMPs that was absent in only one (8.3%). The unilateral and bilateral absence of oVEMPs was diagnosed in one (7.7%) and two (15.4%) patients respectively.

The VHIT wasn’t result reliable in two participants but in five there were a selective damage of semicircular canals: one patient with rod-cone and one with cone-dystrophy had an abnormal function of right and left superior semicircular canals; two with typical RP and one affected by Usher Syndrome presented, respectively, a right-sided deficit of the superior and posterior semicircular canals.

**Conclusions:** The vestibular analysis with video-HIT didn’t demonstrate any selective alteration in patients with RP or USH. The test didn’t show any association between the genetic disorder and vestibular deficit. Neither RP mutated genes or Usher’s genes can be associated with the altered results obtained with the video-HIT.

**Commercial Relationships:** Carmela Carnevale, None; Nicola Iozzo, None; Mario Gagliardi, None; Giuseppe Magliulo, None; Roberto Grenga, None
(GVFs) obtained in patients with inherited retinal degenerations.

**Methods:** GVs collected in 25 patients with moderate to severe visual field loss were scanned and presented on-screen to 10 normally-sighted subjects. The subjects had attended a 1 hr training session explaining the meaning of GVF isopters and the use of the digitization software. During digitization, users mouse-clicked on 5 cardinal points in the GVF grid to establish the horizontal and vertical scales, and then identified each contour as seeing or non-seeing, selected the size of the test light (1-4e through V-4e), and digitally placed the dots of the GVF isopters to the contours. The user repeated the contour process of placing the dots of the GVF isopters to the contours.

**Results:** Each isopter of each test field was analyzed independently to determine the mean retinal area reported by the program, inter- and intra-operator variance of these data, variance as percent of the mean, and the number of operator errors per presentation. Data were subsequently averaged across presented isopters to estimate the expected variances and error rates of GVF digitization. The average inter-operator variance of retinal area calculations was 0.68 ± 1.17 (mm² ± SD), or 2.38 ± 6.70 % of isopter area. Intra-operator variance was similar: 0.94 ± 1.78 mm² or 1.47 ± 2.51 %. Operators had an average error rate of 1.06 ± 1.08 errors per isopter.

**Conclusions:** These results demonstrate that GVF digitization, with minimal training, produces consistent and repeatable retinal area measurements with reasonably small variance. In light of these data, GVF digitization can and will be used to track changes in visual fields of subjects with inherited retinal degenerations, ultimately to demonstrate the efficacy of treatments in clinical trials. Multiple operators and readers will be required to ensure proper labeling and completion of isopters in clinical trials. Data collection will continue to more accurately define the intrinsic variances of these methods.

**Commercial Relationships:** Michael P. Barry, Second Sight Medical Products, Inc. (F), QLT Inc. (F); Liancheng Yang, None; Rebecca Marcus, None; Gislin Dagniclie, None

**Support:** Grant information

**Program Number:** 663 Poster Board Number: D0185

**Presentation Time:** 10:30 AM - 12:15 PM

**A new mouse model for Fam161a-associated retinal ciliopathy Marcus Karlstetter1, Albert Caramoy1, Alexander Aslanidis1, Eva Scheiffert1, Nadine Bremicker1, Herbert Jägle2, Thomas Langmann2, Eva Scheiffert1, Nadine Bremicker1, Herbert Jägle1, Thomas Langmann2

**Department of Ophthalmology, University of Cologne, Cologne, Germany; 2Department of Ophthalmology, University Medical Center Regensburg, Regensburg, Germany.

**Purpose:** Retinitis Pigmentosa (RP) is an inherited retinal degenerative disease leading to progressive vision loss. Nonsense mutations in the photoreceptor-specific Fam161a gene causes RP-28 associated autosomal-recessive RP. Recent studies have shown that Fam161a is a ciliary protein and critically involved in microtubule formation. The goal of this study was the generation of a Fam161a-deficient mouse line to study pathomechanisms involving Fam161a deficiency in the murine retina.

**Methods:** Fam161a gene trap mice were generated from UPA-vector targeted embryonic stem cells derived from the Canadian mouse mutant repository. Genomic locus and orientation of the gene trap in embryonic stem cells were confirmed by sanger sequencing of genomic DNA. Germline transmission of the gene trap was analyzed by PCR-based genotyping and Fam161a expression was studied by qRT-PCR in various tissues. The retinal morphology of Fam161a-deficient mice was analyzed by optical coherence tomography (OCT) and immunohistochemistry.

**Results:** We could confirm a unique gene trap insertion in exon 3 of the Fam161a gene resulting in nonsense mediated mRNA decay. The gene trap was successfully transmitted to the germline of chimeric founder animals and was also detected in all offspring animals. OCT-phenotyping of Fam161a-deficient retinas revealed significant thinning of the retina compared to age-matched littermates. A further detailed temporal histological analysis of Fam161a-deficient retinas showed complete loss of the outer retinal layers in 6 month old animals.

**Conclusions:** In this study we generated and characterized a novel Retinitis Pigmentosa mouse model with Fam161a deficiency. This model could be a useful tool to study Fam161a-associated retinal ciliopathy.

**Commercial Relationships:** Marcus Karlstetter, None; Albert Caramoy, Bausch & Lomb (F), Fluoron GmbH (F), Alamedics GmbH&Co. KG (F); Alexander Aslanidis, None; Eva Scheiffert, None; Nadine Bremicker, None; Herbert Jägle, None; Thomas Langmann, None

**Support:** German Research Foundation DFG/ LA 1203-8-1

**Program Number:** 664 Poster Board Number: D0186

**Presentation Time:** 10:30 AM - 12:15 PM

Modulation of Cellular Signaling Pathways in P23H Rhodopsin Rat Retina

Vishal M. Shinde1, Olga Sizova2, Marina S. Gorbatyuk2, 1Vision Science, University of Alabama, Birmingham, AL; 2cell biology, University of north texas health science center, fort worth, TX.

**Purpose:** The activation of the unfolded protein response (UPR) in P23H rhodopsin (RHO) retinas with autosomal dominant Retinitis Pigmentosa (ADRP) has been reported previously by our lab. In this study we examined the modulation of autophagy, mTOR/akt pathway, Bcl2 family proteins, Ca2+-based toxicity and mitochondria associated apoptosis in ADRP retina.

**Methods:** The RNA and protein extracts were obtained from P21, P30 and P40 P23H RHO (line 3) and Sprague Dawley rat retinas, qRT-PCR and western blot analysis were performed to analyze the modulation of cellular signaling, Calpain m, µ activity assay was conducted to determine the level of active calpains in degenerating retina. Mitochondria and cytosolic fractions of ADRP retina were separated to detect release of the cytochrome C and AIF and translocation of pro-apoptotic BAX protein to the mitochondria.

**Results:** Our results showed that the autophagy- associated proteins ATG5 and Lamp2 were significantly down-regulated by 33% and 31% in P30 P23H RHO retina, while the mTOR signaling was highly activated by 290% and 430% at P30 and P40 respectively. The level of pro-survival pAKT was found to be significantly down-regulated by 75% and 44% at P30 and P40, respectively. Our data also revealed that the Ca2+-induced caspase-12 cleavage was significantly increased by 2.6-fold in P30 P23H RHO retinas. At same point time we also observed that the level of anti-apoptotic Bcl-xL protein was down-regulated by 0.6 fold and the level of pro-apoptotic Bax protein was up-regulated by 136 fold. Another pro-apoptotic protein Puma was elevated by 1.7-fold in P40 P23H RHO retina. Release of the cytochrome C and AIF to the cytosol and translocation of the BAX protein to the mitochondria of P23H RHO photoreceptors was observed in P21 and P40 ADRP retina, respectively which led to elevation of activated caspase-3, 7 and 9 by 1.5 fold, 2 fold and 1.49 fold.

**Conclusions:** This study gives important insight to the activation and alteration of cellular signaling pathways in P23H RHO photoreceptors and validated the mTor and calpains as therapeutic targets for ADRP treatment.

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Changes to the Transition Zone with Progression of X-Linked Retinitis Pigmentosa

Rebecca B. Bausell1, Rithambara Ramachandran4, Cindy X. Cai2, Kirsten G. Locke2, David G. Birch2,4, Donald C. Hood2,3. 1Department of Ophthalmology, University of Texas Southwestern Medical Center, Dallas, TX; 2College of Physicians & Surgeons, Columbia University, New York, NY; 3Rose-Silverthorne Retinal Degenerations Laboratory, Retina Foundation of the Southwest, Dallas, TX; 4Department of Psychology & Ophthalmology, Columbia University, New York, NY.

Purpose: A cross-sectional analysis of the transition zone (TZ), the region between healthy and severely affected retina, is thought to be a model of disease progression in patients with retinitis pigmentosa (RP).[1-4] Here we analyze TZ changes in a group of x-linked (xl)RP patients over time.

Methods: Two 9mm horizontal line scans, taken with optical coherence tomography, were obtained for one eye of 28 xRP patients (15.2 ±6.1 yrs) at least 2 years apart (mean 2.4 yrs). Using a computer-aided manual procedure, outer segment (OS) and outer nuclear layer (ONL) thicknesses were measured.[3] As previously described,[3] to quantify changes across the fovea, the TZ was divided into regions A-E based upon the thicknesses of the OS and ONL relative to healthy controls. Region A: OS and ONL normal; B: OS reduced, ONL normal; C: OS and ONL reduced; D: ONL reduced, OS gone; E: ONL reduced to asymptotic thickness. We compared changes in the TZ regions between the first and last visit based upon: 1) location (distance from fovea) and 2) width. Region A was not analyzed as it was absent in 84% of patients. To determine changes in the TZ with eccentricity, patients were also placed in two groups based upon distance of the border between C and D (the point that OS disappears) from the fovea. Nasal and temporal measurements were averaged and paired t-tests were performed.

Results: As expected, given the central progression of xLRP, the location of regions C (p=.054), D (p<.001) and E (p=.004) shifted towards the fovea (diagonal lines in Fig. 1). Concurrently, the widths of B and C decreased, while D and E expanded (Fig.1). At the final visit, the widths of B and C were narrower, while D and E were wider, in those with C/D borders closer, as compared to farther, from fixation (Fig. 2).

Conclusions: The TZ exhibits consistent changes with time. All borders move closer to the fovea, and the widths of regions (B & C) with the OS layer present decrease, while regions (D & E) without a detectable OS layer expand. Further, changes in the relative size of these regions with eccentricity are consistent with changes over time and support the TZ as a model of disease progression. 1. Jacobson et al. IOVS, 2009, 2. Jacobson et al. IOVS, 2010, 3. Hood et al. IOVS, 2011, 4. Lazow et al. IOVS, 2011.

Commercial Relationships: Rebecca B. Bausell, None; Rithambara Ramachandran, None; Cindy X. Cai, None; Kirsten G. Locke, None; David G. Birch, Acucela (C), QLT (C), Neurotech, USA (C); Donald C. Hood, Topcom, In (F)

Support: NIH/NEI ROI-09076
up interval being 9.1 years. 42% of type 1 showed enlargement of atrophy to progress to type 2. 12% of type 2 progressed to type 3. Median RAE (deg²/yr) based upon baseline AF subtypes was statistically significantly different: 0.70 in type 1, 7.46 in type 2, and 48.51 in type 3. ABCA4 variants were identified in 57 patients. There was a significant association between AF subtype and genotype.

**Conclusions:** The AF pattern at baseline influences the rate of atrophy progression and has genetic correlates. These data are likely to facilitate the study design and monitoring of therapeutic interventions.

AF images of a representative case at baseline and follow-up are shown.

**Commercial Relationships:** Kaoru Fujinami, None; Noemi Lois, None; Rajarshi Mukhopadhyay, None; Vikki A. McBain, None; Kazushige Tsunoda, None; Kazuo Tsubota, AcuFocus, Inc (C), Allergan (F), Bausch Lomb Surgical (C), Functional visual acuity meter (P), JINS (P), Kissei (F), Kowa (F), Santen, Inc. (F), Otsuka (F), Pfizer (C), Thea (C), Echo Denki (P), Nidek (F), Ophitecs (F), Wakasa Seikatsu (F), CEPT Company (P); Fred W. Fitzke, None; Anthony T. Moore, None; Andrew R. Webster, None; Michel Michaelides, Novartis (R)

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**Program Number:** 667

**Presentation Time:** 10:30 AM - 12:15 PM

**The Prevalence Of Residual Visual Field Islands In Retinitis Pigmentosa**

Mary Varsamidis¹, Chi D. Luu¹, ², Peter N. Dimitrov⁴, ², Robyn H. Guymer³, ², Lauren N. Ayton³, ²

¹Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, East Melbourne, VIC, Australia; ²Ophthalmology, University of Melbourne, Melbourne, VIC, Australia.

**Purpose:** Accurate assessment of pre-implant residual visual function is critical for patient selection and determining the efficacy of treatment in retinal prostheses. However this is difficult at very low levels of vision as small areas of residual vision can be hard to detect. The purpose of this study was to determine the prevalence of small islands of peripheral visual field in a group of subjects with Retinitis Pigmentosa (RP).

**Methods:** 49 subjects with RP (55% male, mean age= 56 ±14 years, visual acuity= 6/6 to light perception) were recruited for our Bionic Eye study. Clinical examination was performed using a battery of tests including electroretinography (ERG) and perimetry. Retinal function was assessed using an ISCEV standard full-field ERG protocol. Goldmann kinetic perimetry was performed on both eyes using the smallest white light target size that the subject was able to detect. Visual field islands were defined as any residual areas of vision further than 10 degrees from fixation. The percentage of residual visual field (RVF) islands was estimated using ImageJ software.

**Results:** Four participants were excluded from analysis due to poor fixation (n=1) and intermittent, unreliable visual fields (n=3). Of the remaining 45 participants (90 eyes), 38 (84%, 95% CI= 71-94%) had some measurable visual field using at least the V4e target. Of these

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83 participants (76 eyes), 25 eyes (33%, 95% CI: 23-45%) displayed peripheral islands of vision. 10 of these eyes (40%, 95% CI: 21-61%) had no remaining central vision and 15 eyes (60%, 95% CI: 39-79%) exhibited residual central vision with the addition of one or more peripheral islands. The mean size of the islands was 4.65 ±0.08% with a range of 0.06% to 26.82% of RFV. Clinically detectable ERG responses were observed in 6 eyes (24%, 95% CI: 9-45%) and the remaining 19 eyes had no detectable ERG response (76%, 95% CI: 55-91%), despite having residual islands of vision.

**Conclusions:** Measurement of visual function in patients with end stage RP is extremely difficult as remaining peripheral islands of vision can be missed if we rely only on central visual acuity or ERG. This study has shown that a significant proportion (76%) of patients with a clinically undetectable ERG response still have measurable peripheral visual field islands demonstrating the importance of Goldmann perimetry in the evaluation of residual visual function.

**Commercial Relationships:** Mary Varsamidis, None; Chi D. Luu, None; Peter N. Dimitrov, None; Robyn H. Guymer, Ellex Pty Ltd (F), Novartis (C), Bayer (C), Novartis (R); Lauren N. Ayton, None

**Support:** This research was supported by the Australian Research Council (ARC) through its Special Research Initiative (SRI) in Bionic Vision Science and Technology grant to Bionic Vision Australia (BVA)

**Program Number:** 669 Poster Board Number: D0191

**Presentation Time:** 10:30 AM - 12:15 PM

**Follow-up Of 36 Years In Autosomal Dominant Gyrate-Atrophy Like Choroidal Dystrophy**

Ulrich Kellner1,2, Simone Kellner1,2, Silke Weinitz1,2, Gazaleh Farmand3, Heidi Stoehr3, Bernhard H. Weber3. 1Rare Retinal disease Center, AugenZentrum Siegburg, MVZ ADTC Siegburg GmbH, Bonn, Germany; 2RetinaScience, Bonn, Germany; 3Institute for Humane Genetics, Regensburg, Germany.

**Purpose:** To report the long-term course in a family of autosomal dominant gyrate-atrophy like choroidal dystrophy and the results of molecular genetic testing.

**Methods:** We initially reported a family with an affected father and two affected sons with autosomal dominant gyrate-atrophy like choroidal dystrophy [Kellner et al 1997]. The father was lost two follow-up due to stroke and one son due to brain tumor. The second son could be re-examined at different time intervals since 1994. In addition to clinical examination he underwent visual field testing, multifocal and full-field ERG recording according to ISCEV standards (RETIscan, Roland Consult, Germany), high resolution OCT (SD-OCT; Spectralis OCT, Heidelberg Engineering, Germany), wide-angle fundus and near-infrared autofluorescence (FAX, NIA; HRA2, Heidelberg Engineering, Germany) and molecular genetic testing.

**Results:** The affected father showed severe choroidal atrophy with a residual visual field and a visual acuity of 0.1 at the age of 70 years. Both sons presented with marked peripapillary and midperipheral choroidal atrophy. Ormithin blood levels were normal in all patients. In the index patient first signs of choroidal atrophy nasal to the optic disc were documented at 19 years of age. 36 years later visual acuity was normal on both eyes. Choroidal atrophy had progressed circumferentially involving the peripapillary part of the macula. FAX, NIA and SD-OCT were normal in the non-affected areas, with a sharp border towards the affected areas. Affected areas showed absence of FAX, NIA and a complete loss of outer retinal structures in the SD-OCT. Visual field loss and ERG amplitude reduction progressed corresponding to the slow advance of choroidal atrophy. RetChip v1.0 based genetic testing of 43 genes known to be associated in retinal dystrophies identified a heterozygous, probably pathogenic missense mutation in PDE6A (rs114973968), a gene associated with autosomal recessive retinitis pigmentosa.

**Conclusions:** Autosomal dominant gyrate-atrophy like choroidal dystrophy shows a slow progression with preservation of the foveal area until late adulthood. Molecular genetic findings are currently insufficient to clarify the molecular basis of this rare retinal dystrophy.

**Commercial Relationships:** Ulrich Kellner, None; Simone Kellner, None; Silke Weinitz, None; Gazaleh Farmand, None; Heidi Stoehr, None; Bernhard H. Weber, None

**Program Number:** 670 Poster Board Number: D0192

**Presentation Time:** 10:30 AM - 12:15 PM

**A Comparison of Methods For Tracking Progression in Patients with X-Linked Retinitis Pigmentosa Using Frequency Domain OCT**

Rithambha Ramachandran1, Lisa Zhou1, Kirsten G. Locke1, David G. Birch1, Donald C. Hood1,2, 1Psychology, Columbia University, New York, NY; 2Ophthalmology, Columbia University, New York, NY; 3Retina Foundation of Southwest, Dallas, TX.

**Purpose:** Frequency domain optical coherence tomography (fdOCT) holds promise as a method for following disease progression in clinical studies of retinitis pigmentosa (RP). [1-3] To compare the efficacy of different outer retinal measures, patients with x-linked (xl) RP were followed over time.

**Methods:** 26 xIRD patients (15±6yrs), with regions of healthy central retina and flicker ERG responses greater than 0.3 μV, were studied with fdOCT (Spectralis, Heidelberg). All patients had 9mm horizontal and vertical line scans, and macular volume scans recorded using automated tracking. By manually correcting an automated segmentation program,[3] outer segment (OS), outer nuclear layer (ONL), retinal pigment epithelium (RPE), and total receptor (TotRec) volumes were determined. The ISe contour (black border in Fig. 1, i.e. the location where OS thickness decreases to zero, was marked on all scans. Three parameters were derived from the ISe contour: its horizontal midline width (HW), its vertical midline width (VW), and the area (A) within the contour. Initial and final values over an approximate 2-year period were compared with paired t-tests.

**Results:** OS, ONL and RPE volumes were not significantly different between initial and final visits (Table 1), although TotRec volume did show a marginally significant decrease with time (p = .02). On the other hand, all ISe measures showed changes that were markedly significant (p<0.003). On the cube scan, the ISe HW moved inwards (23/26 patients) by about 10% a year, while the VW moved inwards (25/26 patients) by about 16% a year. The area within the ISe contour was reduced (25/26 patients) on average by 21.7% a year. The horizontal (ISe HW) and vertical (ISe VW) line scan measures had t-scores in the same range as the volume scan measures (Table 1).

**Conclusions:** Measures of the ISe contour are more effective in detecting disease progression than are outer retinal volume measures. Given the similar effectiveness of line and volume scans, the ISe width on vertical and/or horizontal line scans provides the quickest and most effective clinical method for tracking progression in xIRD. 1. Hood et al., Biomed Opt Express, 2011; 2. Locke et al., ARVO, 2012; 3. Yang et al., Biomed Opt Exp, 2011.
Fig.1 OS and ONL volume maps for one patient.

Table 1. t-statistics for all 9 methods. *p<0.05, **p<0.003

<table>
<thead>
<tr>
<th>Method</th>
<th>t-statistic</th>
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<tr>
<td>OS volume</td>
<td>0.56</td>
</tr>
<tr>
<td>ONL volume</td>
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</tr>
<tr>
<td>RPE volume</td>
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<tr>
<td>RetRec volume</td>
<td>1.98**</td>
</tr>
<tr>
<td>De HW</td>
<td>5.67**</td>
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<tr>
<td>De WV</td>
<td>4.53**</td>
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<td>De A</td>
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Table 1. Method

Program Number: 672 Poster Board Number: D0194
Presentation Time: 10:30 AM - 12:15 PM

Therapeutic Effect of Prolonged Treatment with Topical Dorzolamide for Cystoid Macular Edema in Patients with Retinitis Pigmentosa

Yasuhiro Ikeda, Noriko Yoshida, Shoji Notomi, Yusuke Murakami, Toshiro Hisatomi, Hiroshi Enaida, Tatsuro Ishibashi. Dept. of Ophthalmology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan.

Purpose: To evaluate the therapeutic effect of long-term treatment with topical dorzolamide (a carbonic anhydrase inhibitor) for cystoid macular edema (CME) associated with retinitis pigmentosa (RP).

Methods: Eighteen eyes in 10 patients with CME secondary to typical forms of RP were included. Baseline visual acuity, visual field, and optical coherence tomography (OCT) measurements were obtained for all patients. All patients used 1% dorzolamide three times daily in each affected eye. Patients underwent follow-up exams at 1, 3, 6, 12, and 18 months after treatment. The response to treatment was monitored by visual acuity and visual field measurement testing using the Humphrey Field Analyzer (HFA: the central 10-2 Program); in addition, foveal thickness was measured by OCT. Evaluation of “macular sensitivity” was calculated by HFA as the average of twelve central points.

Results: At the end of the observation period, the “macular sensitivity” in 10 eyes (55.6%) in which CME was almost completely resolved was significantly improved (p<0.05). In eight (88.9%) of the 9 eyes in which CME was almost completely resolved within 6 months, the therapeutic efficacy persisted through 18 months. Six eyes (33.3%) showed an initial response and a subsequent rebound of CME. Two eyes showed no response. No severe side effects were observed.

Conclusions: The prolonged use of topical dorzolamide is effective and safe for the treatment of CME in patients with RP. Therefore, we propose topical dorzolamide as a first-line treatment.


Support: This work was supported in part by a Grant-in-Aid (to YI and TI) from the Japanese Ministry of Education, Culture, Sports, Science, and Technology (#24659763 and #24659764).

Clinical Trial: UMIN000005852

Program Number: 672 Poster Board Number: D0194
Presentation Time: 10:30 AM - 12:15 PM

Caspase-7 Ablation Protects the T17M Rhodopsin Mice from Severe Retinal Degeneration through Reprogramming of the UPR and inhibition of TRAF2-JNK Apoptosis

Shreyasi Choudhury1, Yogesh Bhootada1, Oleg Gorbatyk2, Marina S. Gorbatyk1, 2. 1Cell Biology And Anatomy, Univ of North Texas Hlth Sci Ctr, Fort Worth, TX; 2Department of Molecular Genetics and Microbiology, University of Florida, Gainesville, FL.

Purpose: We previously demonstrated that misfolded T17M rhodopsin (RHO) activates the Unfolded Protein Response (UPR) in mouse rod photoreceptor cells eventually leading to Autosomal Dominant Retinitis Pigmentosa. We also have shown that the ablation of the UPR-induced CASP-7 in T17M RHO transgenic mice slows down the rate of retinal degeneration measured by ERG and SD-OCT. Therefore, the goal of this study is to elucidate the molecular mechanisms involved in the preservation of vision in T17M RHO CASP7-/- retinas to validate new therapeutic targets.

Methods: In vitro and in vivo studies were conducted to elucidate the pathway by which CASP-7 ablation promotes the ADRP photoreceptor cell survival. RNA and protein extracts were obtained from the 661W cells co-transfected with either wt or T17M RHO plasmid and control or CASP-7 siRNA. Retinas were harvested from C57BL/6, T17MRHO, T17MRHO CASP7-/- mice at P30 to perform qRT-PCR and western blot analysis.

Results: The study of the cellular signaling in T17M RHO CASP7-/- retina demonstrated that the preservation of the structure and function of ADRP photoreceptors is occurred via down-regulation of the UPR-induced gene and protein expression. The ATF4, pAFT6, mTor and Hif1 proteins were down regulated by 55%, 57%, 31% and 77% correspondingly and the level of pAKT was elevated by 60% in T17M RHO CASP7-/- retina. In addition, the inhibition of PARP1 and TNFa proteins in T17M RHO CASP7-/- retina was observed. All together these modifications lead to diminishing the TRAF2 and p-c-Jun by 31%, 50% correspondingly. In vitro study also confirmed the modulation of cellular signaling observed in T17M RHO CASP7-/- retina.

Conclusions: Both in vivo and in vitro studies indicated that the ablation of CASP-7 in the T17M RHO retina prevents the deterioration of retinal function and structure through reprograming of the UPR and modulation of TRAF2-JNK-induced apoptosis. This reduction is believed to occur through the down-regulation of the
mTOR and Hif1a proteins. The inhibition of the PARP1 and TNFα proteins is also found to be responsible for diminishing the TRAF2-JNK apoptosis. In both scenarios, the reduction in c-Jun apoptosis leads to ADRP photoreceptor survival. This study points out c-Jun as a potential therapeutic target for ADRP treatment.

**Commercial Relationships:** Shreyasi Choudhury, None; Yogesh Bhojota, None; Oleg Gorbatyuk, None; Marina S. Gorbatyuk, None.

**Support:** R01EY020905, Foundation Fighting Blindness

**Program Number:** 673 Poster Board Number: D0195  
**Presentation Time:** 10:30 AM - 12:15 PM  
**Changes in Visual Function during 2-year Follow-up after UF 021 Therapy for Retinitis Pigmentosa**  
Yosuke Nakamura, Akira Hagiwara, Ken Kumagai, Shuichi Yamamoto. Chiba University Graduate School of Medicine, Chiba, Japan.

**Purpose:** We have reported that topical 0.15% unoprostone ophthalmic solution (UF-021) resulted in a dose-dependent improvement in the central retinal sensitivity in patients with retinitis pigmentosa (RP). The purpose of this study was to determine the changes in visual function 2-year after the end of the UF-021 treatment.

**Methods:** We studied 22 eyes of 22 RP patients who had been part of the origin 24-week clinical trial of UF-021. These patients had been randomly assigned to one of the three double-blind treatments: high dose (H, two drops/dose; n=6), low dose (L, one drop/dose; n=8), and placebo (P, n=8). The therapy was terminated in all the patients after the 24 week trial. We examined the mean retinal sensitivity of four central sites using the Humphrey Field Analyzer (HFA) 10-2 program, mean deviation (MD value), and the BCVA at the start and end of the clinical trial. These parameters were also measured 120 weeks after the completion of the trial.

**Results:** We studied 22 eyes of 22 RP patients who had been part of the origin 24-week clinical trial of UF-021. These patients had been randomly assigned to one of the three double-blind treatments: high dose (H, two drops/dose; n=6), low dose (L, one drop/dose; n=8), and placebo (P, n=8). The therapy was terminated in all the patients after the 24 week trial. We examined the mean retinal sensitivity of four central sites using the Humphrey Field Analyzer (HFA) 10-2 program, mean deviation (MD value), and the BCVA at the start and end of the clinical trial. These parameters were also measured 120 weeks after the completion of the trial.

**Conclusions:** The retinal sensitivity in the H group was maintained even 2 years after the UF-021 therapy was stopped. This suggests a long-term preservation of the visual sensitivity by UF-021.

**Commercial Relationships:** Yosuke Nakamura, None; Akira Hagiwara, None; Ken Kumagai, None; Shuichi Yamamoto, None

**Support:** None in the Support field below

**Program Number:** 674 Poster Board Number: D0196  
**Presentation Time:** 10:30 AM - 12:15 PM  
**Exome sequencing as a new approach for genetic screening in inherited retinal degeneration**  
Zi-Bing Jin¹,², Xiao-Feng Huang¹, Dong-Jun Xing¹. ¹Division of Ophthalmic Genetics, Wenzhou Medical College, Wenzhou, China; ²Lab. for Stem Cell & Retinal Regeneration, Wenzhou Medical College, Wenzhou, China.

**Purpose:** Inherited retinal degenerative (IRD) disease is a group of genetic retinal disorders and is a leading cause of inevitable blindness worldwide. Due to phenotypic and genetic heterogeneity, molecular diagnosis using traditional approach is very difficult. This study aimed to develop an approach based on next-generation sequencing to determine the genetic defects in IRD patients precisely and effectively.

**Methods:** One hundred and twenty unrelated Chinese IRD families with retinitis pigmentosa, Usher syndrome, cone dystrophy or Stargardt's disease, were recruited. A total of 285 known and additional genes of inherited retinal diseases were selected for deep exome resequencing.

**Results:** Through systematic data analysis using established bioinformatics pipeline and segregation analysis, a number of genetic variants were released. Over 60% families were successfully identified genetic defects.

**Conclusions:** In conclusion, this study revealed the genetic defects in a serial of disease genes and demonstrated the robustness of targeted exome sequencing to precisely and rapidly determine genetic defects. The methodology provides a reliable strategy for routine gene diagnosis of IRD.

**Commercial Relationships:** Zi-Bing Jin, None; Xiu-Feng Huang, None; Dong-Jun Xing, None

**Support:** National Key Basic Research Program (2013CB967502)

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segments was significantly longer in the KUS group (40.0 ± 0.0 μm) than in the control group (25.0 ± 4.2 μm, p = 0.037), at the area 5 mm superior to the optic disc.

**Conclusions:** These data suggested that this VCP inhibitor can morphologically and functionally suppress photoreceptor degeneration in a rabbit model of RP.

**Commercial Relationships:** Yuki Muraoka, None; Hanako O. Ikeda, Research grants from the Astellas Foundation for Research on Metabolic Disorders (F), Research grants from the Japan Foundation for Applied Enzymology (F); Noriko Nakano, PCT/JP2011/073160 (P); Tomoko Hasegawa, None; Akira Kakizuka, PCT/JP2011/073160 (P); Nagahisa Yoshimura, Canon (C), Canon (F), Nidek (C), Topcon (F), PCT/JP2011/073160 (P)

**Support:** This research was supported, in part, by research grants from the Astellas Foundation for Research on Metabolic Disorders (IOH) and the Japan Foundation for Applied Enzymology (IOH). Support was also received from a Grant-in-Aid for Young Scientists (22791656) and grants (KA) from the Ministry of Education, Culture, Sports, Science, and Technology (MEXT, IOH).

**Program Number:** 676 **Poster Board Number:** D0198

**Presentation Time:** 10:30 AM - 12:15 PM

**GCC and RPE change analysis in Retinitis Pigmentosa (RP) using Fourier domain optical coherence tomography (FD-OCT)**

Chang Ki Yoon, Hyeong Gon Yu. Seoul National University Hospital, Seoul, Republic of Korea.

**Purpose:** To investigate the retinal pigment epithelium (RPE) and ganglion cell complex (GCC) change using FD-OCT in retinitis pigmentosa with various severity and their temporal change after more than 1 year follow up

**Methods:** In a retrospectively designed cross-sectional study, 150 eyes of 150 patients with RP who had retained central vision (better than 20/100) were examined with Cirrus OCT (Carl Zeiss Meditec Inc) and Goldmann perimetry using test target III4e. RPE atrophy area was measured from advanced RPE analysis and mean ganglion cell complex thickness was detected from ganglion cell analysis. En face image of preserved photoreceptor inner segment and outer segment junction was demonstrated with advanced visualization and the area was calculated using photoshop and Image J software. Preserved central visual field was also analysed as a area. Pearson correlation coefficients (p) was used to measure the association between data subsets.

**Results:** A high correlation between mean GCC thickness and preserved IS/OS area was observed (Pearson correlation p=0.642, P<0.0001). Inverse correlation between RPE atrophy area and IS/OS area was observed (p=0.249, P=0.001). RPE atrophy had a tendency to increase exponentially as IS/OS area decreases. Visual field area was related with IS/OS area (p=0.347, P=0.001), mean GCC thickness (p=0.251, P=0.002) and RPE atrophy (p=0.211, P=0.009). IS/OS area was also correlated with LogMar visual acuity (p=-0.273, P=0.001) Sixty two patients were included in follow up group. IS/OS area and GCC thickness was correlated significantly (p=0.311, P<0.01).

**Conclusions:** In RP patients, preserved IS/OS area is related with residual central visual acuity and visual field. Ganglion cell complex comprised of ganglion cell and inner plexiform layer thickness has a strong linear correlation with preserved IS/OS area. RPE atrophy trend to develop after photoreceptor IS/OS layer loss. In consecutive examination suggested also stable correlation between IS/OS area and GCC thickness. This study revealed GCC degeneration and RPE atrophy pattern as photoreceptor degeneration.

**Commercial Relationships:** Chang Ki Yoon, None; Hyeong Gon Yu, None

**Support:** None in the Support field below

**Program Number:** 677 **Poster Board Number:** D0199

**Presentation Time:** 10:30 AM - 12:15 PM

**A comprehensive screen of the USH2A gene in 185 patients with autosomal recessive retinal disease**

Eva Lenassi1,2, Zubin Saifan2, Zheng Li1, Marko Hawlina1, Anthony T. Moore1,2, Linda M. Luxon2, Karen P. Steel2, Maria Bitner-Glindzicz3, Andrew R. Webster1,2, 1UCL Institute of Ophthalmology, London, United Kingdom; 2Moorfields Eye Hospital, London, United Kingdom; 3Ocular Genetics, Singapore Eye Research Institute, Singapore, Singapore; 4Eye Hospital, University Medical Centre, Ljubljana, Slovenia; 5UCL Ear Institute, London, United Kingdom; 6Wellcome Trust Genome Campus, Cambridge, United Kingdom; 7Clinical and Molecular Genetics, UCL Institute of Child Health, London, United Kingdom.

**Purpose:** Mutations in the USH2A gene are the commonest cause of both Usher syndrome and autosomal recessive retinitis pigmentosa (RP). The USH2A gene has multiple transcripts; the longest transcript (72 exons) encodes usherin, a protein of 5,202 amino acids. The aim of this study is to provide insights into the clinical and genetic characteristics of nonsyndromic USH2A-related retinal disease. Of particular interest was the identification of "retina-specific" alleles as these may point to protein domains essential for photoreceptor function.

**Methods:** The USH2A gene was screened in 185 probands with autosomal recessive retinal dystrophy without documented sensorineural hearing loss. Publicly available datasets (NHLBI GO Exome Sequencing Project [ESP], 1000 genomes) were used to distinguish disease-causing alleles from the background of nonpathogenic variation. Clinical investigations of patients with two likely pathogenic mutations were performed including OCT, fundus autofluorescence imaging (FAF) and audiological assessment.

**Results:** A total of 68 coding or splice site variants with a minor allele frequency of 0.20% or less in the ESP dataset were identified (5 nonsense or frameshifting indels, 4 splice site, 47 nonsynonymous); 24/185 (13%) probands were found to harbour at least two such variants. Interestingly, only in one individual were both variants previously associated with syndromic disease. Three alleles that are likely to be specific to those with nonsyndromic disease were found in more than one proband: p.Cys359Phe, p.Cys3358Tyr and c.12295-4T>A. All 24 patients presented with visual symptoms (night blindness and visual field loss; median age 29 years, range 19-43) and none reported early-onset hearing loss. The retinal phenotype was consistent with RP in all cases and a ring of high density on FAF was observed in 19/24 patients. Audiology testing revealed a phenotype consistent with Usher syndrome type 2 in 1/17 patients.

**Conclusions:** USH2A retinopathy is a common cause of nonsyndromic autosomal recessive retinal disease. Identifying disease-causing alleles remains challenging but the extensive catalogues of human genetic variation yielded by exome sequencing projects provide significant insights. Three likely "retina-specific" variants in USH2A were identified. The results of this study are expected to increase the sensitivity of molecular testing in this highly heterogeneous condition.

**Commercial Relationships:** Eva Lenassi, None; Zubin Saifan, None; Zheng Li, None; Marko Hawlina, None; Anthony T. Moore, None; Linda M. Luxon, None; Karen P. Steel, None; Maria Bitner-Glindzicz, None; Andrew R. Webster, None

**Support:** NIHR Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of
Ophthalmology, RP Fighting Blindness, Fight for Sight, Foundation Fighting Blindness

**Program Number:** 678 **Poster Board Number:** D0200  
**Presentation Time:** 10:30 AM - 12:15 PM  
**Does retinitis pigmentosa cause depression?**

**Purpose:** During retinal degeneration, retinal ganglion cells (RGCs) develop rhythmic bursting activity. To correlate abnormal activity with morphological classes of retinal ganglion cells affected by retinal degeneration, we compared electrophysiological recordings to structural features using cluster analysis.  

**Methods:** Excitatory and inhibitory postsynaptic currents were recorded from ~300 RGCs from rd1 mouse whole mount retinas. Cells were infused with sulforhodamine for visualization using a Nikon C1 confocal microscope. Anatomical and physiological parameters were used in a cluster analysis, and were also compared using a general linear model. Fourier analysis was used to determine the dominant frequency component and strength of rhythmic physiological activity. Monostratified and bistratified RGCs were analyzed separately.  

**Results:** All analyzed RGCs exhibited spontaneous oscillatory activity characteristic of rd mutants. This activity correlated to the level of stratification of monostratified RGCs within the innerplexiform layer. Oscillatory currents in bistratified RGCs have a stronger inhibitory component overall. Larger dendritic field size and density are associated with more robust oscillations, varying with stratification level.  

**Conclusions:** The correlation of aberrant activity to stratification suggests that ON and OFF pathways may be differently affected by degeneration. However, differences in dendritic fields within broad classes also contribute to variations in oscillatory activity.

**Commercial Relationships:** Christopher Yee. None; Abduqodir Toychiev. None; Elena Ivanova. None; Botir T. Sagdullaev. None

**Support:** NIH Grant EY020535

**Program Number:** 680 **Poster Board Number:** D0202  
**Presentation Time:** 10:30 AM - 12:15 PM  
**Syndromal Retinitis Pigmentosa Associated with a 12p13.33 Duplication Sings out a Ciliopathy Gene TULP3 as a Candidate for RP**

**Purpose:** Using the HADS, 3 (6.8%) subjects were found to have depressive symptoms, of whom one subject (2.3%) was found to suffer from major depressive disorder as detected by the MINI. The mean VFQ score for the 44 subjects was 51.7 and all 3 subjects who experienced depressive symptoms had VFQ scores lower than the 30th percentile range. In our study, the rate of depression amongst RP subjects compares favourably with the prevalence of major depression in the Singapore population (of about 6%). One limitation of this study was the relatively small sample size, which could have given rise to the low rate of major depression. The 3 subjects who experienced depressive symptoms also scored relatively lower in the VFQ-25. This suggests that reduced visual function may be an important predisposing factor for depressive symptoms.

**Results:** All analyzed RGCs exhibited spontaneous oscillatory activity characteristic of rd mutants. This activity correlated to the level of stratification of monostratified RGCs within the innerplexiform layer. Oscillatory currents in bistratified RGCs have a stronger inhibitory component overall. Larger dendritic field size and density are associated with more robust oscillations, varying with stratification level.  

**Conclusions:** The correlation of aberrant activity to stratification suggests that ON and OFF pathways may be differently affected by degeneration. However, differences in dendritic fields within broad classes also contribute to variations in oscillatory activity.

**Commercial Relationships:** Christopher Yee. None; Abduqodir Toychiev. None; Elena Ivanova. None; Botir T. Sagdullaev. None

**Support:** NIH Grant EY020535

**Program Number:** 679 **Poster Board Number:** D0201  
**Presentation Time:** 10:30 AM - 12:15 PM  
**Aberrant Ganglion Cell Activity varies with Morphology in a Mouse Model of Retinitis Pigmentosa**

**Purpose:** During retinal degeneration, retinal ganglion cells (RGCs) develop rhythmic bursting activity. To correlate abnormal activity with morphological classes of retinal ganglion cells affected by retinal degeneration, we compared electrophysiological recordings to structural features using cluster analysis.  

**Methods:** Excitatory and inhibitory postsynaptic currents were recorded from ~300 RGCs from rd1 mouse whole mount retinas. Cells were infused with sulforhodamine for visualization using a Nikon C1 confocal microscope. Anatomical and physiological parameters were used in a cluster analysis, and were also compared using a general linear model. Fourier analysis was used to determine the dominant frequency component and strength of rhythmic physiological activity. Monostratified and bistratified RGCs were analyzed separately.  

**Results:** All analyzed RGCs exhibited spontaneous oscillatory activity characteristic of rd mutants. This activity correlated to the level of stratification of monostratified RGCs within the innerplexiform layer. Oscillatory currents in bistratified RGCs have a stronger inhibitory component overall. Larger dendritic field size and density are associated with more robust oscillations, varying with stratification level.  

**Conclusions:** The correlation of aberrant activity to stratification suggests that ON and OFF pathways may be differently affected by degeneration. However, differences in dendritic fields within broad classes also contribute to variations in oscillatory activity.

**Commercial Relationships:** Christopher Yee. None; Abduqodir Toychiev. None; Elena Ivanova. None; Botir T. Sagdullaev. None

**Support:** NIH Grant EY020535

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with ocular anomalies particularly in syndromal association including in consanguineous families. Duplication of the TULP3 gene stands out as a possible candidate gene for RP while its deletion has been associated with glaucoma.

Commercial Relationships: Pierre Bitoun, None; Andree Delahaye, None; Brigitte Benzacken, None; Eva Pipiras, None

Program Number: 681 Poster Board Number: D0203
Presentation Time: 10:30 AM - 12:15 PM
30 Year Clinical Follow-Up of Original Family With Autosomal Dominant Vitreoretinochoroidopathy (ADVIRC)

Senad Osmanovic, Clement C. Chow, Norman P. Blair.
Ophthalmology, University of Illinois at Chicago, Chicago, IL.

Purpose: To present the clinical characteristics, including visual acuity (VA), retinal findings, imaging studies, and management of complications over a 30-year period in the original family where Autosomal Dominant Vitreoretinochoroidopathy (ADVIRC) was documented.

Methods: Charts were reviewed for longitudinal data over a 30-year period on the original series of 6 family members of the first ADVIRC cohort, as well as any available members of future generations. Relevant data included visual acuity, visual field testing, fundus photography, fluorescein angiography, OCT and other ancillary testing modalities. Patients' clinical course were assessed for development of any structural or functional ocular complications.

Results: The pedigree of interest was a three-generation family of Welsh extraction. One of the original 6 patients described had expired and 2 did not have sufficient longitudinal data. 3 patients, including the proband, underwent regular ophthalmologic examinations consisting of frequent visual acuity measures, fields, and multimodal retinal imaging. In total, 6 of 9 family members and 5 of 8 living family members examined had findings consistent with ADVIRC. These included, most prominently, a 360 degree demarcated temporal band, a hallmark of ADVIRC, did demonstrate temporal evolution in our patients.

Commercial Relationships: Senad Osmanovic, None; Clement C. Chow, None; Norman P. Blair, None

Program Number: 682 Poster Board Number: D0204
Presentation Time: 10:30 AM - 12:15 PM
Mutations in MVK cause non-syndromic autosomal recessive retinitis pigmentosa

Anna M. Siemiatkowska1, Monique Stoffels2, Kornelia Neveling1, Anna Simon2, Martin van Hagen2, Anneke I. Den Hollander1, 2, Frans P. Cremers2, L. I. van den Born1, Rob W. Collin1. 1Department of Human Genetics, Radboud University Medical Centre, Nijmegen, Netherlands; 2Department of General Internal Medicine, Radboud University Medical Centre, Nijmegen, Netherlands; 3Department of Ophthalmology, Radboud University Medical Centre, Nijmegen, Netherlands; 4Department of Immunology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, Netherlands; 5The Rotterdam Eye Hospital, Rotterdam, Netherlands.

Purpose: Retinitis pigmentosa (RP) is a clinically and genetically heterogeneous retinal disease. Typically beginning with night blindness, RP is characterized by visual field loss followed by deterioration of visual acuity, which may ultimately lead to complete blindness. Despite extensive knowledge about genes involved in RP pathogenesis, the genetic cause remains elusive in many patients. In this study, we aimed to identify novel genes that are involved in the etiology of RP.

Methods: Exome sequence analysis was performed in a proband of Dutch origin that was first diagnosed with non-syndromic autosomal recessive RP. Identified mutations in the mevalonate kinase (MVK) gene were subsequently tested for segregation within the family and in a large cohort of genetically unsolved RP patients. Patients with
mutations underwent extensive clinical re-examination. Mevalonate kinase enzyme (MK) activity was analyzed in cultured lymphoblastoid cells and mevalonic acid levels were measured in urine samples.

**Results:** Exome variant filtering and prioritization led to the identification of compound heterozygous mutations in MVK (p.L268F and p.A334T) in the proband and his affected sibling. Recessive mutations in MVK are known to cause mevalonate kinase deficiencies (MKD): mevalonic aciduria (MVA), sometimes accompanied by RP, and hyper-IgD and periodic fever syndrome (HIDS). Screening of 269 non-syndromic RP patients revealed an individual who was homozygous for the p.A334T alteration. None of these patients displayed any of the other classical extra-ocular symptoms that are usually associated with recessive mutations in MVK, namely elevated IgD levels, recurrent febrile crises psychomotor retardation, progressive cerebellar ataxia or dysmorphic features. In all three affected individuals, mevalonate kinase activity was significantly decreased and mevalonic acid levels in urine were elevated.

**Conclusions:** Although the MK activity in cells and mevalonic acid concentrations in urine are abnormal and within the range of patients with mevalonate kinase deficiency, no apparent other clinical symptoms associated with classical MKD were observed in our patients. This study adds MVK to the group of genes that appear to be associated with non-syndromic retinitis pigmentosa.

**Commercial Relationships:**
- Anna M. Siemiatkowska, None;
- Monique Stoffels, None; Kornelia Neveling, None; Anna Simon, Novartis (C), SOBI Biovitrum (C);
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**Support:** TOP-grant 91209047

**Program Number:** 683 **Poster Board Number:** D0205

**Presentation Time:** 10:30 AM - 12:15 PM

**SD-OCT May Predict Response to QLT091001 in Patients with LCA or RP associated with RPE65 or LRAT Mutations**

Yuquan Wen1,2, David G. Birch1,2, Retina Foundation of the Southwest, Dallas, TX; 1Ophthalmology, UT Southwestern Medical Center, Dallas, TX; 2Visual Function Center, Baylor University Medical Center, Dallas, TX.

**Purpose:** SD-OCT measures were obtained from patients with LCA or RP associated with RPE65 or LRAT mutations as part of a prospective open-label study to evaluate the safety and efficacy of oral QLT091001, a synthetic retinoid replacement for 11-cis-retinal.

Baseline SD-OCT parameters were compared to baseline visual function; baseline SD-OCT and changes were compared to the visual field response to QLT091001.

**Methods:** Comprehensive ophthalmic testing including SD-OCT (Spectralis HRA+OCT) was conducted in 14 patients with LCA and 17 patients with RP at 7 international sites. Oral QLT091001 was administered once daily for 7 days in all study patients. The patients were followed for up to 15 months.

**Results:** Eighteen of 28 eyes (64%) with LCA and 15/34 eyes (44%) with RP responded to QLT091001 (response is defined as expansions of Goldmann visual fields retinal areas by ≥20% at two consecutive study visits). Among these responders, the average baseline thickness of the outer segment (OS) layer (measured from the outer segment/retinal pigment epithelium border to the inner segment ellipsoid band) was calculated with a computer program aided by manual segmentation.

**Conclusions:** Although the primary defect in LCA and RP due to RPE65 or LRAT mutations lies in the visual (retinoid) cycle, photoreceptor degeneration frequently occurs at an early age, even in the first decade of life. The present findings suggest that there is a close parallel between photoreceptor structure and function in these patients. SD-OCT may be useful for predicting the response to oral synthetic retinoid replacement.

**Commercial Relationships:** Yuquan Wen, QLT Inc. (C); David G. Birch, Acucela (C), QLT (C), Neurotech, USA (C)

**Clinical Trial:** NCT01014052

**Program Number:** 684 **Poster Board Number:** D0206

**Presentation Time:** 10:30 AM - 12:15 PM

**Large Animal Model of Autosomal Recessive RP due to a CNGB1 gene mutation**

Simon M. Petersen-Jones1, Paige A. Winkler1, Joshua T. Bartoe1, Patrick J. Ventu2, Kari Ekenstedt1, 1Department of Small Animal Clinical Sciences, Michigan State University, East Lansing, MI; 2Department of Microbiology and Molecular Genetics, Michigan State University, East Lansing, MI.

**Purpose:** Several breeds of dog have recessively inherited retinal dystrophies making them potential large animal models of retinitis pigmentosa (RP). The purpose of this study was to investigate one such retinal dystrophy in the Papillon breed of dog.

**Methods:** A colony of Papillon dogs affected by an inherited progressive retinal degeneration was established. Affected dogs were phenotyped by ophthalmoscopic examination, vision testing and electroretinography. One dog was euthanized and the retina processed for immunohistochemistry. DNA samples were collected from colony dogs and privately owned Papillons with retinal degeneration and unaffected Papillons. 9 affected and 14 unaffected Papillon dogs were genotyped using a SNP microarray (Illumina Canine HD BeadChips).

**Results:** The affected colony dogs had night-blindness from the earliest age that this could be assessed. Ophthalmoscopic signs of retinal thinning developed from between 12 and 18 months of age. The electroretinographic study revealed a marked reduction in rod-mediated responses from an early age. The SNP genotyping results from the affected colony dogs were compared with the control dogs and analyzed using a custom written program to detect regions of homozygosity in the affected dogs compared to the controls.

Following additional microsatellite marker genotyping the cyclic nucleotide-gated channel beta 1 subunit (CNGB1) gene was identified as a positional candidate gene. The homozygous region surrounding CNGB1 was 1.84 Mb. Normal canine retinal cDNA and affected control genomic DNA was sequenced. An exonic one-basepair deletion in CNGB1 predicted to result in a frame shift and premature stop codon was identified. This mutation segregated with the disease status in the colony dogs and was not present in the homozygous state in any unaffected dogs. Retinal immunohistochemistry showed a lack of labeling for CNGB1 in retinal sections from the affected dog whereas the antibody labeled rod outer segments in normal control dog retina.

**Conclusions:** A one-basepair deletion in CNGB1 in Papillon dogs causes a frame shift and premature stop codon, resulting in a lack of...
CNGB1 expression, markedly reduced or absent rod function, and a progressive retinal degeneration. This phenotype recapitulates the reported CNGB1 RP phenotype, making this dog colony a valuable large animal model for studying the effect of CNGB1 mutations and testing therapeutic intervention.

Commercial Relationships: Simon M. Petersen-Jones, None; Paige A. Winkler, None; Joshua T. Bartoe, None; Patrick J. Venta, None; Kari Ekenstedt, None
Support: Myers-Dunlap Endowment for Canine Health

Program Number: 685 Poster Board Number: D0207 Presentation Time: 10:30 AM - 12:15 PM

Effect of Pupil Dilatation on Normative Data for Full-Field Stimulus Threshold (FST) for White, Blue and Red Stimulus Colors
Andre D. Ruppert, Sarah B. Godoi, Nivaldo Sena, Katharina Messias, Rafael S. Arcieri, Andre Messias. Department of Ophthalmology, Otorhinolaryngology and Head and Neck Surgery, USP - University of Sao Paulo, Ribeirao Preto, Brazil.

Purpose: To describe normative data for full-field stimulus threshold (FST), measured with white, blue, red stimulus, and investigate the effects of pupil dilatation on sensitivity thresholds. In addition, data is compared to Retinitis Pigmentosa patients that show typical concentric visual field constriction, but good fixation.

Methods: Data from 20 normally sighted subjects (40 eyes) aging from 18 to 54 years (mean ± SD: 28 ± 9 years) was analyzed. FST was psychophysically determined after 25 minutes dark adaptation using Espion E2 system with the ColorDomeTM LED full-field stimulator (Diagnosys LLC, Lowell, MA), using white (6500 K), blue (465 to 470 nm), and red (635 to 638 nm) stimulus. Only left eyes pupils were dilated for comparison. Data was compared to results from 15 Retinitis Pigmentosa (RP) patients (n=30 eyes).

Results: There was statistically significant difference between FST measured on dilated (DP) vs. non-dilated (nDP) pupils for white stimulus: 43.5 ± 1.0 dB and 41.0 ± 1.0 dB (P=0.0011) and blue: 49.6 ± 1.0 dB and 48.2 ± 0.9 dB(P=0.0084; paired t-Test), for DP and n-DP respectively, but this difference was not observed for the red stimulus: 25.6 ± 0.9 dB and 25.3 ± 0.7 dB (P=0.3303). Mean FST was significantly lower (P<0.05) in RP patients, and the difference between normal and RP was higher for white: 26.3 ± 1.7 dB and blue: 28.4 ± 2.0 dB; than for red stimulus: 12.0 ± 1.2 dB (P<0.05).

Conclusions: The data suggests that pupil dilatation has significant influence on FST for white and blue, but not for red stimulus, and this might be explained by the higher concentration of the red-sensitive photoreceptors on the central retina. As expected, the differences between FST in normal and RP patients are higher for blue and white than for red stimulus.

Commercial Relationships: Andre D. Ruppert, None; Sarah B. Godoi, None; Nivaldo Sena, None; Katharina Messias, None; Rafael S. Arcieri, None; Andre Messias, None
Support: CNPq
Fundus autofluorescence and OCT thickness evaluation in P23H rats

Isabel Pinilla Lozano, Francisco J. Segura Calvo, Lorena Fuentes-Broto, Jose M. Tamari, Eduardo Romanos, Laura Fernandez-Sanchez, Carmen Lopez-de La Fuente, Ana I. Sanchez-Can, Francisco J. Ascaso, Nicolas Cuenca, University of Alicante, Alicante, Spain; Institute of Health Science, Zaragoza, Spain; Surgery, University of Zaragoza, Zaragoza, Spain; Physiology, University of Zaragoza, Zaragoza, Spain; Physics, University of Zaragoza, Zaragoza, Spain; Physics, Genetics and Microbiology, University of Alicante, Alicante, Spain; Bloss Company, Barcelona, Spain; University of Alicante, Alicante, Spain. Program Number: 688 Poster Number: D0210 Presentation Time: 10:30 AM - 12:15 PM

Purpose: The aim of this study was to evaluate fundus autofluorescence (FAF) and OCT changes in an animal model of Retinitis Pigmentosa, the P23H rat and to investigate retinal and choroidal vascularization using fluorescein and indocianin green angiography.

Methods: Twenty albino homozygous P23H line 1 rats aging from 18 postnatal days (P18) to 27 months and albino wild-type Sprague-Dawley (SD rats) (2 and 15 months old) were used for this study. Normal pigmented Long Evans (LE) 2 months old were used to compare FAF findings. Scanning laser ophthalmoscopy (SLO) imaging and Optical Coherence Tomography (OCT) were acquired using a Spectralis HRA OCT system (Spectralis, Heidelberg Engineering, Heidelberg Germany). For checking FAF, fluorescence was excited using diode laser at 488 nm. A single OCT line was performed passing through the optic nerve of the rat. Thickness measurements were evaluated avoiding the ones close to the optic nerve. Immunohistochemistry (ICC) was performed to correlate with the findings of OCT and AF changes.

Results: FAF in LE rats showed no findings. In SD and young P23H rats choroid was seen by transparence. During the course of P23H degeneration, the FAF pattern varied from not findings in young animals, some spotting at 2 months old to a mosaic of hyperfluorescent dots in the rats of 6 months or older. Retinal thicknesses diminished during the time. Young SD rats showed thickness values higher than old ones (205.2 vs 183.18 μm, at 2 and 15 months old respectively). P23H rats showed great changes in morphology in advanced ages, with no clear limit between the retina and the choroid. Mean retinal thickness values varied from 189.88 μm to 73.55 μm at 2 months old and 11 months old respectively, lowering till 58.15 μm at 27 months old. Retinal vascular plexus were diminished with time, and vessels exhibiting an abnormal, tortuous morphology could be observed. Arteries did not change in their diameter.

Conclusions: Autofluorescent ophthalmoscopy is a non-invasive procedure that can detect changes in metabolic activity at the RPE in animal models of retinal degeneration in vivo. Hyperautofluorescent changes appeared with the course of the degeneration with a diminution of retinal thickness. Retinal vascular plexus changes are clear with aging.

Commercial Relationships: Isabel Pinilla Lozano, None; Francisco J. Segura Calvo, None; Lorena Fuentes-Broto, None; Jose M. Tamari, W.M.Bloss SA (E); Eduardo Romanos, None; Laura Fernandez-Sanchez, None; Carmen Lopez-de La Fuente, None; Ana I. Sanchez-Can, None; Francisco J. Ascaso, None; Nicolas Cuenca, Universidad de Alicante (P)

Support: FIS PS0901854, RD07-0062, BAE12/00090, Fundación Gangoi

Program Number: 689 Poster Number: D0211 Presentation Time: 10:30 AM - 12:15 PM

Multiple Rings or Arcs of Hyperautofluorescence in Different Retinitis Pigmentosa Phenotypes

Ana Fakin, Martina Jarc-Vidmar, Maja Šuštar, Jelka Brečelj, Branka Stirn Kranjc, Marko Havlina, University Eye Hospital Ljubljana, Ljubljana, Slovenia. Program Number: 689 Poster Number: D0211 Presentation Time: 10:30 AM - 12:15 PM

Purpose: To characterize retinal structure and function in retina pigmentosa (RP) phenotype patients with multiple rings or arcs of hyperautofluorescence.

Methods: Fifty-nine patients were divided into three groups according to peripheral patterns seen on 55° fundus autofluorescence (FAF) and optical coherence tomography (OCT) imaging (Heidelberg Engineering Spectralis, Germany), in addition to central FAF ring or patch. Group A presented with additional peripheral rings, group B with arcs and group C with no peripheral hyperautofluorescence. Full-field ERG was performed in 35 patients according to ISCEV standard. Rod and cone response amplitudes were averaged between both eyes and expressed as percentages of lower normal limit (5th percentile). Targeted manual microperimetry (MP1, Nidek, Italy; n=5) were performed across fovea and peripheral hyperautofluorescent border.

Results: Peripheral rings were observed in 12% (7/59) and arcs in 20% (12/59) of RP phenotype patients with various types of inheritance (Fig. 1). Average age of patients in groups A-C was 45, 51 and 43 years and was not significantly different. Average disease duration (years since onset of nyctalopia) in groups A and B was significantly lower than in group C (5 and 7 years vs. 22 years, respectively; p<0.05). Average rod response amplitudes were 49%, 20% and 2%, and average cone response amplitudes were 54%, 25% and 16% of lower normal, respectively (p<0.05 except for cone response between B and C). Microperimetry revealed on average of 8 dB increase of retinal sensitivity outside of peripheral hyperautofluorescent borders and OCT in that area showed preserved photoreceptor layer. In one patient with dominant RP expansion of hyperautofluorescent ring was observed in duration of one year (Fig. 2).

Conclusions: Peripheral rings or arcs of hyperautofluorescence were seen in 32% of patients with RP phenotype with various types of inheritance. Peripheral rings were associated with peripherally
A novel heterozygote E2331* mutation in PRPF8 gene causes a severe phenotype of Retinitis Pigmentosa with early loss of visual acuity

Olga Passarin1, Francis L. Munier1,2, Viet H. Tran1, Daniel F. Schorderet1,3, Veronika Vaclavik1,3. 1Hospital Ophtalmique Jules Gomina, Lausanne, Switzerland; 2Institut de Recherche en Ophtalmologie, Sion, Switzerland; 3Ophthalmology, Hopitaux Universitaires de Genève, Geneva, Switzerland.

Purpose: To report a novel mutation E2331* in exon 42 of the PRPF8 gene in 2 generation family with severe form of retinitis pigmentosa.

Methods: Two affected patients (a father and his daughter, aged 60 and 28 years) and the unaffected grandparents were assessed with a complete ophthalmologic examination. All had fundus autofluorescence imaging, standardised electroretinography, Goldmann visual fields and Optical Coherence Tomography. Blood sample was taken for molecular analysis.

Results: The affected patients were severely affected at a young age with early macular involvement. The 28 years old daughter visual acuity of 0.2 according to Snellen EDTRS chart bilaterally. The father’s visual acuity was hand movement. Both had evidence of macular early cone dysfunction, as measured by full field ERGs and autofluorescence imaging. The unaffected grand father was negative for the mutation.

Conclusions: We report a novel E2331* mutation in exon 42 of the PRPF8, which is a rare cause of adRP. Our descriptions report severe phenotype with early macular atrophy, unlike previous reports, although the mutation occurs in the same exon 42, as most of mutations. This finding assist in understanding the pathogenesis of this disorder.

Commercial Relationships: Olga Passarin, None; Francis L. Munier, None; Viet H. Tran, None; Daniel F. Schorderet, None; Veronika Vaclavik, None

141 Retinal Prosthesis II
Sunday, May 05, 2013 1:00 PM-2:45 PM
Exhibit Hall Poster Session
Program #/Board # Range: 1024-1068/C0001-C0045
Organizing Section: Retina

Program Number: 1024 Poster Board Number: C0001
Presentation Time: 1:00 PM - 2:45 PM
Electrically elicited visually evoked potentials (eVEPs) in Argus® II prosthesis wearers

H Christiaan Stronks1,2, Gislin Dagnelie2, Michael P. Barry1.
1Computer Vision, NICTA CRL, Canberra, ACT, Australia; 2Ophthalmology, Johns Hopkins University, Baltimore, MD; 3Biomedical Engineering, Johns Hopkins University, Baltimore, MD.

Purpose: To investigate whether electrically elicited visually evoked potentials (eVEPs) can be used to establish input-output characteristics and predict subjective threshold of electrical stimulation in Argus® II retinal prosthesis wearers.

Methods: We recorded eVEPs in three subjects while systematically varying stimulus level. Subjects provided feedback by rating the brightness and size of the perceived flashes of light (‘phosphenes’). Input-output functions were generated using eVEP amplitude and latency based of the first two positive peaks (P1 and P2). Correlation was determined using linear regression, followed by an F-test on the slope. eVEP thresholds were defined as the amplitude equaling 4 times the standard deviation (4xSD) of the eVEP waveform. We also investigated the effect of stimulating different retinal locations, the maximal feasible pulse rate, and adaptation (‘fading’).

Commercial Relationships: Ana Fakin, None; Martina Jarc-Vidmar, None; Maja Šuštar, None; Jelka Brecelj, None; Branka Stirn Kranjc, None; Marko Hawlina, None
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Program Number: 690 Poster Board Number: D0212
Presentation Time: 10:30 AM - 12:15 PM
Results: P₁ and P₂ amplitudes significantly increased as a function of subjective percept in all three subjects (linear regression and F-test, P<0.05). Only 1 out of 3 subjects showed a significant decrease of eVEP latency with stimulus level and rating (P<0.05). P₂ amplitude yielded accurate predictions of subjective threshold in all three subjects (table 1). Stimulating macular electrodes resulted in higher eVEP amplitudes and shorter latencies compared to more peripheral electrodes (RM ANOVA and Tukey’s post hoc test, P<0.05), while subjective ratings were not different (P>0.05). At pulse rates above 75 Hz, eVEP waveforms became distorted and amplitudes declined. Subjective phosphene brightness decreased over time, which was reflected in P₁ amplitude (linear regression and F-test, P<0.01), but not in P₂ amplitude (P>0.05).

Conclusions: The eVEP P₁ amplitude is a robust measure for generating input-output relationships and is a fairly accurate predictor of subjective threshold. Pulse rates of up to 75 Hz can be used for eVEP recordings. Retinal location affects eVEP amplitudes and latencies irrespective of subjective percept, which has to be taken into account when using the eVEP clinically. We envision that eVEPs may become a diagnostic and monitoring tool that can find important use as an objective measure for rehabilitation purposes.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Subjective threshold (μA)</th>
<th>eVEP threshold (μA)</th>
<th>P₁</th>
<th>P₂</th>
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<tr>
<td>S2</td>
<td>30</td>
<td>38</td>
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<td>S5</td>
<td>11</td>
<td>3</td>
<td>7</td>
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Subjective threshold and interpolated eVEP P₁ and P₂ thresholds.

Commercial Relationships: H Christiana Stronks, Second Medical Products (C), Second Sight Medical Products (P); Gislin Dagnelie. None; Michael P. Barry, Second Sight Medical Products, Inc. (F), QLT Inc. (F)

Support: NIH grant R21EY019991

Program Number: 1025 Poster Board Number: C0002

Presentation Time: 1:00 PM - 2:45 PM

Intra-Retinal Electrical Stimulation: Comparison to Epi- and Sub-Retinal Approaches

David Boinagrov1,2, Susanne Pangratz-Fuehrer3, Keith Mathieson1,4, David V. Palanker1,3, Keith Mathieson1,4, Georgs A. Goetz5,6, Ludwig Galambos7, Daniel V. Palanker1,3

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Purpose: To assess potential improvements in retinal stimulation using close positioning of the electrodes, thresholds were measured with electrodes placed epiretinally, subretinally and penetrating inside the inner and outer plexiform layers (IPL and OPL). The strength-duration relationship of direct and network-mediated responses was determined for each location.

Methods: The whole-cell recordings of action potentials were obtained from RGCs of Long Evans rat retina in vitro. Cathodic and anodic pulses of 0.1-20ms in duration were applied via electrodes in four positions: epiretinal, IPL, OPL, and subretinal. Epiretinal and intraretinal stimulation was applied via 5μm glass pipette electrodes, while subretinal electrode was a 40μm disc.

Results: Stimulation thresholds strongly varied with pulse polarities and electrode locations, but the shape of the strength-duration relationship was independent of electrode location and stimulus polarity. Direct stimulation threshold exhibited chronaxy of about 1ms, while the network threshold continued a constant-slope decrease with increasing pulse duration, at least up to 20ms. The lowest stimulation threshold for direct response was cathodic epiretinal: 1.5μA at 2ms, with corresponding network threshold of 5μA. Epiretinal placement had the highest selectivity for direct stimulation without evoking network response: thresholds ratio was 3.3 for 2ms pulses. Insertion of the electrode into IPL increased both cathodic thresholds: to 3 and 5.5μA, respectively, but decreased anodic thresholds: from 7.9 and 15μA to 4.3 and 7.8μA. In subretinal placement the network thresholds were lower than direct ones, and anodic pulses had lower thresholds (1.5 and 2.2μA for the network and direct responses at 4ms) than cathodic (17.9 and 23.4μA). Upon insertion of the electrode into OPL the thresholds for both polarities decreased, and the direct thresholds remained about twice higher than the network with 4 ms pulses.

Conclusions: Intraretinal positioning of the electrodes may provide better and more stable proximity to the target cells than the epiretinal or sub-retinal arrays. However, electrodes on epiretinal surface still have the lowest thresholds and highest selectivity of direct stimulation of RGCs. OPL position has lower thresholds than subretinal, and the highest selectivity of the network stimulation (7.7) is achieved at longest pulse durations (20ms) for both polarities.

Commercial Relationships: David Boinagrov, None; Susanne Pangratz-Fuehrer, None; Keith Mathieson, None; Georgs A. Goetz, None; Ludwig Galambos, None; Daniel V. Palanker, None

Support: This project was supported in part by NIH grant # R01EY018608, Stanford University Bio-X Research Grant, Air Force Office of Scientific Research Grant FA9550-10-1-0503, SU2P RCUK Science Bridges award.

Program Number: 1026 Poster Board Number: C0003

Presentation Time: 1:00 PM - 2:45 PM

Comparison of Electrically Evoked Retinal Ganglion Cell (RGC) Responses by Square Pulse and Triangle Pulse in rd1 mice

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1Physiology, Chungbuk National Univ Med School, Cheongju, Republic of Korea; 2Nano Artificial Vision Research Center, Seoul National University Hospital, Seoul, Republic of Korea.

Purpose: Retinal prostheses have been developed for the patients with retinitis pigmentosa (RP) and age related macular degeneration (AMD), and is regarded as the most feasible method to restore vision. Extracting optimal electrical stimulation parameters for the prostheses is one of the most important elements for the success of retinal prostheses. Here, we used charge balanced biphasic current pulse and we compared efficiency of three different pulse shapes evoking RGC responses in rd1 mice.

Methods: The well-known animal model for RP, rd1 (Pde6brd1) mice at postnatal 8 weeks were used (n=9). From the ex-vivo retinal preparation, retinal waveforms were recorded with 8 x 8 MEA. Biphasic current pulses in the form of cathodic phase-1st and anodic phase-2nd were applied once per second (1 Hz, x50). We tested 3 different pulse shapes with same charge; 1) biphasic square pulse (I: intensity, D: duration), 2) biphasic triangle pulse with intensity doubled (2Ix, D) to satisfy same charge requirement with square pulse, 3) biphasic triangle pulse with duration doubled (I, 2xD) to satisfy same charge requirement with square pulse. For intensity modulation, duration of the pulse was fixed to 500 μs and the intensities of the pulse were modulated from 5 to 40 μA. For duration modulation, intensity of the pulse was fixed to 30 μA and the durations of the pulse were modulated from 60 to 500 μs. The electrically-evoked RGC spikes were defined as positive when the
number of RGC spikes for 400 ms after stimulus was 1.3 times higher than that for 400 ms before stimulus in post-stimulus time histogram.

**Results:** RGC responses were well modulated both with square pulse and triangle pulse by varying the intensity and duration of the pulse. Amplitude modulation shows that RGC response is preferentially activated by biphasic triangle pulse with duration doubled especially with 5 μA (p<0.001) and 10 μA (p<0.01). Duration modulation shows that RGC response is preferentially activated by biphasic triangle pulse with duration doubled especially with 60 and 100 μs (p<0.001) and 200 μs (p<0.05).

**Conclusions:** Biphasic triangle pulse with duration doubled is always efficient than square pulse and biphasic triangle pulse with intensity doubled both in amplitude modulation and duration modulation.

**Methods:**

1) Square Pulse 2) Triangle Pulse with Intensity Doubled and 3) Triangle Pulse with Duration Doubled

**Commercial Relationships:** None; Lauren N. Ayton, None; Penelope J. Allen, None; Seol A Jae, None; Joo Yun Kim, None

**Support:** Korean MEST grant (2010-0020852 )

**Program Number:** 1027 Poster Board Number: C0004

**Presentation Time:** 1:00 PM - 2:45 PM

**The Feasibility of Explanting a Suprachoroidal Electrode Array in a Feline Model**

**Ronald T. Leung**1, 2, David A. Nayagam1, 2, Richard A. Williams2, 4, Penelope J. Allen2, 5, Cesar M. Salinas-La Rosa1, Chi D. Luu2, 5, Lauren N. Ayton6, 5, Meri Basa7, 8, Robert K. Shepherd1, 2, Chris E. Williams1, 2, 1Bionics Institute, East Melbourne, VIC, Australia; 2Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Parkville, VIC, Australia; 3Department of Anatomical Pathology, St. Vincent’s Hospital Melbourne, Fitzroy, VIC, Australia; 4Royal Victorian Eye & Ear Hospital, East Melbourne, VIC, Australia; 5Centre for Eye Research Australia, East Melbourne, VIC, Australia; 6Centre for Eye Research Australia, East Melbourne, VIC, Australia; 7Bionics Institute, Melbourne, VIC, Australia; 8Department of Anatomical Pathology, The University of Melbourne, Melbourne, VIC, Australia.

**Purpose:** To determine whether chronically implanted suprachoroidal electrode arrays can be safely explanted in a feline model.

**Methods:** Six healthy subjects were unilaterally implanted with suprachoroidal electrode arrays which were surgically explanted after one month. Fundus photography and optical coherence tomography (OCT) was performed pre- and post-operatively. The subjects were overdosed two months post-explanation and the eyes were prepared for histological study.

**Results:** All the arrays were explanted with no intra-operative complications. OCT and fundus photography showed that the tapetum and retina was disrupted near the tip of the implant within two weeks of implantation and that explantation did not result in further disruption. Staphylomas were observed in five subjects upon macroscopic dissection. There was no change in the thickness of the chorioid, photoreceptor layer or inner retina compared to the contralateral unimplanted control eye following array implantation or explantation. Histological results showed that the morphology of the retina was well preserved except for focal disruption of the tapetum and photoreceptors near the optic disk which corresponded to the same damaged regions observed in fundus photographs and OCT. There was a minor foreign body response with mild episcleral acute inflammation and mild chronic inflammation in the suprachoroidal space.

**Conclusions:** The feasibility of explanting a suprachoroidal retinal prosthesis has been demonstrated. This procedure can be safely performed provided that there is good management of the scleral wound. There was minimal damage to the globe and surrounding tissues. These findings have important implications for suprachoroidal array explantation in the clinical setting.

**Commercial Relationships:** Ronald T. Leung, None; David A. Nayagam, None; Richard A. Williams, None; Penelope J. Allen, Bionic Vision Australia (P); Cesar M. Salinas-La Rosa, None; Chi D. Luu, None; Lauren N. Ayton, None; Meri Basa, None; Robert K. Shepherd, None; Chris E. Williams, Bionic Vision Australia (P)

**Support:** The Bionics Institute and the Centre for Eye Research Australia acknowledge the support they receive from the Victorian Government through its Operational Infrastructure Support Program. This research was supported by the Australian Research Council (ARC) through its Special Research Initiative (SRI) in Bionic Vision Science and Technology grant to Bionic Vision Australia (BVA) and the Harold Mitchell Foundation. The Bionics Institute would also like to acknowledge support from the Bertalli Family Trust.

**Program Number:** 1028 Poster Board Number: C0005

**Presentation Time:** 1:00 PM - 2:45 PM

**Development of a surgical procedure for implanting a wide view electrode array in the suprachoroidal space**

Jonathan Yeoh1, 2, Alexia Saunders2, David A. Nayagam2, 4, Chris E. Williams2, 4, Mark McCombe1, 3, Burns Owen2, Joel Villalobos2, Michelle McPhedran2, Robert Briggs2, 1, Penelope J. Allen1, 2, 1The Royal Victorian Eye and Ear Hospital, Melbourne, VIC, Australia; 2Bionics Institute, Melbourne, VIC, Australia; 3Centre for Eye Research Australia, Melbourne, VIC, Australia; 4Department of Anatomical Pathology, The University of Melbourne, Melbourne, VIC, Australia.

**Purpose:** The goal of this study was to develop the surgical procedure for implanting a suprachoroidal retinal prosthesis in patients. The preclinical implant was adapted to conform to human orbital anatomy.

**Methods:** A surgical technique for suprachoroidal implantation of a conformable electrode array (19 mm x 8 mm) and lead was developed. Human cadavers (n = 5) were used to adapt the approach which was previously used in a pre-clinical model. A method of tunnelling the array forward from behind the pinna towards the orbit was used, with a custom trocar. First, an anteriorly based C-shape flap was created behind the pinna to position the percutaneous pedestal. Next a lateral canthotomy was made. An orbitotomy was performed provided that temporary compression placed behind the pinna. A flap was created behind the pinna to position the percutaneous pedestal. The lead was anchored inside this notch with a compression fit and by a conformable patch sutured onto the sclera.
The lateral rectus muscle was detached and a 9 mm full scleral thickness incision was made 1-4 mm behind the muscle insertion point, according to eye size. A pocket was created in the suprachoroidal space. The moulded array was inserted into the suprachoroidal space. The incision was closed and scleral anchor point sutured.

Results: Dissection of the cadaver eyes confirmed that the retinal prostheses were reliably positioned in the suprachoroidal space and beneath the macula. A conformable anchor point sutured to the sclera stabilised the transscleral lead exit. This anchor point was angled accordingly to ensure a simple fit of the intraorbital lead with minimal strain. Safe tunnelling was achieved with the use of a tunnelling trocar beneath the temporalsis fascia. The 150 mm lead reliably reached the pedestal behind the pinna.

Conclusions: A surgical approach for suprachoroidal prosthetic implantation was developed for successful anatomical placement, mechanical stability and safe tunnelling, to be used in subsequent patient testing. Electrode impedance measurements and psychophysics testing in patients have shown the retina to be functional after uncomplicated surgery and several months of implantation.

Commercial Relationships: Jonathan Yeoh, None; Alexa Saunders, None; David A. Nayagam, None; Chris E. Williams, Bionic Vision Australia (P); Mark McCombe, Bionic Vision Australia (P); Burns Owen, Bionics Institute (P); Joel Villalobos, The Bionics Institute of Australia (P); Michelle McPhedran, None; Robert Briggs, Cochlear (C); Penelope J. Allen, Bionic Vision Australia (P)

Program Number: 1029 Poster Board Number: C0006
Presentation Time: 1:00 PM - 2:45 PM

In Vivo Electrical Stimulation of a Retinal Prosthesis Containing Conductive Diamond Electrodes

Mohit N. Shivdasani1, David J. Garrett2, David A. Nayagam1, Joel Villalobos1, Penelope J. Allen1,2,3, Alexa Saunders1, Michelle McPhedran1, Ceara McGowan1, Hamish Meffin2, Robert K. Shepherd1,2, Bionics Institute, East Melbourne, VIC, Australia; 1School of Physics, The University of Melbourne, Melbourne, VIC, Australia; 2Centre for Eye Research Australia, East Melbourne, VIC, Australia; 3Royal Victorian Eye and Ear Hospital, East Melbourne, VIC, Australia; 4Victoria Research Laboratory, National ICT Australia, Melbourne, VIC, Australia; 5Electrical & Electronic Engineering, The University of Melbourne, Melbourne, VIC, Australia.

Purpose: Nitrogen incorporated ultrananocrystalline diamond (N-UNCD) has recently been shown to be a promising material as a stimulating electrode. The aim of this study was to assess if N-UNCD electrodes are capable of stimulating retinal ganglion cells (RGCs) in vivo, at stimulus intensities considered safe for this material.

Methods: Hermetic arrays containing 120x120 µm N-UNCD electrodes were fabricated on a polycrystalline diamond substrate and inserted through a 5mm incision and fixed epiretinally using a titanium tack. Impedances were measured before implantation and inserted into the suprachoroidal space of 60 current pulses (500 µs duration, 1029 µA, 10 ms interstimulus interval). The lateral rectus muscle was detached and a 9 mm full scleral thickness incision was made 1-4 mm behind the muscle insertion point, according to eye size. A pocket was created in the suprachoroidal space. The moulded array was inserted into the suprachoroidal space. The incision was closed and scleral anchor point sutured.

Results: Impedances in vivo (26.6±2 kΩ, Mean±SEM) did not differ (p>0.05) to those measured in vitro (26.4±2.3 kΩ). Epiretinal stimulation led to robust activation of the visual cortex with reliable thresholds measured from stimulating 30 of 42 electrodes. Best thresholds ranged between 29.5-442.6 µC/cm². Cathodic first pulses (54.9±2.8 nC) resulted in significantly lower (paired t-test, p<0.001) thresholds than anodic first pulses (73±5.2 nC). Histological analysis revealed focal damage to the retina surrounding the tacked edge of the implant. The retina beneath the diamond array remained attached. The extent of damage attributed to tacking alone versus the combined pressure from the tack and silicone implant body was unclear.

Conclusions: For all but three electrodes, charge densities required to evoke cortical responses were well within the previously established electrochemical safe limit for diamond (300 µC/cm²). N-UNCD electrodes were successfully used to acutely stimulate RGCs via an epiretinal approach with some electrodes requiring very low intensities to activate the visual cortex. Variability in impedances and thresholds, along with histological analyses, suggest that further optimization of the implant shape and tack insertion procedure is required to consistently obtain low thresholds and minimize damage. In addition, performance of these electrodes needs to be evaluated in chronic studies.

Commercial Relationships: Mohit N. Shivdasani, None; David J. Garrett, None; David A. Nayagam, None; Joel Villalobos, The Bionics Institute of Australia (P); Penelope J. Allen, Bionic Vision Australia (P); Alexa Saunders, None; Michelle McPhedran, None; Ceara McGowan, None; Hamish Meffin, NICTA (P); Robert K. Shepherd, None

Support: This work was supported by the Australian Research Council through its Special Research Initiative in Bionic Vision Science and Technology awarded to Bionic Vision Australia. The Bionics Institute wishes to acknowledge the support it receives from the Victorian Government through its Operational Infrastructure Program.

Program Number: 1030 Poster Board Number: C0007
Presentation Time: 1:00 PM - 2:45 PM

A Suprachoroidal Retinal Prosthesis with a Flexible Lead is Reliable for Patient Testing

Joel Villalobos1, Penelope J. Allen1,2,3, Chi D. Liu1,2, Lauren N. Ayton1,2, Jonathan Yeoh1,3, David A. Nayagam1, Nicholas L. Opte1,3, Mohit N. Shivdasani1, Robert K. Shepherd1,2, Chris E. Williams1,2, Bionics Institute, East Melbourne, VIC, Australia; 1Centre for Eye Research Australia, East Melbourne, VIC, Australia; 2Royal Victorian Eye and Ear Hospital, East Melbourne, VIC, Australia; 3Victoria Research Laboratory, National ICT Australia, Melbourne, VIC, Australia; 4Electrical & Electronic Engineering, The University of Melbourne, Melbourne, VIC, Australia.

Purpose: A flexible intraorbital lead was developed to minimise risk and simplify implantation of a retinal prosthesis. The microwire based prostheses was tested in a preclinical model, then optimised in cadavers and tested in a clinical pilot study.

Methods: Initially, a suprachoroidal (SC) electrode array was developed with a transcleral lead of 14-22 platinum microwires in silicone. It was implanted in cats (n = 16) for 3 months. The lead was sutured on the sclera with a silicone patch and tunnelled under conjunctiva to a patch on the orbital rim. It followed either a straight path (3 implants) of 12 mm; or a curved path (13 implants; Fig. 1) of 16 mm with 1 mm strain relief cones. Histological assessment was performed on the tissue around the lead. The lead routing was then fitted to a human orbit and tested in cadavers. This lead, with strain relief cones, was 34 mm to the lateral orbit where it was fitted inside a channel. Lead durability was then tested in a mechanical model of a skull and eye moving to 25° of abduction/adduction. A 24-channel electrode array with optimised lead and a percutaneous connector (on the parietal bone) was then implanted in a clinical pilot. The lead location was monitored with X-
ray and CT imaging. **Results:** The SC implant and orbital lead were well tolerated in all 16 cat eyes, with no conjunctival or skin erosion around the eye. From 197 individually wired electrodes with a curved lead, 177 were connected following 3 months of implantation; which contrasted with 24 connected out of 36 implanted using a straight lead (Chi-square P < 0.001). Implant and lead were stable in all but one case where the implant’s anterior end eroded the sclera. The typical tissue response around the moving lead was a thick granulomatous fibrous capsule. The leads in mechanical durability testing have undergone 65 million eye movements with no wire breakages. In humans, the implant with extraorbital lead was stable during the initial 6 months of implantation (Fig. 2). All the electrodes remained connected. **Conclusions:** The SC retinal implant with flexible lead allowed for minimal surgical manipulation of the eye and distal placement of larger components. The strain-relieved lead was reliable during chronic implantation in a preclinical model and in a clinical pilot.

**Fig 1.** Suprachoroidal implant with curved lead for cat

**Fig 2.** CT scan of patient with retinal prosthesis and strain-relieved lead (blue)

**Commercial Relationships:** Joel Villalobos, The Bionics Institute of Australia (P); Penelope J. Allen, Bionic Vision Australia (P); Chi D. Luu, None; Lauren N. Ayton, None; Jonathan Yeoh, None; David A. Nayagam, None; Nicholas I. Opie, None; Mohit N. Shrivastadi, None; Robert K. Shepherd, None; Chris E. Williams, Bionic Vision Australia (P)

**Support:** Australian Research Council through its Special Research Initiative in Bionic Vision Science and Technology grant to Bionic Vision Australia

**Clinical Trial:** NCT01603576

**Program Number:** 1031 Poster Board Number: C0008

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Operation and Performance of Eye-conformable Retinal Prosthesis using Liquid Crystal Polymer

Joonsoo Jeong1, Seung Woo Lee2, Kyoo sik Min1, Soowon Shin1, So Hyun Bae1, 2, Tae Wan Kim1, 2, Bum-Joo Cho1, Jong-Mo Seo1, 2, Hum Chung1, Sung June Kim1. 1Electrical Engineering and Computer Science, Seoul National University, Seoul, Republic of Korea; 2Neurosurgery, Massachusetts General Hospital, Harvard Medical School, Boston, MA; 3Ophthalmology, Seoul National University, Seoul, Republic of Korea; 4Ophthalmology, Kangnam Sacred Heart Hospital, Seoul, Republic of Korea; 5Ophthalmology, Seoul Nat’l Univ Boramae Medical Ctr, Seoul, Republic of Korea.

Purpose: A miniaturized and eye-surface conformable novel retinal prosthesis using monolithic encapsulation and deformation of biocompatible Liquid Crystal Polymer (LCP) was developed, and its in vivo functionality and long term reliability was assessed.

Methods: A miniaturized and eye-conformable retinal implant was fabricated through monolithic integration of all the electronic components on a multilayered LCP substrate. Electronics include 16-channel electrode array, multilayered planar coil and 16-channel current stimulator IC (AMS HV CMOS 0.35um). The LCP substrate was spherically deformed to fit the curvature of the eyeball. Stimulation parameters were controlled using a touchscreen-based external unit which can generate power and pulse-width-modulated (PWM) data for the wireless transmission via an inductive link at 2.5MHz. The device was implanted into the rabbit eye to evaluate its functionality and long-term stability by attaching the package on the superotemporal quadrant of the scleral surface under the Tenon’s capsule and inserting the electrode array into the suprachoroidal space via superonasal incision.

Results: The developed LCP-based monolithic retinal implant with circular package of 14mm in diameter and 1.5 mm in the maximum thickness was fabricated. Stimulation patterns and waveforms could be adjusted through the graphic user interface of an external unit and the transmitter coil attached on the skin up to coil distance of 17 mm in vivo. The device could be successfully implanted into the rabbit eye and has been stably implanted for more than 4 months without showing any adverse sign.

Conclusions: The exterior unit as well as the implantable unit performed as designed. Accelerated soak tests and in vivo animal test to verify their reliability and stability for an extended period of time are ongoing at this moment.

Commercial Relationships: Joonsoo Jeong. None; Seung Woo Lee. None; Kyoo sik Min. None; Soowon Shin. None; So Hyun Bae. None; Tae Wan Kim. None; Bum-Joo Cho. None; Jong-Mo Seo. None; Hum Chung. None; Sung June Kim. None

Support: Korea Health 21 R&D Project A050251 by MIHWF, Public Welfare and Safety Program 2012-0065666 by MEST, BK21, GPhD Fellowship from NRF

Program Number: 1033 Poster Board Number: C0010

Presentation Time: 1:00 PM - 2:45 PM

A bottom-up visual saliency-based image processing strategy for object recognition under simulated prosthetic vision

Xinyu Chai, Yanyu Lu, Weizhen Fu, Yao Chen, Chuangqing Zhou, Jing Wang. School of Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, China.

Purpose: Object recognition is among the most important visual tasks for the patients with visual protheses. This study is to propose an image processing strategy of visual prostheses based on a bottom-up saliency-based visual attention model to detect, extract and enhance the object in a daily scene.

Methods: 18 subjects with normal or corrected-to-normal vision participated in this study. 70 object images taken under indoor scene with 20° × 20° visual angle were chosen as experimental materials. The images were processed with a visual attention model (Itti et al, 1998) to produce salient points. These points were clustered into some regions by applying FCM algorithm and the closet-to-center region was chosen as the ROI. The object in the ROI was separated from the scene by using an image segmentation method, GrabCut. We adopted two foreground/background contrast-enhancing strategies to present images under simulated prothetic vision compared with a directly pixelization strategy (DP): the foreground with 8 gray levels while the background with 4 lower gray levels (8-4 separated pixelization, 8-4 SP) and the foreground with 8 gray levels while the background with edge extracted information (Background edge extraction, BEE).

Results: Subjects achieved above chance (1/70 = 1.43%) recognition accuracy (26.41 ± 8.83%) under DP condition. The two foreground/background separated strategies, 8-4 SP (41.73 ± 7.29%) and BEE (44.44 ± 7.70%), significantly increased the object recognition accuracy compared with DP (P < 0.05); however, there was no significant difference between these two strategies (P > 0.05). 70 objects were classified into 3 categories (perfect, good and bad) according to Jaccard Coefficient (JC) which evaluated the effectiveness of the object extraction from background. As JC (segmentation quality) increased, the object recognition accuracy significantly increased using 8-4 SP and BEE strategies (P < 0.05), while there was no significant difference among the categories using DP strategy.

Conclusions: The results showed the foreground/background contrast-enhancing strategies based on a saliency-based visual attention model can significantly improve the recognition accuracy of objects under daily scenes. We hope our study on image processing strategies will be helpful to the future design and development of visual prosthesis to restore functional vision for the blinds.

Commercial Relationships: Xinyu Chai, None; Yanyu Lu, None; Weizhen Fu, None; Yao Chen, None; Chuangqing Zhou, None; Jing Wang. None

Support: The National Basic Research Program of China (973 Program, 2011CB707503/2); The National Natural Science Foundation of China (61273368, 91120304)

Program Number: 1034 Poster Board Number: C0011

Presentation Time: 1:00 PM - 2:45 PM

Immunohistochemical and electrophysiological analysis of rat retinas after subretinal implantation of photovoltaic arrays

Jacob G. Light1, 2, James W. Fransen3, Alice Adkins4, Gobinda Pangenti5, James Loudin6, 7, Keith Mathiesen6, 7, Daniel V. Palanker6, 7, Maureen A. McCall8, Machelle T. Parada1, 2, 4, Ophthalmology, Emory University, Atlanta, GA; 2Rehab Center of Excellence, Atlanta VA Medical Center, Atlanta, GA; 3Anatomical Sciences & Neurobiology, University of Louisville, Louisville, KY; 4Ophthalmology & Visual Sciences, University of Louisville, Louisville, KY; 5Hansen Experimental Physics Laboratory, Stanford University, Stanford, CA; 6Ophthalmology, The Byers Eye Institute at Stanford University, Palo Alto, CA; 7Santa Cruz Institute for...

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Physiological Response of RD Mouse Retinal Ganglion Cells to Electrical Stimulation

Alice Cho, Alapakkam P. Sampath, Mark S. Humayun, James D. Weiland
1Biomedical Engineering, University of Southern California, Los Angeles, CA; 2Ophthalmology, University of Southern California, Los Angeles, CA.

Purpose: The aim of this study was to assess how the intrinsic properties of retinal ganglion cells (RGC) in a mouse model of retinal degeneration affect thresholds to electrical stimulation.

Methods: The animal model used for this study was the rd10 mouse, aged 6-10 weeks. The rd10 mutation is caused by a missense mutation on the gene encoding the PDE-beta subunit and results in almost complete loss of photoreceptors by the end of two months. Spontaneous baseline activity and spikes elicited by external stimulation were recorded from RGCs using whole-cell patch clamp. The stimulating electrode was a 75 μm diameter Pt-Ir disk positioned approximately 50 μm above and 50 μm laterally from the targeted RGC; the ground electrode was positioned behind the retina on the photoreceptor side. Charge-balanced biphasic square pulses (cathodic-phase first, 50 μs/phase) were delivered at 10 Hz frequency.

Results: For each ganglion cell, measurements for threshold, soma diameter, resting membrane potential, spontaneous firing rate, and presence/absence of rebound excitation were recorded. Since a subset of rd10 RGCs exhibited a high rate of spontaneous activity that was not observed in wildtype mice, cells were classified into two groups - low rate (spontaneous rate < 10 Hz) and high rate (spontaneous rate ≥ 10 Hz) - based on their baseline activity. RGCs with high spontaneous rates had significantly lower electrical thresholds than cells with lower spontaneous rates (μlow = 46.66 μA, μhigh = 27.67 μA, p = 0.0423); the relationships between threshold/resting membrane potential and spontaneous rate were not significant. RGCs were also functionally classified into ON or OFF cells based on their ability to exhibit rebound excitation (D.J. Margolis, 2007). OFF ganglion cells had higher spontaneous firing rates than ON ganglion cells (μOFF = 4.93 Hz, μON = 0.238 Hz, p = 0.0114) but their threshold and resting potential measurements were not statistically different.

Conclusions: OFF ganglion cells appear to exhibit higher rates of spontaneous activity compared to ON ganglion cells and RGCs with higher spontaneous rates had lower electrical thresholds than cells with lower rates. These results suggest that intrinsic spontaneous activity may increase sensitivity to extracellular stimulation and may enable OFF RGCs to be selectively stimulated at lower thresholds than ON RGCs due to their elevated spontaneous firing rates.

Commercial Relationships: Alice Cho, None; Alapakkam P. Sampath, None; Mark S. Humayun, Bausch & Lomb (F), Bausch & Lomb (C), Bausch & Lomb (B), Bausch & Lomb (R), Alcon (C), Alcon (R), Iridex (P), Iridex (R), Replenis (I), Replenis (C), Replenis (R), Replenis (S), Second Sight (F), Second Sight (I), Second Sight (C), Second Sight (P), Second Sight (R), Second Sight (S), Regenerative Patch Technologies (I), Regenerative Patch Technologies (C); James D. Weiland, Second Sight Medical Products, Inc. (F)

Support: NSF EEC-0310723; Research to Prevent Blindness, W.M. Keck Foundation

Program Number: 1036 Poster Board Number: C0013
Presentation Time: 1:00 PM - 2:45 PM

Re-alignment and explantation of subretinal prostheses: surgical aspects and proteomic analyses


Purpose: Active subretinal implants are highly complex, constantly improved devices requiring sophisticated surgical procedures. Under certain circumstances corrections, such as realignments, explantations, and reimplantations become necessary. Intracellular tissue reactions to devices, e.g. from scleral, retinal or RPE cells, have been described on a histologic (Gekeler, ARVO 2010) but not on a proteomic level.

Methods: 34 patients have been implanted with a subretinal MPDA; 2 patients underwent re-alignment (avg. 1.5), 10 patients after the pilot trial had explantation (avg. 9.5), and 1 re-implantation surgery (2.5, all in months). 3 removed implants were analyzed using liquid
chromatography coupled to electrospray Orbitrap mass spectrometry (nHPLC-MS/MS) following limited proteolysis of the proteins that covered the surfaces.

**Results:** Longer intervals since implantation resulted in more scarring around the polyimide (PI) foil on the sclera but no adhesion was found; implants were retrieved in 2-3 pieces, unharmed for technical analyses. PI foils and MPDAs were pulled out without silicone oil exchange. One patient (with initial subretinal hemorrhage) suffered from retinal detachment after explantation requiring oil exchange. Retinas over the MPDA remained unaltered in funduscopy and SD-OCT. In case of the first explant, proteomic analysis exhibited more than 900 protein identifications over the MPDA and 364 on the section of the implant on the sclera. Besides a huge overlap of common housekeeping, e.g. GAP-dehydrogenase and aldolase, and plasma proteins like serotransferrin a set of eye-, and/or retina-specific proteins like alpha-crystallin, beta arrestin and retinol-converting enzymes were identified from the chip section. All sections of the explanted device showed slight coverage by immunoreactive proteins like immunoglobulins lambda and J, integrins alpha and beta, and by complement factors.

**Conclusions:** Explantation and reimplantation surgery is feasible in subretinal implants as tissue reactions in the subretinal space are minimal. Proteomic analyses of explanted subretinal MPDAs revealed common protein sets on the surface as reported for other types of implants, e.g. silicone devices, reflecting both, minor irritation of the surrounding tissue and the body’s tendency to coat implants with an extracellular matrix. Proteomics can be valuable to improve biocompatibility tests in retinal implants.

**Commercial Relationships:** Florian Gekeler, Retina Implant AG (F), Okuvision GmbH (F), Retina Implant AG (C), Retina Implant AG (P); Helmut G. Sachs, Retina Implant AG (R), Retina Implant AG (C); Veronique Kitiratschky, None; Katarina Stigl, Retina Implant AG (F); Udo Greppmaier, Retina Implant AG (E), Okuvision GmbH (E); Eberhart Zrenner, Retina Implant AG (F), Retina Implant AG (I), Retina Implant AG (C), Retina Implant AG (P), QLT Inc (C), Servier, Paris (C), Steinbeis GmbH&CoKG, Stuttgart (I), Steinbeis GmbH&CoKG, Stuttgart (C), Neurotech, USA (C), Pfizer, USA (C); Karl-Ulrich Bartz-Schmidt, Retina Implant (P); Marius Ueffing, None; Sascha Dammeier, None

**Support:** Retina Implant AG, Reutlingen, Germany

**Clinical Trial:** NCT00515814, NCT01024803, NCT01497379

**Program Number:** 1038 Poster Board Number: C0015

**Presentation Time:** 1:00 PM - 2:45 PM

**Long-term Reliability of Argus® II Retinal Implants**


**Purpose:** Retinal prostheses are susceptible to damage by body fluids over time. Long-term reliability of retinal prostheses requires hermetic packaging to protect the electronic circuitry of the implant from the harsh environment of the human body and a robust high-density electrode array for safe chronic stimulation. In addition to lifetime testing under normal use conditions, accelerated lifetime testing has been widely used to predict the implants’ life and to better understand their failure modes.

**Methods:** Lifetime testing of the Argus II implant has been conducted at the component, subsystem and final device levels. Long-term stability of the implants is assessed in vitro through active soak tests under constant pulse stimulation. The implants are tested in buffered saline at body temperature, or elevated temperatures for accelerated tests. The implants are attached to the silicone eye model to simulate the actual implanted condition. In some tests, a motor moves the entire eye model to simulate micromotion of a human eye. The device functionality, visual appearance, and material changes are monitored through the course of the lifetime test.

**Results:** Electrode material lifetime has reached 7 years in real-time testing under constant pulse stimulation and predicted equivalent of over 50 years of use in accelerated testing. Thin-film polymer electrode array insulation has reached 7 years in real-time testing and an equivalent lifetime of over 26 years in accelerated testing. Finished implants have reached more than 10 year lifetime in accelerated testing. These bench-test results are supported by clinical trial data: 30 subjects have been implanted an average of 4.2 years (range 3.3 to 5.5, excluding one explant at 18 months). Cumulatively, this represents 125 patient-years with only one device failure at 4 years post-implant.

**Conclusions:** The Argus II Retinal Implant has been tested at the component and system levels for long-term reliability. Thin-film electrode arrays withstood aggressive constant pulse stimulation and provided long-term safe stimulation without corrosion or material degradation. The hermetic package demonstrated the functional lifetime of the implant by preventing the moisture level accumulated inside the device. Lifetime tests support long-term reliability of Argus II Retinal Implants. Such long-term reliability is of paramount concern with respect to regulatory approval, and clinical utility, safety, and adoption.

**Commercial Relationships:** David Zhou, Second Sight Medical Products (E); Alexander Istomin, Second Sight Medical Products (E); Amy Hines, Second Sight Medical Products (E); Alina Agazaryan, Second Sight Medical Products, Inc (E); Charles A. Byers, None; James Little, Second Sight Medical Products Inc (I), Second Sight Medical Products Inc (E), Second Sight Medical Products Inc (P); Brian V. Mech, Second Sight (E), Second Sight (I), Second Sight (P); Robert J. Greenberg, Second Sight Medical Products, Inc (I), Second Sight Medical Products, Inc (E), Second Sight Medical Products, Inc (P), Second Sight Medical Products, Inc. (S)

**Support:** NIH grant EY012893

**Program Number:** 1038 Poster Board Number: C0015

**Presentation Time:** 1:00 PM - 2:45 PM

**Morphological comparisons of flat and 3-dimensional subretinal photovoltaic arrays in rat and pig models of retinitis pigmentosa**

Alice Adkins¹, Wei Wang³, Henry J. Kaplan², Douglas Emery⁴, Juan P. Fernandez de Castro⁵, Sang-Joon Lee²,³, Philip Huie⁴,⁵, Daniel V. Palanker⁴,³, Maureen A. McCall⁶,⁷, Michelle T. Pardue⁶,⁷

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**Purpose:** Retinal prosthetics are designed to restore vision to patients with photoreceptor degeneration. Theoretically, close proximity of inner retinal cells to stimulating electrodes is needed for their optimal activation. We evaluated the morphology of retinas with subretinal inactive polymer arrays (IPAs) containing gaps between the pixels or pillar electrodes. In addition, we compared IPAs to active silicon photovoltaic arrays (PVAs) with only gaps.

**Methods:** IPAs or PVAs were implanted into the subretinal space of P23H-1 rats (8-11 wks of age) and P23H-1 transgenic and wildtype (WT) pigs (6-14 wks age). Implanted IPAs were either: (1) flat
devices with 70 or 140 micron pixels separated by 5 or 10 micron gaps or (2) vertical pillar devices of various densities but without gaps. PVAs had a similar flat design. SD-OCT images visualized the placement of the implant 2 weeks after implantation and subsequently at regular biweekly intervals to monitor changes in retinal morphology. At the end of the experiment, rat (8 and 16 wks post-implantation) and pig eyes (2, 4 and 8 wks post-implantation) were enucleated and fixed. The tissue under the implant was examined in histological sections for migration of inner retinal cells through the implant gaps and any other morphological changes and compared to tissue near and distal to the implant.

**Results:** IPAs with 10 micron gaps showed significant migration of inner retinal cells to the RPE-side of the implant compared to 5 micron gap devices (36% vs 15%, p<0.001). Similar to IPAs, PVAs with 5 micron gaps showed little migration in rats or pigs. Surgical implantation of pillar devices was significantly more difficult than flat devices and created greater tissue trauma and glial reactions. In 38% of the cases, the ends of some pillars protruded through the rat retina over time.

**Conclusions:** The retinal response to PVAs or IPAs is similar. Ten micron gaps created significant inner retinal cell migration while 5 micron gaps allow close proximity of the inner retina to the device without excessive migration through the gaps. Flat devices with gaps are much easier to implant, they produced less trauma than the pillar arrays, and results in better inner retinal proximity.

**Commercial Relationships:** Alice Adkins, None; Wei Wang, None; Henry J. Kaplan, None; Douglas Emery, None; Juan P. Fernandez de Castro, None; Sang-Joon Lee, None; Philip Huie, None; Daniel V. Palanker, None; Maureen A. McCull, None; Machelle T. Pardue, None

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**Program Number:** 1039 Poster Board Number: C0016

**Presentation Time:** 1:00 PM - 2:45 PM

**Combining holographic stimulation with cellular resolution imaging in the rodent eye**

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Nairouz Farah¹

¹Biomedical Engineering, Technion, IIT, Haifa, Israel; ²Medical Engineering, Ruppin Academic Center, Emek Hefer, Israel

**Purpose:** Optical retinal prostheses for patients with outer-retinal degenerative diseases could interface directly with surviving retinal neurons in order to mimic the normal input obtained from photoreceptors in healthy retinas. Recently, we introduced an artificial photo-stimulation technique based on the projection of holographic patterns with high spatio-temporal resolution onto optogenetic probes, to selectively control large retinal neuronal populations in the isolated retina. Here, we explore the ability to target single optogenetic-expressing retinal ganglion cells (RGCs) with holographic patterns at a cellular resolution, in-vivo.

**Methods:** For image-guided neuronal targeting, we constructed a system that combines precise spatiotemporal holographic photo-stimulation with high resolution fundus imaging. The system is also integrated with a multiphoton microscope to enable functional imaging of the responses to artificial stimulation.

**Results:** The system was utilized to acquire both brightfield and fluorescence fundus images of mice and rats in-vivo, enabling the identification of single fluorescent RGCs for stimulation. Holographic patterns were projected onto the rods’ retinas and imaged. The stimulation spot diameter is sufficient for cellular targeting using patterned photo-stimulation.

**Conclusions:** Our system enables single-cell resolved patterned holographic photo-stimulation of RGCs in-vivo which will enable the further development of a novel optical retinal prosthesis.

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**Support:** European Research Council (grant #211055)

**Program Number:** 1040 Poster Board Number: C0017

**Presentation Time:** 1:00 PM - 2:45 PM

**Argus® II Retinal Prosthesis System safety profile in post-market patients**

Robert J. Greenberg¹, Peter Walter³, Albert J. Augustin⁵, Bernd Kirchhoff⁶, Lyndon daCruz⁴, Hannah Schimitzek³, Gernot Roessler³, Stanislao Rizzo⁵

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**Purpose:** The Argus II Retinal Prosthesis System (Argus II) is the first and only artificial retina approved for market use (2011 CE mark in Europe, US FDA approval pending) and has since been implanted in 16 severely vision impaired retinitis pigmentosa patients in 5 surgical centers in Italy, Germany and the UK. A post-market surveillance study has been initiated with the purpose to evaluate the safety profile of the approved device during commercial use compared to that observed in the investigational clinical study.

**Methods:** Safety data has been collected from the day of surgery to early December 2012, covering on average 6.2 months (median 6.6 months, range from 2 days to 13.3 months; 8.2 patient years) of exposure. Vigilance requirements have ensured complete capture of all safety related events in all implanted patients, independently from their participation in the post market study. The demographic distribution is: 6 female and 10 male patients, average age 50.8 years (range 31.0 - 74.0 years); 9 OD and 7 OS implanted eyes.

**Results:** No surgical procedure or device-related serious adverse event has occurred to date. Ten patients experienced no surgery- or device-related adverse events. The other six patients experienced 7 surgery related non-serious adverse events, which occurred between the day of surgery up to 1 month post operatively: two instances of IOP elevation, and one each of nausea, vomiting, fainting, conjunctival irritation, and retinal tear (occurred during surgery when a retinal membrane was peeled prior to placing the implant). The first 5 events resolved between the same day and 9 days with medical treatment; the last two are ongoing. One patient also experienced device induced headache that is mitigated by adjustment of the device settings.

**Conclusions:** The first group of Argus II patients using the commercially available device demonstrates a safety profile that is at 6 months post implantation markedly better than that observed in the developmental phase of Argus II.

**Commercial Relationships:** Robert J. Greenberg, Second Sight Medical Products, Inc. (I), Second Sight Medical Products, Inc. (E), Second Sight Medical Products, Inc. (P), Second Sight Medical Products, Inc. (S); Peter Walter, Novartis (R), Bayer (R), Second Sight (R), Bayer (F), Novartis (F); Albert J. Augustin, 2nd sight (F), Alcon (C), Allergan (C), Novartis (F); Bernd Kirchhoff, None; Lyndon daCruz, Second Sight Medical products Inc. (R); Hannah Schimitzek, None; Gernot Roessler, None; Stanislao Rizzo, None

**Program Number:** 1041 Poster Board Number: C0018
Presentation Time: 1:00 PM - 2:45 PM
Simulating current focusing and steering in penetrative optic nerve stimulation: a computational model
Qiushi Ren1, Menghui Li2, Yan Yan1, Liming Li2. 1Biomedical Engineering, University of Southern California, Los Angeles, CA; 2Biomedical Engineering, Peking University, Beijing, China.

Purpose: A visual prosthesis based on penetrative optic nerve (ON) stimulation is a potential way for vision recovery. The fact that an enormous number of RGC axons of various diameters are tightly packed in mammalian optic nerve makes it difficult to implant more numbers of stimulating electrodes. Here we presented a computational model to simulate and evaluate two widely used field shaping strategies, current steering and current focusing, in penetrative stimulation of rabbit ON.

Methods: Finite element models with were established to compute the 3D electric potential distribution generated with different stimulating parameters under 2 and 3-electrode configurations. Then the external electric potential was fed to a large number of randomized multi-compartment cable models to calculate the membrane potential of each ON fibre to predict whether AP could be elicited in each sampled position. Finally a statistical process was conducted to quantify the recruitment region and three indicators were statistically derived to evaluate effects of current steering and current focusing.

Results: The shifting rate (SR) value of the 2-electrode configuration showed consistent correlation to the steering coefficient, whereas no such significant correlation could be detected in that of the 3-electrode configuration. For the 3-electrode configuration, large values of compensation coefficient resulted in a large recruitment area in the (ON) under arbitrary stimulus amplitude, which was contrary to the intention of current focusing. Both configurations demonstrated rather localized neural fibre recruitment compared with the surface ON stimulation.

Conclusions: The simulation results show that the 2-electrode configuration excels in current steering whereas the 3-electrode configuration performs poorly in both current steering and focusing. The localized recruitment of both configurations implies that current focusing might be unnecessary in penetrative optic nerve stimulation.

Program Number: 1042 Poster Board Number: C0019

Presentation Time: 1:00 PM - 2:45 PM
Retinal Prostheses: Functional Use of Monocular Depth Perception in the Low Resolution Limit
Noelle R. Stiles1, Ben P. McIntosh2, Armand R. Tanguay2, Mark S. Humayun1. 1Computation and Neural Systems Program, California Institute of Technology, Pasadena, CA; 2Electrical Engineering-Electrophysics, University of Southern California, Los Angeles, CA; 3Electrical Engineering-Electrophysics, Biomedical Engineering, and Ophthalmology, University of Southern California, Los Angeles, CA; 4Ophthalmology, Cell and Neurobiology, and Biomedical Engineering, University of Southern California, Los Angeles, CA.

Purpose: Monocular depth perception (using cues such as perspective and relative size) persists to very low resolution in both static and dynamic images (at video frame rates), with potential implications for limited resolution retinal prostheses that are currently implanted in only one eye. An image depth-rating task previously demonstrated a significant improvement in depth perceived by Gaussian filtering of pixelated images that exhibit false depth cues (N=11). The depth-rating task also showed that depth could be perceived even at very low resolutions (e.g., 8 x 10 pixels or electrodes) when dynamic depth cues (such as motion parallax) were present. This study investigates the degree to which image representation and resolution affects the performance of functional tasks. Furthermore, the role of foveation in improving the performance of such tasks at low resolution with restricted field-of-view was studied. Foveation may improve the functionality of retinal prostheses that currently use a head-mounted camera without eye-tracking capability, and can be implemented either with an intraocular camera or with eye-tracking and a wide field-of-view scene camera.

Methods: A functional reaching task with a head-mounted display (HMD) was used to determine monocular depth perception capabilities at low resolution with different image representations. Images were acquired from a head-mounted wide-field-of-view camera, processed to low resolution (pixelation and blur or pixellation alone), and then displayed in real time within the HMD. In the eye-pointed mode, the subject’s gaze directed the subregion of the wide-field-of-view (FOV) image displayed to the user; head position alone determined the subregion of the image displayed in the head-pointed mode.

Results: Subjects (N=3) were able to reach and grasp a bottle while avoiding obstacles with pixellated and blurred images in the eye-pointed mode faster than with pixellated images in either mode. The task with 32 x 32 pixels, Gaussian post-pixelation blurred and eye-pointed took on average 5.3 seconds, as compared with 2.4 seconds on average with normal vision.

Conclusions: Results show that appropriate presentation of images as well as the implementation of foveation in retinal prostheses improve the efficiency of depth task performance. The functional task also affirms that subjects with a retinal prosthesis may be able to perceive depth monocularly.

Commercial Relationships: Noelle R. Stiles, Patent (not licensed) (P); Ben P. McIntosh, None; Armand R. Tanguay, University of Southern California (P); Mark S. Humayun, Bausch & Lomb (F), Bausch & Lomb (C), Bausch & Lomb (P), Bausch & Lomb (R), Bausch & Lomb (S), Alcon (C), Alcon (R), Iridex (P), Iridex (R), Replensih (I), Replensih (C), Replensih (R), Replensih (S), Second Sight (F), Second Sight (I), Second Sight (C), Second Sight (P), Second Sight (R), Second Sight (S), Regenerative Patch Technologies (I), Regenerative Patch Technologies (C)

Support: National Science Foundation, National Science Foundation Graduate Research Fellowship

Program Number: 1043 Poster Board Number: C0020

Presentation Time: 1:00 PM - 2:45 PM
Relative efficiency of voltage vs. current pulses for retinal stimulation
Navya S. Davuluri1, Mark S. Humayun2, 3, James D. Weiland2, 3. 1Biomedical Engineering, University of Southern California, Los Angeles, CA; 2Ophthalmology, Doheny Eye Institute, Los Angeles, CA.

Purpose: This in-vivo study is aimed at comparing supra-threshold responses of rat retinal ganglion cells (RGC) to rectangular current controlled and rectangular voltage controlled pulses. This is motivated by the need to determine efficient stimulation strategies for an electronic retinal prosthesis.

Methods: In 10 Long-Evans rats, we inserted a Pt/Ir electrode (D=75 μm) in the left eye and exposed the right SC. The left retina was stimulated with current controlled and voltage controlled pulses of varying pulse width and amplitude. A large needle electrode distant from the eye was used as a current return. While stimulating the
retina, evoked potentials were recorded from the superior colliculus (SC), a midbrain structure in the visual pathway. The pulse widths were 0.3 ms, 0.5 ms, 1 ms and 2 ms. For each pulse width, 4 amplitudes between 10 and 60 nC were applied in both current and voltage mode.

**Results:** Power in the evoked potentials recorded from the SC was used to determine stimulation efficiency. In general, whether current controlled or voltage controlled pulses are more efficient depends on the stimulus pulse width. For 0.3 ms pulse width, at every charge level both current controlled and voltage controlled pulses were equally efficient (student t-test, p > 0.05). For 0.5 ms pulse width, voltage controlled pulses generated evoked potentials with significantly higher power than current controlled pulses (student t-test, p < 0.05). For 1 ms case, current controlled pulses were significantly efficient than voltage controlled pulses for the lower charge levels (student t-test, p < 0.05). And for 2 ms pulse width, current controlled pulses were significantly efficient than voltage controlled pulses for all charge levels (student t-test p < 0.05).

**Conclusions:** The efficiency of retinal stimulation depends on the pulse width and the stimulation mode. Other factors that may affect stimulation efficiency include electrode size and electrode material.

**Commercial Relationships:** Navya S. Davuluri, None; Mark S. Humayun, Bausch & Lomb (F), Bausch & Lomb (C), Bausch & Lomb (P), Bausch & Lomb (R), Bausch & Lomb (S), Alcon (C), Alcon (R), Iridex (P), Iridex (R), Replenish (I), Replenish (C), Replenish (R), Replenish (S), Second Sight (F), Second Sight (I), Second Sight (C), Second Sight (P), Second Sight (R), Second Sight (S), Regenerative Patch Technologies (I), Regenerative Patch Technologies (C); James D. Weiland, Second Sight Medical Products, Inc. (F)

**Support:** Research to Prevent Blindness, W.M. Keck Foundation; NSF EEC-0310723;

**Program Number:** 1044 Poster Board Number: C0021
**Presentation Time:** 1:00 PM - 2:45 PM

**Psychophysics of a suprachoroidal retinal prosthesis**


1Bionics Institute, East Melbourne, VIC, Australia; 2Medical Bionics, The University of Melbourne, Melbourne, VIC, Australia; 3Centre for Eye Research Australia, Melbourne, VIC, Australia.

**Purpose:** The hypothesis was tested that electrodes implanted in the suprachoroidal space would produce phosphene images for the representation of visual information in patients with profound vision loss.

**Methods:** Two patients with retinitis pigmentosa were implanted with a suprachoroidal electrode array having 17 600µi and three 400µi platinum electrodes and several return configurations. Preoperatively, both patients had bare light perception and could not recognise shapes. A specially designed stimulator and psychophysics test setup were used to measure electrode impedance, threshold, dynamic range, perceived shape, size, position, and intensity of phosphenes produced by stimulating one electrode at a time. These data were included in phosphene maps suitable for encoding images or creating complex shapes by stimulating multiple electrodes in an interleaved fashion.

**Results:** Electrode impedances were around 20 kΩ for stimulation with biphasic current pulses with durations 500µs per phase and 500µs interphase gap. All electrodes produced phosphenes. Thresholds were lowest (down to 50 nC per phase) when the anodic phase preceded the cathodic phase of the pulse, the monopolar electrode configuration was used, and pulse rates of 200 to 500pps were used. Dynamic ranges were limited by the maximum electric charge density per phase. Phosphenes varied from quite complex (including dark and light regions) for electrodes close to the fovea, and became simpler for more peripheral electrodes (such as grey cloudy convex shapes). Phosphene shape, size, and position did not vary much between electrode configurations (monopolar, common ground, hexagonal) or with pulse parameters. Pulse rates of 220

**Conclusions:** A suprachoroidal retinal prosthesis with relatively large electrodes produces distinct phosphenes when stimulated in monopolar or common ground electrode configurations, and these phosphenes can be used to “paint” distinctive shapes.

**Commercial Relationships:** Peter J. Blamey, Bionics Institute (P); Cochlear Limited (P); Nicholas C. Sinclair, None; Kyle Slater, None; Hugh J. McDermott, None; Thushara Perera, None; Peter N. Dimitrov, None; Mary Varsamidis, None; Lauren N. Ayton, None; Robyn H. Guymet, Novartis Advisory board (C), Bayer Advisory Board (C), Novartis (R); Chi D. Lau, None

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**Clinical Trial:** NCT01603576

**Program Number:** 1045 Poster Board Number: C0022
**Presentation Time:** 1:00 PM - 2:45 PM

**Determination of Electrode Proximity to the Retinal Surface from the Stimulus Pulse Waveform**

*Joseph Majdi*, 1, 2, *Saugandhika Minnikanti*, 1, 2, *Anant Agrawal*, 1, 2, *Nathalia Peisoso*, 1, 2, *Ethan D. Cohen*, 1, 2, 3

1Division of Physics, Office of Science and Engineering Laboratories, Center for Devices and Radiological Health, FDA, Silver Spring, MD; 2Electrical & Computer Engineering Department, George Mason University, Fairfax, VA.

**Purpose:** To determine the proximity of an stimulus electrode to the retinal surface for effective activation of the underlying local retinal neurons by epiretinal prostheses.

**Methods:** Using a superfused rabbit eye cup preparations, we advanced a thick fluoropolymer insulated (1.6mm) Pt electrode (0.25mm diameter, cut at a 37° angle) parallel to the retinal surface, while applying 0.95msec biphasic 10µA pulses and recorded the resulting voltage waveform. Using a micromanipulator, we advanced the electrode from 1000µm towards the retinal surface, while simultaneously monitoring the electrode’s charging characteristics and position using Fourier domain optical coherence tomography. A series of proximity experiments were performed by applying 10mVrms sine waves from frequencies of 1Hz to 100kHz in order to evaluate changes in the electrode impedance and phase angle.

**Results:** We found that the voltage step at pulse onset increased as the electrode approached the retinal surface. The series resistance of electrical stimulation rose indirectly proportional to the electrode-retina proximity by 3300±680Ω with the 50% midpoint averaging 32µm from the surface and the charging characteristics fit closely to exponential decay for greater distances. The resistance increased an additional 1300±640Ω as the electrode depressed the retina 50µm against the choroid. A similar impedance relation was seen for retinal proximity with impedance spectroscopy. At 100kHz, the impedance modulus increased 4.6±0.9 fold (n=6) at the retinal surface compared to a distance of 1000µm. Interestingly, at 10kHz we observed a 25° difference in phase between the 1000µm and 0µm electrode.
configurations. This difference was significant and observed in all experiments we performed (n=6). These results point to signature impedance spectral features (modulus and phase) for proximity of electrode to the retinal surface.

**Conclusions:** We found several different methods to measure retinal proximity from an epiretinal stimulus electrode. An inverse relationship was found between the voltage step on the stimulus pulse and its proximity to the retinal surface and there were also differences using impedance spectroscopy.

**Commercial Relationships:** Joseph Majdi, None; Saugandhika Minnikanti, None; Anant Agrawal, None; Nathalia Peixoto, None; Ethan D. Cohen, None

**Support:** Critial Path Initiative (FDA)

**Program Number:** 1046

**Poster Board Number:** C0023

**Presentation Time:** 1:00 PM - 2:45 PM

**Evaluation of safety of porous surface electrodes for STS Retinal prosthesis**

Hiroaki Kando	extsuperscript{1}, Takeshi Morimoto	extsuperscript{1}, Yasuo Terasawa	extsuperscript{2}, Yukari Nakano	extsuperscript{1}, Kohji Nishida	extsuperscript{2}, Takashi Fujikado	extsuperscript{1,3}.

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	extsuperscript{2}Vision Institute, NIDEK Co., Ltd., Gamagori, Japan; 
	extsuperscript{3}Ophthalomology, Osaka University Graduate School of Medicine, Suita, Japan.

**Purpose:** We have reported that our originally developed retinal prostheses with suprachoroidal-transretinal stimulation (STS) effectively elicited phosphene with current less than 1.0 mA in patients with advanced retinitis pigmentosa (Fujikado, IOVS 2010). Now we have developed a novel porous stimulating electrode (porous electrode) for retinal prostheses for STS system (Terasawa, ARVO 2012). The porous electrode has a large surface area introducing porous surface of the platinum bulk electrode with a femtosecond laser irradiation. To verify their safety, we investigated the threshold current for retinal damage by a 48-h continuous-stimulation test.

**Methods:** Ten eyes of 10 pigmented rabbits were used in this study. We created a scleral pocket at the posterior pole of the eye and implanted the stimulating electrode. The stimulating electrode comprised a single-channel porous electrode (diameter, 0.5 mm; height, 0.3 mm). The rabbits were divided into four groups and stimulated with electrical currents of different intensities: 1.0 mA (n = 2), 1.5 mA (n = 3), 2.0 mA (n = 3), and 3.0 mA (n = 2). Continuous biphasic pulses of 0.5 ms/phase were applied at a frequency of 20 Hz for 48 h under general anesthesia. Fundus photography, fluorescein angiography (FA), and optical coherence tomography (OCT) were performed before and after applying the electrical currents. After the experiment was concluded, the eyes were enucleated and the retinas were stained with hematoxylin and eosin, and examined by light microscopy.

**Results:** In the 1.0 mA and 1.5 mA groups, changes were not observed on fundus photography, FA, OCT, or histological examination. Leakage of fluorescent dye was observed in one of three cases in the 2.0 mA group and in all cases in the 3.0 mA group. Probit analysis of the relationship between retinal pigment epithelium (RPE) damage and stimulus intensity suggested that 2.1 mA led to an RPE damage incidence rate of 50%.

**Conclusions:** These results indicate that the threshold current to induce retinal damage is greater than the current to elicit phosphene in STS. Therefore, the porous electrodes are feasible as stimulating electrodes for STS retinal prostheses.

**Commercial Relationships:** Hiroyuki Kanda, Nidek Co., Ltd. (P); Takeshi Morimoto, None; Yasuo Terasawa, Nidek Co., Ltd. (E); Yukari Nakano, NIDEK CO., LTD. (E); Kohji Nishida, Alcon (C), Alcon (F), HOYA (F), Senju (F), Pfizer (F), Santen (F), Osaka University (P); Takashi Fujikado, Nidek (P)

**Support:** None in the Support

**Program Number:** 1047

**Poster Board Number:** C0024

**Presentation Time:** 1:00 PM - 2:45 PM

**A monolithic diamond microelectrode array fabricated for a high acuity retinal prosthesis**

Kumaravela Ganesan	extsuperscript{1,2}, David J. Garrett	extsuperscript{1,2}, Mohit N. Shivadasani	extsuperscript{1}, David A. Nayagam	extsuperscript{1,3}, Joel Villalobos	extsuperscript{2}, Hamish Meffin	extsuperscript{2}, Kate E. Fox	extsuperscript{2,3}, Samantha G. Lichter	extsuperscript{1,2}, Robert K. Shepherd	extsuperscript{1}, Physic, The University of Melbourne, Parkville, VIC, Australia; 2Bionic Vision Australia, Melbourne, VIC, Australia; 3The Bionics Institute, East Melbourne, VIC, Australia; 4Department of Pathology, The University of Melbourne, Fitzroy, VIC, Australia; 5NICTA, Department of Electrical and Electronic Engineering, The University of Melbourne, Melbourne, VIC, Australia.

**Purpose:** To fabricate and test a biocompatible, chemically inert, hermetically sealed, near-conformable microelectrode array comprised of two kinds of diamond materials.

**Methods:** Feedthroughs were made on insulating polycrystalline diamond (PCD) substrate using laser milling and electrically conducting nitrogen incorporated ultrananocrystalline diamond (N-UNCD) was grown on top of it using chemical vapour deposition. Finally, the N-UNCD electrodes were electrically isolated by laser milling. An optical 3D profile image of the flat part of a 16x16 electrode array is shown in Fig. 1. The electrode array was tapered in order to reduce the space between the electrode and the retina with approximate radius of 12 mm as shown in the Fig. 2. In order to test the stimulation efficacy, diamond electrodes were tested using acute in vivo preclinical models. The hermeticity of the array was tested using a helium leak tester by attaching the electrode array by a Viton® O-ring.

**Results:** A high density hermetic diamond microelectrode array was fabricated and implanted in vivo with a PDMS carrier and the average minimum charge density required to produce cortical activity was 151 µC cm⁻². The in vivo electrode impedances were between 2.5-76kΩ and stable over the course of the acute testing phase. The helium leak rate was found lower than the detection limit of the helium mass spectrometer (10-11 mbar L s⁻¹) for approximately 30s and thereafter helium is found to leak through the O-ring.

**Conclusions:** The average threshold charge density exhibited by the diamond arrays presented here is well within the safe charge injection limit. The hermeticity of the high density electrode array means that the array can also function as encapsulation for implantable microelectronics. The use of a single material for construction of the array eliminates any potential materials mismatches that could lead to device failure. The results are evidence that diamond shows potential for both active and passive components of an implantable neural prosthesis.

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Fig. 1: A 3-D optical profile image of the 16x16 diamond micro electrode array.

Fig. 2: A schematic of the near-conformable diamond electrode array and the high acuity implant. (Not to scale). 1. Retina. 2. N-UNCD electrode. 3. Electrical feedthrough. 4. Indium contact bump. 5. Diamond Encapsulation. 6. PCD substrate. 7. microprocessor chip.

**Commercial Relationships:** Kumaravelu Ganesan, None; David J. Garrett, None; Mohit N. Shivdasani, None; David A. Nayagam, None; Joel Villalobos, The Bionics Institute of Australia (P); Hamish Meffin, NICTA (P); Kate E. Fox, University of Melbourne (P); Samantha G. Lichter, National Information and Communication Technology Australia (NICTA) (F), Bionic Vision Australia (E), Bionic Vision Australia (P); Robert K. Shepherd, None.

**Support:** Australian Research Council (ARC) through its Special Research Initiative (SRI) in Bionic Vision Science and Technology Program Number: 1048 Poster Board Number: C0025

**Presentation Time:** 1:00 PM - 2:45 PM

**Program Number:** 1048 Poster Board Number: C0025

**New Advancements to High-Density Packaging Technology for the Boston Retinal Prosthesis**


**Purpose:** This work is related to the efforts of the Boston Retinal Implant Project to develop a sub-retinal prosthesis to restore vision to the blind. We present new high density packaging advancements for the Boston prosthesis, and bonding processes for the exterior of the packages.

**Methods:** Co-fired ceramic structures with signal feedthroughs formed from a platinum-rhodium alloy were fabricated to mate with hermetic packages for the retinal implant; feedthrough discs were gold brazed to the miniature titanium housings. In subsequent assembly steps, flexible electrode arrays with electroplated gold contact pads were joined to the feedthrough assemblies by thermo-compression bonding. A custom fixture for making temporary contact to the bonded prostheses for testing purposes was designed and built, which allowed the bonded devices to be wirelessly tested before affixing the protective headers.

**Results:** Tests of the retinal implant assemblies' quality were performed by helium leak testing and bond pull tests. In the Figures, the co-fired ceramic discs and the bonded prosthesis assemblies are shown. When thermo-compression bonds to the prosthesis' iridium oxide electrode arrays were performed at 150 degrees C had an average shear strength of more than 50 grams force, indicating good quality bonding. Room temperature bonds were markedly weaker. Helium leak rates better than 1.0x10E-09 standard cc He / second were measured. The completed assemblies were extensively tested wirelessly in vitro and can monitor individual electrode voltage waveforms via on-chip analog to digital converters.

**Conclusions:** Improved feedthrough fabrication and bonding methods to miniature implantable titanium retinal prosthesis assemblies have been demonstrated, and completed retinal implants having 256+ channels were successfully tested wirelessly. These results pave the way for clinical testing of the Boston retinal prosthesis in the near future.

A high-density co-fired ceramic disc for the Boston Retinal Prosthesis, prior to hermetic sealing and bonding of the electrode array.
Flexible electrode Array for the high-density Boston Retinal Prosthesis bonded to the exterior of the ceramic feedthrough disc, prior to attachment of the protective header.

**Commercial Relationships:** Douglas B. Shire, VA CIVR (P); Thomas Salzer, Hermetic, Inc. (C); William K. Jones, None; Ali Karbasi, None; Oscar D. Mendoza, None; Shawn K. Kelly, Bionic Eye Technologies (P); John L. Wyatt, Bionic Eye, Ltd. (P); Joseph F. Rizzo, Bionic Eye Technology (I), Bionic Eye Technology (P)

**Support:** CNF Facility; VA Merit Review Grant; NIH Grant 2R01EY016674; NSF Grant IIS -1117093; Massachusetts Lions Eye Research Fund

**Program Number:** 1049 Poster Board Number: C0026

**Presentation Time:** 1:00 PM - 2:45 PM

**Evaluating Lanczos2 Image Filtering for Visual Acuity in Simulated Prosthetic Vision**

Paulette Lieby1, 2, Adele F. Scott1, 2, Nick M. Barnes1, 2, Ashley Stacey1, 2, Lauren N. Ayton1, Janine G. Walker1, 2, 3

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**Purpose:** Optimising visual acuity is an important challenge in prosthetic vision. With a small pupil size, the eye optics can result in low-pass filtering of the retinal image at the Nyquist frequency with respect to the photoreceptor density so that aliasing is not apparent. The Lanczos2 filter offers a better compromise than other image filters in reducing aliasing while retaining image sharpness. We evaluated the performance of Lanczos2 image filtering for visual acuity in simulated prosthetic vision using a validated clinical measure.

**Methods:** 26 normally-sighted (20/20) adult participants each completed on average 22 trials of the Freiburg Visual Acuity Test (FrACT) during one experimental session. The test material consisted of a black background with a white Landolt C whose gap orientation was presented randomly in any of eight directions. The participants had to determine the gap orientation using a keypad. Visual acuity was automatically computed by the FrACT program. Before presentation on a computer monitor, the test material was processed to simulate prosthetic vision using 98 phosphesones rendered over eight levels of brightness. Interphosphene spacing was 1.79° of visual field. A Lanczos2 filter was applied to the test material image prior to sampling. Five cut-off frequencies, \( f_c = \{2.0, 1.33, 1.0, 0.80, 0.66\} \), were Nyquist frequency, and a no-filtering case were used. Participants were masked to the presentation order of the six filtering conditions which were randomly allocated and equally represented in the session. Institutional Ethics Board approval was obtained.

**Results:** The highest mean VA scores were obtained for the cut-off frequencies of 1.33°/\( f_c \) (n=96, mean logMAR 1.655) and 0.66°/\( f_c \) (n=96, mean logMAR 1.644) which were not significantly different (p=0.985). However both were significantly higher than the mean VA scores obtained for the three other cut-off frequencies and no-filtering (p<0.001). The lowest mean VA score was obtained for no-filtering (n=97, mean logMAR 1.816). All the mean VA scores obtained were significantly higher than the highest score predicted by the Nyquist theorem (i.e., 2.031 logMAR) at this phosphene spacing.

**Conclusions:** Lanczos2 filtering with cut-off at or just above the Nyquist frequency may be used as an effective approach for enhancing visual acuity under conditions of limited resolution and dynamic range characterising current prosthetic vision devices.

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Support: NIH Grant EY018608 and an unrestricted Research to Prevent Blindness Grant

Program Number: 1051 Poster Board Number: C0028
Presentation Time: 1:00 PM - 2:45 PM

Magnetic Resonance Imaging (MRI) Brain Scan in Argus II Retinal Prosthesis Patients
Yvonne H. Luo1, 2, 3, Indran Davagnanam4, Lyndon da Cruz5, 1.
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Purpose: To report the safety and feasibility of MRI brain scanning on 2 blind retinitis pigmentosa patients fitted with Argus II retinal implant for prosthetic vision. To our knowledge, these are the first two patients ever to undergo MRI brain scan in the presence of Argus II device. Being commercially available in Europe and with recent FDA recommendation for marketing approval, it is foreseeable that clinicians will encounter more and more patients with Argus II implants in the near future.

Methods: Two Argus II retinal prosthesis patients underwent MRI brain scans at 1.5 Tesla field strength for investigations of unrelated medical conditions. Changes in implant position are assessed by comparing color fundus photographs and OCT scans of the implant taken before and after MRI. Changes in implant function are assessed by comparing the impedances and thresholds of the 60 electrodes. Artifacts produced by the implant on MRI image are estimated. The subjects have been followed-up for 3 months and 15 months respectively and ongoing to report any adverse event. Results: Visual and quantitative comparison of the fundus photographs and OCT images respectively did not show any positional change of the implant in both patients. The frequency distributions of impedance readings for both implants are comparable before and after MRI indicating no significant change in retinal contact. Some deterioration in electrode thresholds are noted for both patients, but these are no greater than the general trend of threshold deterioration with time observed due to disease progression. The implant produces local moderate artifacts of up to 29mm x 37mm x 40mm (AP x TR x SI) which preclude visualization of intraorbital contents immediately adjacent to the implant, but interpretation of other orbital and retroorbital structures are possible. There is no adverse event e.g. implant dislocation, retinal detachment during the follow-up.

Conclusions: MRI brain scans have been performed on 2 patients fitted with Argus II retinal prosthesis to date with no adverse effect on patient safety and implant function. The implant produces a moderate size artifact on MRI to preclude visualization of intraorbital contents, but interpretations of adjacent structures are reasonable.
filters for different environments, and what types of activities can be practiced at home.

**Conclusions:** The purpose of this work is to support patients so they can maximize the benefit of the Argus II System. We believe that applying standard low vision rehabilitation principles to the development of visual skills with the Argus II System will offer the best opportunity for patients to optimize the benefits from this technology.

**Commercial Relationships:** Jessy D. Dorn, Second Sight Medical Products (E); Duane Geruschat, second sight medical products (F);

Fatima Anaflous, Second Sight Medical products (E); Robert J. Greenberg, Second Sight Medical Products, Inc. (I), Second Sight Medical Products, Inc. (E), Second Sight Medical Products, Inc. (P), Second Sight Medical Products, Inc. (S)

**Support:** NIH Grant EY020778

**Clinical Trial:** NCT00407602

**Program Number:** 1053 Poster Board Number: C0030

**Presentation Time:** 1:00 PM - 2:45 PM

**Chronic Electrical Stimulation Of The Retina Via Suprachoroidal Electrodes Is Safe**

David A. Nayagam1,2, Richard A. Williams2,4, Mohit N. Shivdasani2,3, Ceser M. Salinas-La Rosa2,4, Penelope J. Allen2, Ceara McGowan1, Chi D. Luu1, Lauren N. Ayton1, Chris E. Williams1,2, Robert K. Shepherd1. 1Bionics Institute, East Melbourne, VIC, Australia; 2Pathology, University of Melbourne, Melbourne, VIC, Australia; 3Centre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital, Melbourne, VIC, Australia; 4Anatomical Pathology, St. Vincent's Hospital Melbourne, Fitzroy, VIC, Australia.

**Purpose:** To assess the safety and efficacy of chronic retinal stimulation with a suprachoroidal electrode array.

**Methods:** 6 normally-sighted feline subjects were stimulated above physiological and perceptual, but below aversive, levels with a medical grade, conformable, suprachoroidal electrode array (containing: 12 Ø600µm Pt electrodes; and 3 large Pt return electrodes). Charge balanced, biphasic, current pulses (100-600µA; 400µs; 86µC/cm2; ≤200Hz) were used. Retinal structure and function was assessed monthly with ERG, OCT and fundus photography. Electrode impedances were measured weekly and electrically evoked cortical potentials (EEPs) measured monthly to confirm that stimuli were activating visual cortex. At the end of 3 months continuous stimulation, an acute experiment was conducted and thresholds re-measured. Eyes were enucleated and prepared for histopathology. Randomized, blinded assessments were performed by 2 independent pathologists to compare stimulated and non-stimulated H&E stained 5µm sections of eye-tissue using contralateral eyes as controls.

**Results:** All subjects accepted the surgical and stimulation procedure with no evidence of discomfort or unexpected adverse outcomes. Electrode impedances were stable over the total implantation period (up to 6 months), with typical impedances between 10-30kΩ (compared with 5-10kΩ, measured pre-implantation in saline). Clinical eye assessments were normal. EEPs were recorded throughout the chronic stimulation period. The changes in threshold between consecutive measurements (Fig. 1) did not significantly differ from each other (one-way ANOVA; p>0.05). In 70/73 electrode-adjacent tissue samples examined, there were no discernible histopathological differences in the minor scarring, fibroblastic response, or foreign body response between stimulated and unstimulated regions. There was no necrosis, acute/chronic inflammatory response or secondary retinal damage in any of the samples examined (Fig. 2). In the other 3 tissue samples there were minor focal fibroblastic and acute inflammatory responses for which there was no obvious cause.

**Conclusions:** Chronic suprathreshold electrical stimulation of the retina using Pt electrodes in a planar silicone carrier located in the suprachoroidal space evokes a minimal tissue response and no adverse histological findings. Moreover thresholds and electrode impedance remained stable over the duration of the study.

**Figure 1:**

**Figure 2:**

**Commercial Relationships:** David A. Nayagam, None; Richard A. Williams, None; Mohit N. Shivdasani, None; Ceser M. Salinas-La Rosa, None; Penelope J. Allen, Bionic Vision Australia (P); Ceara McGowan, None; Chi D. Luu, None; Lauren N. Ayton, None; Chris E. Williams, Bionic Vision Australia (P); Robert K. Shepherd, None

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**Program Number:** 1054 Poster Board Number: C0031

**Presentation Time:** 1:00 PM - 2:45 PM

**In vivo chronological observation of electrochemical properties of porous electrodes with chronic suprachoroidal-transretinal stimulation**

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Institute of Science & Technology, Ikoma, Japan; 2Nidek Co., Ltd., Gamagori, Japan; 3Department of Health Sciences, Kyushu University, Fukuoka, Japan.

**Purpose:** Stabilizing electrochemical properties of stimulating electrodes in vivo for long term is a key issue for visual prostheses. We previously proposed stimulating electrodes with porous surface [Terasawa et al., Invest Ophthalmol Vis Sci 2012;53: E-Abstract 5538]. The purpose of this study is to confirm the stability of electrochemical properties of stimulating electrodes with chronic suprachoroidal-transretinal stimulation in vivo.

**Methods:** An electrode array with two porous electrodes was developed for this study. The diameter and height of an electrode were 0.5mm and 0.3mm respectively. The electrode array was inserted into a scleral pocket of a rabbit eye and sutured onto the sclera. Charge-balanced biphasic pulses were applied to one of two electrodes on the array for eight hour per day for one month. Electrode impedance spectra were obtained periodically. In addition, charge injection capacities (CIC) of the electrodes were determined both in saline and in vivo. All in vivo experiments were conducted in accordance with the Association for Research in Vision and Ophthalmology statement for the use of animals in ophthalmic and vision research, and institutional guidelines for the care and use of laboratory animals.

**Results:** Data analysis using equivalent circuit fitting suggested that double-layer capacitances in vivo were two orders of magnitude lower than that in vitro. No significant changes were observed in impedance spectra during chronic electrical stimulation. However increase of electrode impedance was observed at sixth day after cessation of stimulation. Double-layer capacitances decreased by half after cessation of stimulation. The CIC decreased from 225μC/cm² to 78μC/cm² after one month stimulation. Inter pulse potential (electrode potential before onset of each pulses) decreased from 0.217V (vs. Ag/AgCl) to 0.005V after stimulation. The decrease of inter pulse potential moved electrode potential closer to the lower limit of water window, which resulted in the decrease of the CIC of stimulating electrodes.

**Conclusions:** Impedance spectra in vivo kept unchanged during one-month chronic stimulation. The increase of impedance after cessation of stimulation suggested that electrical stimulation significantly affects the electrochemical properties of stimulating electrodes. Studies with longer period of stimulation are ongoing.

**Commercial Relationships:** Yasuo Terasawa, Nidek Co.,Ltd. (E); Hiroyuki Tashiro, Nidek Co., Ltd. (F); Yukari Nakano, NIDEK CO.,LTD. (E); Koji Osawa, NIDEK (E); Motoki Ozawa, Nidek Co., Ltd. (E)

**Program Number:** 1055 Poster Board Number: C0032

**Presentation Time:** 1:00 PM - 2:45 PM

**Comparison of Ankyrin-G Labeling of Axon Initial Segments on Ganglion Cells in Normal and Degenerate Rat Retina**

Steven T. Walston1, Eun-Jin Lee1, Mark S. Humayun1,2, James D. Weiland1,2. 1Biomedical Engineering, University of Southern California, Los Angeles, CA; 2Ophthalmology, University of Southern California, Los Angeles, CA.

**Purpose:** To compare the position and length of the axon initial segment (AIS) on retinal ganglion cells (RGCs) as it relates to activation thresholds in normal and degenerate retina.

**Methods:** Immunohistochemistry was used to label the AIS and the corresponding RGCs. Studies were conducted on normal Long-Evans, and heterozygous S334ter-line-3 rat retina. Antibodies against ankyrin-G, calretinin, and Bm3 were used to label the AIS, RGC somas and axons, and confirm RGC identity, respectively. The length of the AIS and its distance from the soma was acquired using fluorescence microscopy and measured using ImageJ.

**Results:** RGCs and their corresponding AIS are identified in the ganglion cell and nerve fiber layer with fluorescence microscopy. The average length of the AIS is 1.8μm shorter in degenerate retina when compared to normal (p=0.022, Student t-test). The mean AIS length is 21.1 ± 7.17μm (mean ± std) (n=173) in normal retina and 19.3 ± 6.09μm (n=122) in degenerate retina. The distance between the soma and proximal edge of the AIS along the axon is not significantly different between normal and degenerate retina (p=0.183). The mean position of the AIS is 13.4 ± 8.97μm (n=173) in normal retina and 12.1 ± 7.21μm (n=122) in degenerate retina.

**Conclusions:** Based on population statistics, the average length of the AIS is statistically shorter in degenerate retina than in normal retina. Although there is significant overlap of the data, this decrease in length may, in theory, increase the threshold at which the neuron fires action potentials. Further study is necessary to determine if there are differences within individual ganglion cell subtypes for normal and degenerate retina.

![Figure 1. Histogram plots of A AIS length and B distance from soma to proximal edge of AIS on RGCs of normal Long-Evans (black) and S334ter-line-3 retina (blue).](image-url)

**Commercial Relationships:** Steven T. Walston, None; Eun-Jin Lee, None; Mark S. Humayun, Bausch & Lomb (F), Bausch & Lomb (C), Bausch & Lomb (P), Bausch & Lomb (R), Bausch & Lomb (S), Alcon (C), Alcon (R), Iridex (P), Iridex (R), Replenis (I), Replenis (C), Replenis (R), Replenis (S), Second Sight (F), Second Sight (I), Second Sight (C), Second Sight (P), Second Sight (R), Second Sight (S), Regenerative Patch Technologies (I), Regenerative Patch Technologies (C); James D. Weiland, Second Sight Medical Products, Inc. (F)

**Support:** Research Innovation Fund from USC; Research to Prevent Blindness; W.M. Keck Foundation; NSF EEC-0310723

**Program Number:** 1056 Poster Board Number: C0033

**Presentation Time:** 1:00 PM - 2:45 PM

**An Optimal Power Coil Configuration to Minimize Surgical Cut for Intraocular Retinal Prostheses**

Yu Zhao1, Charles DeBoer1, Mandheerej S. Nandra1, James D. Weiland1,2, Mark S. Humayun1,2, Yu-Chong Tai1,2. 1Electrical

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Engineering, California Institute of Technology, Pasadena, CA; Doheny Eye Institute, Los Angeles, CA.

**Purpose:** Power coils used in current telemetries powering the epiretinal, subretinal and suprachoroidal prosthetic devices, such as microfabricated planar coil with metal electroplating and wire-wound coil, are not suitable/ideal for intraocular implantation as they are usually thick, rigid and large. For intraocular implantation, we propose a foil coil as an optimized configuration. It demonstrates not only better electrical performance, but also superior mechanical flexibility and bendability allowing the surgeon to implant through a minimal incision.

**Methods:** The lens capsule is a possible intraocular implantation site for the telemetry coils, which also sets the size and mass constraints. This implantation is similar to the common intraocular lens implantation. While making the best use of the coil winding window, it is still necessary to make the coil flexible for minimally invasive surgical implantation. Flexural stiffness, i.e., resistance to bending, equals to the product of the Young’s modulus $E$ and second moment of area $I$ reflecting the material stiffness and its geometrical cross section, respectively. Given same constructing metal, second moment of area varies with cross-sectional size and geometry (Fig. 1). The long-span high-aspect ratio foil strip can achieve smallest $I$ and therefore the most flexibility. The strip was fabricated using a parylene-metal-parylene sandwich structure. The thermally deposited metal is thin (0.25 μm) and patterned to form a 1-mm-wide stripe to fit into lens capsule. After the foil was dry-peeled off from the silicon substrate and manually wound into a circular coil, the original width of the encapsulated metal foil becomes the equivalent thickness of the coil.

**Results:** To demonstrate the surgical feasibility, the coil was implanted into the lens capsule of a porcine eye (Fig. 2). The coil was compressed and inserted into a porcine lens capsule through a capsulorhexis. After implantation the forceps were withdrawn and the coil regained its circular shape (dotted circle in the middle panel). By observing the implanted coil after removal of the iris, the full recovery of the coil shape was achieved in vitro.

**Conclusions:** Foil coil configuration has been theoretically proven and experimentally demonstrated to be more bendable, thus less invasive during implantation. The resulting smaller surgical incision has the potential to reduce post operative recovery time.

**Commercial Relationships:** Yu Zhao, None; Charles DeBoer, None; Mandheerej S. Nandra, None; James D. Weiland, Second Sight Medical Products, Inc. (F); Mark S. Humayun, Bausch & Lomb (F), Bausch & Lomb (C), Bausch & Lomb (P), Bausch & Lomb (R), Bausch & Lomb (S), Alcon (C), Alcon (R), Iridex (P), Iridex (R), Replenish (I), Replenish (C), Replenish (R), Replenish (S), Second Sight (F), Second Sight (I), Second Sight (C), Second Sight (P), Second Sight (S), Regenerative Patch Technologies (I), Regenerative Patch Technologies (C); Yu-Chong Tai, None.

**Program Number:** 1057 **Poster Board Number:** C0034 **Presentation Time:** 1:00 PM - 2:45 PM **Visual Prosthesis Simulation: Effects of Foveation on Visual Search**

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Commercial Relationships: Ben P. McIntosh. None; Noelle R. Stiles. Patent (not licensed) (P); Mark S. Humayun, Bausch & Lomb (F), Bausch & Lomb (C), Bausch & Lomb (R), Bausch & Lomb (S), Alcon (C), Alcon (R), Iridex (P), Iridex (R), Replensh (I), Replensh (C), Replensh (R), Replensh (S), Second Sight (F), Second Sight (I), Second Sight (C), Second Sight (P), Second Sight (R), Second Sight (S), Regenerative Patch Technologies (I), Regenerative Patch Technologies (C); Armand R. Tanguay, University of Southern California (P)

Support: National Science Foundation, National Science Foundation Graduate Research Fellowship

Program Number: 1058 Poster Board Number: C0035
Presentation Time: 1:00 PM - 2:45 PM

Decrease in Electrode-Retina Distance over Time and its Effect on Electrical Impedances in a Suprachoroidal Retinal Prosthesis

Lauren N. Ayton1,2, Nicholas C. Sinclair2,3, Peter J. Blamey2,3, Thushara Perera2,3, David A. Nayagam1,3, Peter N. Dimitrov1,3, Penelope J. Allen1,3, Mary Varsamidis1, Robyn H. Guymer1,3, Chi D. Lu1,3.

1Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, East Melbourne, VIC, Australia; 2Bionics Institute, East Melbourne, VIC, Australia; 3University of Melbourne, Parkville, VIC, Australia.

Purpose: The initial patient tests of a suprachoroidal retinal prosthesis prototype have shown success in both the surgical procedure and initial psychophysics testing. In this study, we investigated the relationship between electrode-retina separation and electrical impedances in a patient with an implanted suprachoroidal device.

Methods: Three patients with end stage retinitis pigmentosa (light perception vision) were implanted with a suprachoroidal retinal prosthesis prototype, which consisted of 24 electrodes. Optical coherence tomography scans were taken weekly, and high quality images were obtained from one patient (52yo female) with steady fixation. From these scans the array position, distance between electrode and retina, and retinal thickness above the electrodes were measured. Scans were taken both horizontally and vertically through all rows and columns of electrodes. Electrical impedances were measured weekly using a 500µs phase width and 20µs interphase gap biphasic pulse. The results of 50 pulses delivered at 500Hz were averaged.

Results: The average electrode-retina separation decreased gradually with time from an average of 422µm at the initial stimulation (55 days postop) to 362µm at 6 months postop (p=0.02). Average retinal thickness did not change significantly over this time (186µm to 184µm, p=0.71). The electrical impedances increased over this same time period, from an initial average impedance of 17.75kΩ to 20.08kΩ at 6 months postop (p<0.005). The decrease in electrode-retina distance was significantly correlated with the increased impedances (r=-0.59, p<0.005).

Conclusions: Following suprachoroidal retinal prosthesis implantation, the electrode-retina distance gradually decreases with time. The improved proximity of electrode to retinal tissue correlated with increased electrical impedances in this patient.

Commercial Relationships: Lauren N. Ayton, None; Nicholas C. Sinclair, None; Peter J. Blamey, Bionics Institute (P), Cochlear Limited (P); Thushara Perera, None; David A. Nayagam, None; Peter N. Dimitrov, None; Penelope J. Allen, Bionic Vision Australia (P); Mary Varsamidis, None; Robyn H. Guymer, Ellex Pty Ltd (F), Novartis (C), Bayer (C), Novartis (R); Chi D. Luu, None

Support: This research was supported by the Australian Research Council (ARC) through its Special Research Initiative (SRI) in
Bionic Vision Science and Technology grant to Bionic Vision Australia (BVA).

Clinical Trial: NCT01603576

Program Number: 1059 Poster Board Number: C0036
Presentation Time: 1:00 PM - 2:45 PM

Analysis of retinal and cortical response to electrical stimulation by subretinal implant in rodent model

Frederic Matonti1, 2; Sebastien Roux2; Virginie Donnadieu1, 2; Henri Lorach1, Olivier Marre2, Serge A. Picaud2, Frederic Chavane2.

1Ophthalmology, Hopital Nord, Marseille, France; 2Institut de Neurosciences de la Timone, Aix Marseille Université, Marseille, France; 3Institut de la Vision, Université Pierre et Marie Curie, Paris, France.

Purpose: This research aims to develop and improve the use of retinal prosthesis in animal model. For that purpose, we measured retinal and cortical response to direct subretinal electrical stimulation to understand how the patterns of stimuli can be adapted to improve stimulation to get closer to the response evoked by natural visual stimuli.

Methods: In a rat model, a comparative analysis of the functional impact of similar stimulation of a subretinal implant is done at two levels, (i) in the retina in vitro by multi electrodes array and (ii) in vivo in the primary visual cortex by optical imaging recordings. Optical imaging permits a functional mapping of the cortex, using light reflection and absorption changes depending on the rate of blood oxygenation. Diverse parameters were investigated: stimulus shape and polarity, intensity, size and location.

Results: At the cortical level, we have quantified the size, position and intensity of the point-spread function in response to the various electrical stimulations and compared them to those generated by calibrated light stimuli. The point-spread function was much larger for electrical stimulations compared to visual stimulation. We are currently performing retinal recordings of ganglion cells, while the prosthesis is on the photoreceptor side. We will compare the size of ganglion cell receptive fields to the size of the electric field activation to see if a difference in the size of the region activated by the two stimulations in the retina could explain the difference observed at the cortical level.

The ability to evaluate in vitro within the retina and in vivo the cortical responses induced by the prosthesis allowed us refining the patterns of electrical stimulation to get closer to a natural visual activation.

Conclusions: These results offer interesting prospect for improving the design of prostheses as well as their patterns of stimulation for a medical application.

Commercial Relationships: Frederic Matonti, Allergan (C), Alcon (R), Théa (R); Sebastien Roux, None; Virginie Donnadieu, None; Henri Lorach, None; Olivier Marre, None; Serge A. Picaud, UPMC (P), Pixmap Vision (C); Frederic Chavane, None.

Support: Bourse de recherche de la SFO

Program Number: 1061 Poster Board Number: C0038
Presentation Time: 1:00 PM - 2:45 PM

Development of large multielectrode arrays for epiretinal stimulation - feasibility of implantation procedures

Gernot Roessler1, Thomas Laube1, Florian Waschkowski2, Anne C. Rieck2, Claudia Brockmann2, Wilfried Mokwa3, Peter Walter1. 1Dept of Ophthalmology, RWTH Aachen University, Aachen, Germany; 2Dept of Materials in Electrical Engineering, RWTH Aachen University, Aachen, Germany; 3Dept of Ophthalmology, University of Duisburg-Essen, Essen, Germany.

Purpose: To demonstrate the feasibility of implantation surgery of Very Large Retinal Stimulation arrays (VLARS) to provide artificial vision with enlarged visual fields.

Methods: Polymide foils with a star-shaped pattern and a diameter of 12.5 mm have been fabricated for implantation. Each foil carries 244 gold electrodes divided into 63 electrodes for central and 181 electrodes for peripheral stimulation of the retinal surface. Openings for tack fixation were embedded paracentrally and into each arm of the star-shaped electrode array. Implantation was performed in pigs’ eyes including lens removal, vitrectomy and the implantation via corneal incision.

Results: Following lens removal by phacoemulsification and three-port vitrectomy, a decaline bubble was installed into the vitreous cavity. Via a corneal incision the folded stimulator was inserted into the eyeball, pushed through a posterior capsulotomy and positioned contacts of the electrode implanted just anterior to the chiasm in the ON by Veraart et al., it is still unknown the topography and spatial resolution of penetrative ON prosthesis implanted close to ON head. In this study, we investigated retinotopic organization of the ON stimulation and its spatial resolution in vivo cat experiments.

Methods: A five-electrode array was inserted perpendicular to the ON axis or a single electrode was advanced at different depths within the ON ~1-2 mm behind the eyeball in 13 cats. Cortical responses were recorded by a 5 x 6 epidural electrode array. A sparse noise method was used to map electrode position in ON and the visual cortex to establish ON and cortical visuo-topic maps. Then we compared the visual field positions of ON stimulation sites and their elicited greatest cortical response (M-Channels) sites. Finally, we estimated the spatial resolution of the penetrative ON prosthesis by calculating the difference in M-channel visual field positions corresponding to neighboring ON sites with an inter-electrode distance of 150 μm.

Results: Electrical stimulation with penetrating ON electrodes inserted just posterior to eyeball could elicit cortical responses with visuotopographical correspondence in cats. The electrical stimulation through electrodes within the temporal ON can elicit cortical responses corresponding to the central visual field. According to the increment of penetrating depth, the corresponding elicited cortical responses shift from lower to central visual field. About 2° to 3° spatial resolution within a limited visuotopic representation in the cortex could be obtained by this approach.

Conclusions: Visuotopic electrical stimulation with relatively fine spatial resolution could be accomplished by penetrating electrodes implanted at multi-sites and different depths within ON close to the optic nerve head. This study also provided useful experimental data for the design of electrode density and distribution of penetrating ON electrodes for a visual prosthesis.

Commercial Relationships: Yao Chen, None; Yiliang Lu, None; Yan Yan, None; Liming Li, None; Xinyu Chai, None.

Support: The National Basic Research Program of China (973 Program, 2011CB707502), the National Natural Science Foundation of China (31070981, 61171174, 91120304).

Program Number: 1060 Poster Board Number: C0037
Presentation Time: 1:00 PM - 2:45 PM

Spatial resolution of the Penetrative Optic Nerve Visual Prosthesis estimated by epidural cortical recording

Yao Chen, Yiliang Lu, Yan Yan, Liming Li, Xinyu Chai. Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, China.

Purpose: A visual prosthesis based on penetrating stimulation electrodes within the optic nerve (ON) is a potential way to restore partial functional vision for the blind patients. Although a rough visuotopographical relationship was found between each of the four visuotopic electrical stimulation with relatively fine spatial resolution could be accomplished by penetrating electrodes implanted at multi-sites and different depths within ON close to the optic nerve head. This study also provided useful experimental data for the design of electrode density and distribution of penetrating ON electrodes for a visual prosthesis.

Commercial Relationships: Frederic Matonti, Allergan (C), Alcon (R), Théa (R); Sebastien Roux, None; Virginie Donnadieu, None; Henri Lorach, None; Olivier Marre, None; Serge A. Picaud, UPMC (P), Pixmap Vision (C); Frederic Chavane, None.

Support: Bourse de recherche de la SFO

Program Number: 1061 Poster Board Number: C0038
Presentation Time: 1:00 PM - 2:45 PM

Development of large multielectrode arrays for epiretinal stimulation - feasibility of implantation procedures

Gernot Roessler1, Thomas Laube1, Florian Waschkowski2, Anne C. Rieck2, Claudia Brockmann2, Wilfried Mokwa3, Peter Walter1. 1Dept of Ophthalmology, RWTH Aachen University, Aachen, Germany; 2Dept of Materials in Electrical Engineering, RWTH Aachen University, Aachen, Germany; 3Dept of Ophthalmology, University of Duisburg-Essen, Essen, Germany.

Purpose: To demonstrate the feasibility of implantation surgery of Very Large Retinal Stimulation arrays (VLARS) to provide artificial vision with enlarged visual fields.

Methods: Polymide foils with a star-shaped pattern and a diameter of 12.5 mm have been fabricated for implantation. Each foil carries 244 gold electrodes divided into 63 electrodes for central and 181 electrodes for peripheral stimulation of the retinal surface. Openings for tack fixation were embedded paracentrally and into each arm of the star-shaped electrode array. Implantation was performed in pigs’ eyes including lens removal, vitrectomy and the implantation via corneal incision.

Results: Following lens removal by phacoemulsification and three-port vitrectomy, a decaline bubble was installed into the vitreous cavity. Via a corneal incision the folded stimulator was inserted into the eyeball, pushed through a posterior capsulotomy and positioned contacts of the electrode implanted just anterior to the chiasm in the ON by Veraart et al., it is still unknown the topography and spatial resolution of penetrative ON prosthesis implanted close to ON head. In this study, we investigated retinotopic organization of the ON stimulation and its spatial resolution in vivo cat experiments.

Methods: A five-electrode array was inserted perpendicular to the ON axis or a single electrode was advanced at different depths within the ON ~1-2 mm behind the eyeball in 13 cats. Cortical responses were recorded by a 5 x 6 epidural electrode array. A sparse noise method was used to map electrode position in ON and the visual cortex to establish ON and cortical visuo-topic maps. Then we compared the visual field positions of ON stimulation sites and their elicited greatest cortical response (M-Channels) sites. Finally, we estimated the spatial resolution of the penetrative ON prosthesis by calculating the difference in M-channel visual field positions corresponding to neighboring ON sites with an inter-electrode distance of 150 μm.

Results: Electrical stimulation with penetrating ON electrodes inserted just posterior to eyeball could elicit cortical responses with visuotopographical correspondence in cats. The electrical stimulation through electrodes within the temporal ON can elicit cortical responses corresponding to the central visual field. According to the increment of penetrating depth, the corresponding elicited cortical responses shift from lower to central visual field. About 2° to 3° spatial resolution within a limited visuotopic representation in the cortex could be obtained by this approach.

Conclusions: Visuotopic electrical stimulation with relatively fine spatial resolution could be accomplished by penetrating electrodes implanted at multi-sites and different depths within ON close to the optic nerve head. This study also provided useful experimental data for the design of electrode density and distribution of penetrating ON electrodes for a visual prosthesis.

Commercial Relationships: Yao Chen, None; Yiliang Lu, None; Yan Yan, None; Liming Li, None; Xinyu Chai, None.

Support: The National Basic Research Program of China (973 Program, 2011CB707502), the National Natural Science Foundation of China (31070981, 61171174, 91120304).

Program Number: 1060 Poster Board Number: C0037
Presentation Time: 1:00 PM - 2:45 PM

Spatial resolution of the Penetrative Optic Nerve Visual Prosthesis estimated by epidural cortical recording

Yao Chen, Yiliang Lu, Yan Yan, Liming Li, Xinyu Chai. Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, China.

Purpose: A visual prosthesis based on penetrating stimulation electrodes within the optic nerve (ON) is a potential way to restore partial functional vision for the blind patients. Although a rough visuotopographical relationship was found between each of the four
onto the decaline bubble. While the stimulator showed a good overall contact to the retinal surface after removal of the decaline bubble, implantation was finished by fixation using retinal tacks.

**Conclusions:** Our experiments demonstrated the feasibility of implantation surgery of large electrode arrays. Long term implantation for biocompatibility testing as well as stimulation experiments for the generation of cortical activation in animal experiments will follow.

**Commercial Relationships:** Gernot Roessler, None; Thomas Laube, None; Florian Waschkowski, None; Anne C. Rieck, None; Claudia Brockmann, None; Wilfried Mokwa, None; Peter Walter, Novartis (R), Bayer (R), Second Sight (R), Bayer (F), Novartis (F)

**Support:** Jackstaedt Foundation

**Program Number:** 1062 Poster Board Number: C0039

**Presentation Time:** 1:00 PM - 2:45 PM

**In vivo evaluation of the liquid crystal polymer-based retinal prosthesis by optical coherence tomography**


**Purpose:** Liquid crystal polymer (LCP) - based, monolithic retinal prosthesis was developed, and in vivo biocompatibility and biostability were evaluated in the rabbit eye by using optical coherence tomography (OCT).

**Methods:** LCP-based gold electrode array was fabricated and the electrical retinal stimulator was integrated into the LCP package to form a monolithic prosthetic system. After making scleral tunnel in the rabbit eye, electrode part was implanted suprachoroidally or subretinally, and the stimulator package was positioned and fixed over the sclera, in the sub-tenon space. Regular post-operative evaluation was done by OCT, fundus photography and electoretinography (ERG).

**Results:** OCT showed the chorioretinal structure over the electrodes in detail. However, LCP was opaque to the light, thus there were shadows under the electrodes. This made the choroidal evaluation difficult in the eye with subretinal LCP electrode. Localized tenting or stretching of the retina or choroid over the electrode was well visualized by OCT, and this could not be identified easily on the fundus photograph. Some structural changes of the retina over the LCP electrodes were found in 7 out of 14 eyes, and these might be due to the intraoperative surgical events, not due to the toxicity of the LCP itself. ERG waveform was correlated with the change on the OCT finding.

**Conclusions:** LCP retinal prosthesis showed good in vivo biocompatibility and biostability. OCT was useful for the evaluation of anatomical and histological outcome of LCP retinal prosthesis implantation and the physical characteristics of the LCP implants.

**Commercial Relationships:** Hum Chung, None; Bum-Joo Cho, None; Hee Sun Park, None; So Hyun Baek, None; Tae Wan Kim, None; Jong-Mo Seo, None; Hyeong Gon Yu, None; Joosoo Jeong, None; Soowon Shin, None; Sung June Kim, None

**Support:** Korea Health 21 R&D Project A050251 by MHWAF, Technology Innovation Program 10033634 by MKE, Public Welfare and Safety Program 2012-0006566 by MEST

**Program Number:** 1063 Poster Board Number: C0040

**Presentation Time:** 1:00 PM - 2:45 PM

**Optimal electrode conditions for surprachoroidal-transretinal stimulation system to elicit electrically-evoked potentials**

Kentaro Nishida, Hirokazu Sakaguchi, Takashi Fujikado, Motohiro Kamei, Kohji Nishida. Osaka University Graduate School of Medicine, Suita, Japan; Sakai City Hospital, Sakai, Japan.

**Purpose:** To determine the effects of the height and the surface area of the stimulating electrode on the electrical evoked potentials (EEPs) elicited by surprachoroidal-transretinal stimulation (STS) in rabbit eye.

**Methods:** A scleral pocket (3x5 mm) was created just over the visual streak in anesthetized rabbits (weight, 2.2-2.5 kg). The STS stimulating electrode system was implanted into the pocket. We varied the height of the stimulating electrode (300µm or 500µm) and the surface of the electrode (smooth or porous, Figure). EEPs were then elicited by each type of electrode conditions. Three sessions were repeated for each group.

**Results:** For the height of the stimulating electrode, the implicit times of the EEPs were 31.6±0.5 ms (300µm) and 31.9±0.8 ms (500µm), respectively, and the amplitudes were 78.2±9.5 µV (300µm) and 70.0±5.1 µV (500µm) respectively. These differences were not significant (P=0.588; P=0.261). The surface area of the stimulating electrode has no significant effect on the implicit times and the amplitudes of the EEPs (P>0.05).

**Conclusions:** The height and the surface area of the stimulating electrode do not significantly affect the implicit times and amplitudes of the EEPs elicited by the STS system.

**Commercial Relationships:** Kentaro Nishida, None; Hirokazu Sakaguchi, HOYA Corporation (R); Takashi Fujikado, Nidek (P); Motohiro Kamei, None; Kohji Nishida, Alcon (C), Alcon (F), HOYA (F), Senju (F), Pfizer (F), Santen (F), Osaka University (P)

**Program Number:** 1064 Poster Board Number: C0041

**Presentation Time:** 1:00 PM - 2:45 PM
Reducing the Number of Stimulators and Electrical Tracks in High-Resolution Visual Prostheses

Milan Djilas¹, Ryad Benosman¹, Philippe Bergonzo², Christoph Posch³, Jose A. Sahel¹,², Serge A. Picaud¹,³

¹Institut de la Vision, INSERM/UPMC Univ Paris 6/CNRS/CHNO des XV-XX, Paris, France; ²LIST, CEA, Saclay, France; ³Fondation Ophthalmologique Adolphe de Rothschild, Paris, France.

Purpose: Retinal diseases such as RP and AMD cause photoreceptor degeneration while other cell layers partially remain. Retinal prostheses restore useful vision by activating these cells. The NxN electrode matrix and stimulators are coupled with N² electrical tracks. With the increase of pixel resolution, this inter-connection becomes difficult to fabricate. The foil also becomes more rigid, making the implantation surgery more challenging. Here we propose an alternative electrode design and connectivity layout that significantly reduces the required number of metal tracks and stimulators.

Methods: The proposed layout is shown on Figure 1. To stimulate a particular pixel, segments from one row, one column and two diagonals containing that pixel are activated simultaneously. To excite only the tissue at the target pixel, the stimulation intensity of each active segment is kept below threshold, whereas the intensity of simultaneous activation of four active segments at the target pixel is above threshold.

Results: The proposed layout requires a total of 6(N-1) electrical tracks and only 4 stimulators (1 for row, 1 for column, and 2 for diagonals) regardless of implant resolution. One additional track is needed for a common counter-electrode. Finite-element method simulations clearly confirm significantly higher stimulation intensity at the target pixel compared to other pixels stimulated with 4x lower intensity. This range should be sufficient to activate only the former.

Conclusions: The proposed strategy requires 6N-5 tracks and 4 stimulators, compared to N²+1 tracks and N² stimulators in the standard one-track-per-electrode layout. The downside of such an approach is that only a single pixel at a time can be activated. This would however not be a limiting factor if asynchronous image acquisition is implemented. Future work includes experimental validation of the proposed strategy.

Figure 1 A 5x5 electrode layout with 4 stimulating electrodes per pixel. Segments designated with the same number are electrically connected. Simultaneous electrical stimulation through segments from one column (segments 7), one row (segments 2), and two diagonals (segments 14 for \ and 19 for /) produces maximal stimulation in the target pixel located in the intersection of the four lines (thick outline). A metalized grid surrounding the electrodes serves as the counter-electrode.

Conclusions: The flexibility and the edge sharpness of the electrode were important for decreasing the tissue damage during implant surgery. The size and the weight of the external part also affected the stability of the electrode by leverage effect. Optimized design according to the size and the shape of the eyeball is necessary for the successful implantation of the mololithic retina prosthesis.

Commercial Relationships: Mila Djilas, Ryad Benosman, Philippe Bergonzo, Christoph Posch, Jose A. Sahel, Serge Picaud.

Support: The proposed spark gap electrode and the system package were evaluated. The electrode with the maximum diameter of 3 mm could be safely implanted into the subretinal or suprachoroidal space through scleral tunnel. Meticulous hemostasis of the choroid with high-frequency electrocauterization increased the success rate of the operation. Sharp angulation between the stimulator package and the electrode shaft affected the surgical outcome.

Flexible Microelectrode array

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Xiaohong Sui, Yan Yan, Jingjing Sun, Liming Li, Qiushi Ren, Xinyu Chai. Shanghai Jiao Tong University, Shanghai, China.

Purpose: To explore the spatial characteristics of indirect stimulation of the retina by MEMS based flexible microelectrode arrays and to evaluate the spatial characteristics of suprachoroidal stimulation for visual prosthesis.

Methods: Based on MEMS techniques, a 16 microelectrode array in a 4 × 4 arrangement was fabricated using single metal layer, and a wide-view electrode array with 60 stimulating sites was also fabricated with dual metal layers. Arrays were implanted into the suprachoroidal space of rabbits for in-vivo test. For the 4 × 4 electrode array, diagonal “L” shapes stimulation and two square shapes - small square using the central four electrodes and large square using the peripheral 12 electrodes - stimulation were applied. Row stimulations were applied with the 60 one. The electrical evoked responses (EEPs) from the primary visual cortex were recorded by a silver-ball electrode array. The amplitudes, maximum locations and spatial spreads of the cortical activities were analyzed.

Results: Cortical responses could be consistently evoked by suprachoroidal stimulation using both types of MEMS microelectrode array. In two diagonal “L” shapes stimulations, maximum cortical responses locations and spatial spreads were similar. While in square stimulations, maximum EEPs locations were at the same place but the responses amplitudes increased and the spatial spread expanded in the large square shape stimulation. Rows stimulation in 60 electrode array showed that horizontally orientated cortical responses could be evoked, which were consisted visuotopically with the row-electrodes horizontal position on the retina. The amplitudes of EEPs increased with increasing stimulus intensity, but the maximum EEPs positions remained unchanged. Differentiated maximum EEPs positions showed up in different row stimulations. The spatial spreads varied with a relatively large responded cortical area resulted in stimulation by rows located under the visual streak.

Conclusions: Preliminary pattern differentiated cortical responses could be evoked by simultaneously stimulation of multiple selected electrodes using the suprachoroidal MEMS based array. Results indicated that this approach may be feasible to potentially restore functional vision for the blinds.

Commercial Relationships: Xiaohong Sui, None; Yan Yan, None; Jingjing Sun, None; Liming Li, None; Qiushi Ren, None; Xinyu Chai, None


Program Number: 1067 Poster Board Number: C0044

Presentation Time: 1:00 PM - 2:45 PM

A Center-Surround-Selectable, High-Acuity, Large-Field-of-View, Flexible Retinal Prosthesis

Long-Sheng Fan1, Chia-He Chung1, Frank Yang1, Eunice Liu1, Jasmine Lin1, Zung-Hua Yang1, Grace Teng1, Chang-Hao Yang1, Kea-Tiong Tang1. 1Institute ofMEMS, National Tsing Hua University, Hsinchu, Taiwan; 2Institute of Electronics, National Tsing Hua University Hospital, Hsinchu, Taiwan; 3Ophthalmology, National Taiwan University Hospital, Taipei, Taiwan.

Purpose: We previously reported a 4,096-pixel flexible retinal prosthesis generating bi-phase electrical stimulations 30 μm in pitch to enable the possibility of high visual acuity (VA) and cover a field of view (FOV) around 40o. The pixel electrical output is a function of the light intensity on that pixel. However, retinal photo sensors influence retinal neurons across hundreds of micrometers, and the retinal networks exhibit a center-surround receptive field through lateral inhibition. Various stages of retina degeneracy may also need certain artificial restoration of such neural function through electronics. We target to implement a 16,328-pixel prosthesis that is selectable to have an electrical output consistent with the center-surround receptive field, and the chip covers up to 20o FOV with 30 μm pixel pitch, and conform to the surface of a 25 mm eyeball.

Methods: Since the ratio of the number of photo sensors to that of ganglion cells is low near the fovea, the center-surround characteristics is expected to be the key feature of the coding in this region. The new retinal prosthesis chip includes the option that the pixel electrical output from the pixel signal processing circuitry can be selected to be a function of the light intensities on neighboring pixels to a range of the typical receptive field in additional to the light intensity on that pixel. The primary weight matrix is a Laplacian Gaussian.

Results: We have implemented a flexible 16,328-element retina chip 30 μm thick using a 180nm, flexible CIS technology. The electrodes are 10 μm in size and photo sensors 30 μm in pitch. The retina chip with a large FOV is 6 mm in size including multiplexing electronics for pixel characterizations and perfusion openings, and formed into a spherical-shaped patch during the packaging process. We have previously shown that the identical 10 μm-sized electrode arrays are capable of inducing RGC spiking in vitro, and details are under characterization.

Conclusions: This study demonstrates the feasibility to integrate a high-acuity, large-field-of-view, flexible retinal prosthesis in a spherical-shaped patch with the selectable feature to have an electrical output characteristic consistent with the center-surround receptive field using a 180 nm mixed-signal CMOS Image Sensor technology. Detailed characteristics of this retinal chip will be reported.

Commercial Relationships: Long-Sheng Fan. National Tsing-Hua University (P); Chia-He Chung. None; Frank Yang. None; Eunice Liu. None; Jasmine Lin. None; Zung-Hua Yang. None; Grace Teng. None; Chang-Hao Yang. None; Kea-Tiong Tang. None

Support: NTHU

Program Number: 1068 Poster Board Number: C0045

Presentation Time: 2:45 PM - 4:25 PM

Design of a Compact Wide-Field-of-View Camera for Retinal Prostheses

Furkan E. Sahin1, Ben P. McIntosh1, Patrick J. Nasiatka1, James D. Weiland2, Mark S. Humayun3, Armand R. Tanguay4. 1Department of Electrical Engineering-Electrophysics, University of Southern California, Los Angeles, CA; 2Departments of Biomedical Engineering, and Ophthalmology, University of Southern California, Los Angeles, CA; 3Departments of Ophthalmology, Cell and Neurobiology, and Biomedical Engineering, University of Southern California, Los Angeles, CA; 4Departments of Electrical Engineering-Electrophysics, Biomedical Engineering, and Ophthalmology, University of Southern California, Los Angeles, CA.

Purpose: To design and implement an ultraminiature, head-mounted, wide-field-of-view extracocular camera that can be used in conjunction with an ultraminiature eye-tracking camera to restore natural foveation capabilities to patients implanted with intraocular retinal prostheses.

Methods: In the proposed approach, a wide-field-of-view image of the outside world is captured with the wide-field-of-view camera. The eye-tracking camera in conjunction with appropriate software algorithms extracts the direction of gaze, and the corresponding subregion of the full camera field of view is exported to the microstimulator array of the retinal prosthesis. Custom compact multi-element 90° and 120° wide-field-of-view lenses were first designed. Based on these designs, less optimal but

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commercially available miniature lenses were chosen with matching parameters, and the optical system design reoptimized. The wide-field-of-view extraocular camera can easily fit on a pair of eyeglasses in such a way as to be relatively unobtrusive yet add minimal weight and volume.

**Results:** A compact, low mass, wide-field-of-view optical system has been designed and successfully implemented. This lens system has four commercially available spherical lens elements. The lens system provides a diagonal field of view of 100°, and fits into a housing with dimensions of only 8 mm diameter and 8 mm overall length. This lens design was coupled with a commercially available wide dynamic range image sensor (OV10633) from OmniVision Technologies and test images have been successfully captured. Any wide field of view optical system generates a degree of unwanted image (typically barrel) distortion that may cause adverse complications with either direct stimulation of the visual system or the implementation of subsequent image processing algorithms. To this end, an image dewarping algorithm capable of removing this distortion in real time has been developed that has the additional feature of greatly reducing the associated chromatic aberration in the image.

**Conclusions:** A very compact wide field of view camera was designed to be used in conjunction with an eye-tracking camera to restore natural foveation for retinal prosthesis patients.

**Commercial Relationships:** Furkan E. Sahin, None; Ben P. McIntosh, None; Patrick J. Nasiatka, None; James D. Weiland, Second Sight Medical Products, Inc. (F); Mark S. Humayun, Bausch & Lomb (F), Bausch & Lomb (C), Bausch & Lomb (P), Bausch & Lomb (R), Bausch & Lomb (S), Alcon (C), Alcon (R), Iridex (P), Iridex (R), Replenis (I), Replenis (C), Replenis (R), Replenis (S), Second Sight (F), Second Sight (I), Second Sight (C), Second Sight (P), Second Sight (R), Second Sight (S), Regenerative Patch Technologies (I), Regenerative Patch Technologies (C); Armand R. Tanguay, University of Southern California (P)

Test image of common grocery items captured with the designed and implemented wide-field-of-view camera.

Same image, but following software dewarping with chromatic aberration correction to achieve a rectilinear, chromatically corrected image.

**Support:** National Science Foundation

**143 Endophthalmitis Poster**

Sunday, May 05, 2013 1:00 PM-2:45 PM

Exhibit Hall Poster Session

**Program #/Board # Range:** 1100-1126/C0077-C0103

**Organizing Section:** Retina

**Program Number:** 1100 Poster Board Number: C0077

**Presentation Time:** 1:00 PM - 2:45 PM

**Crystal-induced endophthalmitis after intravitreal triamcinolone**

Hiroki Otsuka, Hiroki Kawano, Shozo Sonoda, Taiji Sakamoto.

ophthalmology, Kagoshima Univ Sch of Medicine, Kagoshima, Japan.

**Purpose:** To determine the cause of sterile endophthalmitis after intravitreal triamcinolone acetoneate (IVTA).

**Methods:** The clinical records of 21 eyes that developed sterile endophthalmitis after IVTA were reviewed. Cytological studies were performed and cytokine and chemokine profiles of the aqueous humor (AqH) were determined. The effects of direct contact of TA crystals with cultured lens epithelial cells (B3) or retinal pigment epithelial cells (ARPE-19) on cytokine production were determined. Non-contact culture studies were performed in a Boyden chamber. 11-deoxycortisol was used for non-bioactive crystals.

**Results:** Inflammation appeared one day after the IVTA, and the incidence of severe sterile endophthalmitis was 13.0% (6/46), which was reduced to 4.3% (2/47) after switching to preservative-free TA. Most cells found in the AqH were granulocytes. The concentrations of interleukin (IL)-6 (447.8 to <5000 pg/mL) and IL-8 (47.2 to <5000 pg/mL) were significantly increased but IL-1β, IL-10, IL-12p70 and tumor necrosis factor-α were not significantly changed. The level of IL-8 increased significantly when B3 cells made direct contact with TA crystals (1.33X times that of PBS; P <0.05, Student’s t test) but not in non-contact cultures. A similar reaction was found in ARPE-19 cells. These effects were also observed when the cells were exposed to 11-deoxycortisol crystals.

**Conclusions:** Sterile endophthalmitis after IVTA is characterized by an immediate granulocytic infiltration and an increase of IL-6 and IL-8 in the AqH. TA crystals can cause mechanical stress on the lens epithelial cells leading to the up-regulation of IL-8.

**Commercial Relationships:** Hiroki Otsuka, None; Hiroki Kawano, None; Shozo Sonoda, None; Taiji Sakamoto, None

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**Program Number:** 1101 Poster Board Number: C0078

**Presentation Time:** 1:00 PM - 2:45 PM

**Clinical Features and Treatment Outcomes of Endogenous Endophthalmitis**

Nicole H. Siegel, Achal J. Patel, Deeba Husain. BMC- Dept of Ophthalmology, Boston Medical Center, Boston, MA.

**Purpose:** To review the risk factors, clinical features, prognostic factors, treatment and outcomes of patients diagnosed with endogenous endophthalmitis at Boston Medical Center.

**Methods:** The medical records of patients diagnosed with endogenous endophthalmitis between 2005 and 2012 were reviewed. Variables included age, gender, existing medical conditions, systemic infections, ocular infections, immune status, risk factors and

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treatment. 

**Results:** Endogenous endophthalmitis was diagnosed in 14 patients and the charts of 12 patients were evaluated. One patient had bilateral involvement, 6 (50%) involved the right eye and 5 (41.7%) the left eye. The mean age at diagnosis was 49.5 years (range 24 to 80), with 5 (41.7%) patients under the age of 35 years. Seven patients (58.3%) were female and 5 (41.7%) were male. Four (33%) had a previous diagnosis of Hepatitis C and 2 (16.6%) had decreased mental status on presentation. None of the patients had HIV. The most common risk factor, intravenous drug use, was seen in 6 (50%) of the patients. Five (41.7%) initially presented with best corrected visual acuity (BCVA) of counting fingers and improved to a BCVA between 20/50 and 20/400. The majority of ocular cultures yielded no growth. Five (41.7%) of the patients had a presumed or culture positive Candida spp. infection. 1 (8.3%) was culture positive for Serratia marcescens, 2 (16.6%) had presumed methicillin-resistant Staphylococcus aureus and 4 (33%) did not have a known infection or culture diagnosis. Seven (58.3%) patients had cardiac imaging with transthoracic or transesophageal echocardiography but no study revealed vegetations. Seven (58.3%) patients underwent a pars plana vitrectomy. Two (16.6%) patients were ultimately treated with evisceration of the affected eye secondary to panophthalmitis on presentation.

**Conclusions:** Endogenous endophthalmitis can have a devastating visual outcome and most commonly occurs in patients with underlying medical conditions such as diabetes, septicemia or immunosuppression. In contrast, intravenous drug use was the most prevalent risk factor in our series, especially those under the age of 40. The diagnostic yield of cardiac imaging to evaluate for endocarditis is unclear in this setting, especially in the absence of cardiopulmonary symptoms. A thorough skin examination may be warranted at the time of diagnosis, as 2 (16.6%) patients presented with skin abscesses requiring treatment.

**Commercial Relationships:** Nicole H. Siegel, None; Achal J. Patel, None; Deeba Husain, None

**Program Number:** 1102 Poster Board Number: C0079

**Presentation Time:** 1:00 PM - 2:45 PM

**The Incidence of Curvularia Keratitis and A Case Series of Curvularia Endophthalmitis**


**Purpose:** To report a case series of Curvularia endophthalmitis and to determine the number of Curvularia positive corneal cultures at a single academic center in five year increments from January 1, 1980 to October 17, 2012.

**Methods:** Retrospective review of Bascom Palmer Eye Institute microbiology archives and patient charts for demographic information, clinical features, etiology, treatment, and outcomes in Curvularia endophthalmitis. The number of corneal cultures positive for Curvularia in five year increments was determined.

**Results:** Seven adult patients with exogenous Curvularia endophthalmitis (4 post-operative, 3 posttraumatic) were seen between 1980 and 2012. In 3 cases the endophthalmitis followed trauma. In 4 postoperative cases, patients became symptomatic 2-5 months following surgery and the time to definitive diagnosis ranged from 7-19 months. In post-operative cases, successful treatment was achieved 8-25 months following the original surgery and often required surgical removal of an infectious nidus, in addition to the lens capsule. When assessed by five-year increments, the number of Curvularia keratitis cases increased over the study period. No cases of Curvularia keratitis were seen between 1980 and 1984, while 30 cases were seen between 2005 and 2009.

**Conclusions:** The incidence of Curvularia keratitis increased from 1980 to 2009 in an academic center. In postoperative endophthalmitis cases, patients typically present with chronic inflammation and the diagnosis requires a high index of suspicion as it can be difficult to establish. Definitive treatment often requires removal of an infectious nidus, in addition to removal of the lens capsule.

**Commercial Relationships:** Ashvini Reddy, None; Aleksandra V. Rachitskaya, None; Darlene Miller, None; Harry W. Flynn, None; William E. Smiddy, None; Wilfredo C. Lara, None; Thomas A. Albini, Bausch and Lomb (C), Allergan (C), Genentech (F), Eleven Biotherapeutics (C)

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**Program Number:** 1103 Poster Board Number: C0080

**Presentation Time:** 1:00 PM - 2:45 PM

**Differentiation of culture positive endophthalmitis from non-infectious endophthalmitis following intravitreal anti-VEGF injections**

Kamal Kishore1, 2, Bharti Kashyap2, 1, Anthony S. Ekon2, 1, Illinois Retina Institute, Peoria, IL; 2Kashyap Memorial Eye Hospital, Ranchi, India; 1Department of Surgery, University of Illinois College of Medicine Peoria Campus, Peoria, IL.

**Purpose:** To analyze clinical findings at presentation in culture positive and culture negative eyes suspected of acute endophthalmitis following intravitreal anti-VEGF injections.

**Methods:** Retrospective chart review of 10 eyes of 10 patients suspected of acute endophthalmitis following intravitreal injection of either Avastin or Lucentis. Patient’s age, time to presentation, presenting VA, pain score, severity of conjunctival congestion, corneal edema, hypopyon, retinal hemorrhages were compared between culture positive (CP, n= 4, all after Avastin) and culture negative (CN, n= 6, 5 after Avastin and one after Lucentis) eyes.

**Results:** Hypopyon was noted in 3/4 CP, and 0/6 CN eyes, retinal hemorrhages in 3/4 CP and 0/6 CN eyes. Both hypopyon and retinal hemorrhages had specificity of 100%, but sensitivity of 75% each. However, using OR criteria, patients with either hypopyon or retinal hemorrhages had 100% sensitivity and specificity for being culture positive. Patient age (years) [Mean 85 CP, 78.8 CN, p=0.3], Time to presentation (days) [Mean 5.75 CP, 5.1 CN, p=0.87], logMAR VA at presentation [Mean 1.6 CP, 1.4 CN, p=0.28], pain score [Mean 2 CP, 1 CN, p=0.02], were not statistically significant between the two groups. Conjunctival congestion (Mean 3 CP, 0.5 CN, p=0.00038) was more severe in CP group. All eyes had varying degree of corneal edema at presentation. Cultures revealed S aureus (2), coagulase negative Staph (1) and Staph capitis (1) eye. All CN eyes responded well to treatment, 3 CP eyes responded well to initial tap/inject procedure, one required a PPV 4 days after tap/inject. One CP eye treated with tap/inject alone developed retinal detachment which was repaired by PPV, SB and silicone oil injection. One CN eye developed recurrent inflammation after subsequent anti-VEGF injections.

**Conclusions:** Hypopyon and retina hemorrhages were specific for culture positive endophthalmitis following intravitreal anti-VEGF injections. Culture positive eyes exhibited more severe conjunctival congestion compared to culture negative eyes.

**Commercial Relationships:** Kamal Kishore, None; Bharti Kashyap, None; Anthony S. Ekon, None

**Program Number:** 1104 Poster Board Number: C0081

**Presentation Time:** 1:00 PM - 2:45 PM
The Incidence of Noninfectious Intraocular Inflammation after Intravitreal Aflibercept Injection

Kunjal K. Modi1,2, Daniel B. Roth1, Howard F. Fine1,2, Harold M. Wheatley3, Jonathan L. Prenner2,3, Stuart N. Green1,2, David L. Yarian2,3. Ophthalmology, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ; 2Retina-Vitreous Center, New Brunswick, NJ; 3Ophthalmology, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ.

Purpose: Aflibercept (Eylea), an anti-VEGF agent approved for neovascular age-related macular degeneration (AMD) since November 2011, has been associated with reports of post-injection intraocular inflammation. In February 2012, 14 cases were reported after an estimated 30,000 injections (0.047%), however 11 of these cases came from a single practice. Recent studies have reported post-Aflibercept inflammation ranging from 1.2-6.7%. This study aims to evaluate the incidence and nature of inflammatory reactions, or noninfectious endophthalmitis, in eyes injected with Aflibercept in patients with an initial 120 days of use, and initial 8 months of use.

Methods: The subjects in this study were patients who received intravitreal Aflibercept (IAI) injections. All eyes were prepped with 5% povidone-iodine solution, followed by anesthesia consisting of 4% topical Lidocaine and 2% subconjunctival Lidocaine injection. Injections were administered in the superotemporal quadrant of the eye. Injections were performed by Aflibercept (Eylea), an anti-VEGF agent approved for neovascular age-related macular degeneration (AMD) since November 2011, has been associated with reports of post-injection intraocular inflammation. In February 2012, 14 cases were reported after an estimated 30,000 injections (0.047%), however 11 of these cases came from a single practice. Recent studies have reported post-Aflibercept inflammation ranging from 1.2-6.7%. This study aims to evaluate the incidence and nature of inflammatory reactions, or noninfectious endophthalmitis, in eyes injected with Aflibercept in patients with an initial 120 days of use, and initial 8 months of use.

Results: Initial 8 months: Total of 477 injections in 372 patients. 3 eyes (0.6% of injections, 0.8% of patients) had some adverse reaction. 2 of these (0.4% of injections, 0.5% of patients) had moderate inflammation and vitritis consistent with noninfectious endophthalmitis—follow-up cultures from these 2 eyes were negative. The 1 eye other eye had mild anterior chamber reaction and discomfort. Initial 8 months Total of 2856 injections in 799 patients. 8 eyes in (0.28% of injections, 1.0% of patients) had some adverse reaction. 3 eyes (0.1% of injections, 0.4% of patients) with inflammation consistent with noninfectious endophthalmitis—follow-up cultures from these 3 eyes were negative.

Conclusions: Noninfectious endophthalmitis (NIE) can occur after anti-VEGF injections: *0.28% of injections developed some form of an AC reaction which was easily treated with topical steroids, consistent with anti-VEGF associated uveitis. 0.1% of injections developed iritis, vitritis, and vision loss, consistent with noninfectious endophthalmitis. *Clinicians should be aware of possibility of developing uveitis and even NIE after anti-VEGF injections, including Aflibercept (Eylea). Fortunately, these conditions usually resolve without residual vision loss.

*Patients should be counseled to return for evaluation for any symptoms of visual blur, even without pain or metamorphopsia, lasting more than 24 hours after an injection.

Commercial Relationships: Kunjal K. Modi, None; Daniel B. Roth, Allergan (C), Genentech (C), Regeneron (C), QLT (C); Howard F. Fine, Genentech (C), Regeneron (C), Allergan (C), Auris Surgical Robotics (P); Harold M. Wheatley, None; Jonathan L. Prenner, Genentech (C), Regeneron (C), Thrombogenics (C), Panoptica (C), Ophthotech (I); Stuart N. Green, None; David L. Yarian, None

Program Number: 1105 Poster Board Number: C0082
Presentation Time: 1:00 PM - 2:45 PM
Endophthalmitis following intravitreal injection: spectrum of causative organisms and antimicrobial susceptibility


Purpose: To describe patient demographics and microbiological features of patients with clinically diagnosed endophthalmitis following intravitreal injection

Methods: Retrospective review of consecutive cases of endophthalmitis seen at a university referral center between January 2005 and August 2012

Results: Thirty one eyes from 31 patients presented clinically diagnosed endophthalmitis following intravitreal injection in the study period. Most patients were women (58%) and the mean age was 68 ± 10.34 years old. The majority of the patients received injections of bevacizumab (61.3%) followed by steroids (16.12%), ranibizumab (3.22%) and miscellaneous (19.35%). Overall, the positivity of bacterial culture was 48.4% (15 out of 31 patients). The higher culture positivity was achieved for diphtheria from vitrectomy (55.5%; 5/9) and vitreous tap samples (47.8%; 11/23). Aqueous humor was culture positive in 14.3% (2/14) of the samples. At the time of sample collection, at least 9 out of 15 patients were in use of topical fluoroquinolone (for the remaining information was not available). The most common organism isolated was coagulase-negative Staphylococci - CoNS (73.3%; 11/15) followed by S. aureus (20%; 3/15) and viridans group Streptococci (6.6%; 1/15). Gatifloxacin (GAT) and moxifloxacin (MOX) susceptibility rate was 80% (MIC90 2 µg/mL) among all bacterial isolates. All S. aureus isolates were susceptible to fourth-generation fluoroquinolone, methicillin and vancomycin. For CoNS, 72.7% of isolates were susceptible to GAT and MOX (MIC90 4µg/mL for both). The frequency of methicillin-resistant CoNS (MRCoNS) was 36.3% (4/11). Only MRCoNS isolates demonstrated resistance to fourth-generation fluoroquinolones (75%; 3/4). All CoNS isolates were susceptible to vancomycin.

Conclusions: Culture-proven endophthalmitis following intravitreal injection was documented in the last 3 years for 15 patients in our setting. Staphylococci remained as the main causative organism and was isolated even from patients using post-injection topical fluoroquinolones. The frequency of endophthalmitis was higher among the patients that received bevacizumab intravitreal injection, probably due to the greater number of this type of injection.
Commercial Teno Virus Associated with Endophthalmitis

Aaron Y. Lee1, Lakshmi Akileswaran2, Michael D. Tibbetts3, Sunir J. Garg1, Russell N. Van Gelder1. 1Department of Ophthalmology, Washington University in St Louis, St Louis, MO; 2Department of Ophthalmology, University of Washington School of Medicine, Seattle, WA; 3Mid Atlantic Retina, Wills Eye Institute, Philadelphia, PA.

**Purpose:** To investigate the presence of viral pathogens in culture-positive and -negative infectious endophthalmitis using deep DNA sequencing techniques.

**Methods:** In a prospective fashion, 7 fluid samples from uninflamed eyes and 21 consecutive samples from infectious endophthalmitis diagnosed by a retinal specialist were collected by vitreous or aqueous tap. Using Biome Representational in Silico Karyotyping (BRiSK), a type IIB DNA restriction enzyme (BsaX1) was used to create a representational set of 27-mer DNA tags for each sample and sequenced using a massively parallel sequencing platform. Tags that uniquely matched viral DNA were included for further analysis. Quantitative PCR was performed to verify the presence of pathogens.

**Results:** Fifteen of the 21 endophthalmitis samples (71.4%) were positive for the Torque Teno Virus (TTV) including 7 out of 7 (100%) of culture-negative samples. In contrast, 0 out of 7 (0%) of the normal vitreous samples were positive for TTV (p = 0.001 by Fisher Exact). No other viruses were recovered in these samples, and the presence and absence of TTV were verified by PCR. A mean of 369.4 TTV tags were recovered per sample (range of 1 to 3,580 tags).

Quantitative PCR showed relative multiplicity of infection compared to human genomic DNA of up to 258, suggesting a productive infection.

**Conclusions:** BRiSK is an effective method for identifying viral presence in culture-positive and culture-negative endophthalmitis. TTV is a small non-enveloped single stranded DNA virus with a genome size of approximately 3.8 kb found frequently in the serum of normal individuals (90%) with no clear pathogenic role. TTV has been shown to modulate the immune system by increasing proinflammatory cytokine production of interferon γ, IL-6, and IL-12 through Toll-like receptor 9. The finding of TTV in high viral load in infectious endophthalmitis samples leads to a number of possible hypotheses including: inflammation directly related to infection, TTV modulating the immune system to increase susceptibility to bacterial co-infection, a proinflammatory state causing negative endophthalmitis, or breakdown of the blood-retinal barrier allowing the virus to replicate in the vitreous.

Commercial Relationships: Aaron Y. Lee, Cogent 14 Productions LLC (threeplus.org) (F); Lakshmi Akileswaran, None; Michael D. Tibbetts, None; Sunir J. Garg, Lux (F), EyeGate (F), Regeneron (F), Genentech (F), Allergan (C); Russell N. Van Gelder, Novartis (F)

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Program Number: 1107 Poster Board Number: C0084
Presentation Time: 1:00 PM - 2:45 PM
Intraocular Penetration of Systemic Antibiotics Following Scleral or Corneal Penetrating Injury

Shareef Ahmed, Himanshu Aggarwal, Oscar C. Kuruvilla, David S. Chin Yee, Yue Li, Paul A. Edwards, Xiaoxi Qiao, Hua Gao. Henry Ford Hospital, Detroit, MI.

**Purpose:** To determine if penetrating injury can enhance intraocular penetration of systemic moxifloxacin, vancomycin, and ceftazidime.

**Methods:** Thirty New Zealand rabbits were divided into 3 groups, 10 rabbits for each of 3 antibiotics. In each group, 5 rabbits were used for scleral injury and 5 for corneal injury. Right eyes were used for injury while left eyes served as controls. For scleral injury, a 4 mm laceration was made 5 mm posterior to the temporal limbus, and for corneal injury, a 3 mm laceration was made in the central cornea. Moxifloxacin 20 mg/kg, vancomycin 15 mg/kg, or ceftazidime 50 mg/kg was administered intravenously 10 minutes after injury. Eyes were enucleated 20 minutes later, frozen, and the vitreous harvested. Intra-cardiac blood was collected before animals were sacrificed. HPLC was performed to determine vitreous and plasma concentration of antibiotics.

**Results:** Intravitreal moxifloxacin concentration was unchanged by injury (3.34 and 3.28 ug/ml in scleral and corneal injury eyes, respectively) when compared to control eyes (3.48 and 3.26 ug/ml). It reached 47% to 51% of plasma concentration. MIC90 (minimum inhibitory concentration) was achieved in the vitreous against the most common endophthalmitis-causing organisms. Intravitreal vancomycin levels were not significantly enhanced by injury (0.4 and 0.22 ug/ml in scleral and corneal injury eyes, respectively) when compared to control eyes (0.28 ug/ml to non-detectable). It reached only 1-2% of plasma level and did not reach the MIC90 for organisms commonly causing intraocular infection. Intravitreal ceftazidime was increased in the injured eyes, 1.78 ug/ml (67% higher) and 1.50 ug/ml (73% higher) in scleral and corneal injury eyes, respectively compared to 1.065 and 0.74 ug/ml in control eyes. It reached 0.98% to 1.36% of plasma concentration and reaches MIC90 of many gram-negative bacteria.

**Conclusions:** Intravitreal antibiotic penetration of systemic antibiotics with or without penetrating injury varies depending on the antibiotic. For prevention or treatment of gram-positive bacteria-causing endophthalmitis from penetrating ocular injury, intravitreal injection is required when vancomycin is considered, whereas systemic administration can be used for moxifloxacin. Systemic ceftazidime can be used for many gram-negative bacteria, but intravitreal injection is recommended for better coverage, especially for more potent organisms.

Commercial Relationships: Shareef Ahmed, None; Himanshu Aggarwal, None; Oscar C. Kuruvilla, None; David S. Chin Yee, None; Yue Li, None; Paul A. Edwards, None; Xiaoxi Qiao, None; Hua Gao, None

Support: Graduate Medical Education - Henry Ford Hospital

Program Number: 1108 Poster Board Number: C0085
Presentation Time: 1:00 PM - 2:45 PM
Incidence of Endophthalmitis After Wearing Surgical Masks During Intravitreal Injections

Erin Lessner1, Rebecca Lessner2, 1Ophthalmology, University of South Carolina, Columbia, SC; 2Lincoln Memorial University-DeBusk College of Osteopathic Medicine, Harrogate, TN.

Purpose: To assess whether wearing surgical masks during intravitreal injections reduces the incidence of endophthalmitis.

Methods: This retrospective chart review compares the rate of endophthalmitis in 25 patients following intravitreal injections performed by a physician wearing a surgical mask and in 25 patients when a mask was not worn. The same physician performed each of the 50 intravitreal injections in this study. Patients were pre-treated with a fourth generation fluoroquinolone four times a day for four days before their intravitreal injection. Patients used a fourth generation fluoroquinolone four times a day for four days post injection. The same sterile preparation and superior temporal intravitreal injection technique was used in all 50 procedures. Each patient was given endophthalmitis precautions and instructed to call the clinic immediately if such symptoms occurred. Each patient had a follow up exam within a 4-8 week period.

Results: There were no reported cases of endophthalmitis in either arm of the study. There were no cases of respiratory infections in patients receiving injections or in the physician administering injections. The physician delivering each injection did not talk during the procedure when a mask was not worn. There was no difference in the number of endophthalmitis cases after intravitreal injection in either the masked or unmasked patient groups.

Conclusions: This study suggests wearing a surgical mask does not significantly alter the risk of endophthalmitis following an intravitreal injection. A cost-benefit analysis of wearing surgical masks to prevent the risk of endophthalmitis in a larger prospective randomized control study should be performed. Further studies may consider analyzing the benefit of wearing a mask when a physician performing an intravitreal injection has a respiratory infection. Routine precautions such as not talking during the procedure should continue to be followed in future investigations when masks are not worn. This study used topical antibiotics before and after each intravitreal injection without any cases of endophthalmitis. The risk of bacterial resistance when topical antibiotics are used in this fashion compared to the risk of endophthalmitis should continue to be studied.

Commercial Relationships: Erin Lessner, None; Rebecca Lessner, None

Program Number: 1109 Poster Board Number: C0086
Presentation Time: 1:00 PM - 2:45 PM

Outbreak of Fusarium endophthalmitis following Brilliant Blue G (BBG) dye-assisted vitrectomy procedures

Michael Davis1, Kristie Lin2, Tom Chang1, Mike Samuel1, Ritwan Bhattacharya3, Steven Friedlander2, Nishita Patel1, Pravin U. Dugel1.
1Retina Institute of California, Los Angeles, CA; 2Western University of Health Sciences, Pomona, CA; 3Retina Consultants of Arizona, Phoenix, AZ.

Purpose: To review the presentation of fungal endophthalmitis and the diagnostic dilemma it presents to the clinician, and to review the treatment regimen required to treat these resilient organisms.

Methods: This is a case review of 12 patients from two locations in the United States afflicted with probable fungal endophthalmitis following vitrectomy surgery with BBG dye. Patient symptomatology and presentation, treatment regimens (both surgical and medical), and responses to therapy will be reviewed. Co-morbidity factors that may affect patient outcomes will also be examined.

Results: There are 12 patients from 3 Retina practices at 2 locations (further possible cases are pending) affected by a recent outbreak of Fusarium endophthalmitis. All patients underwent vitrectomy with BBG dye. The dye was compounded from a single compounding pharmacy and Fusarium was cultured from unused vials returned to the pharmacy. All patients presented with an insidious inflammation weeks after the procedure and were treated initially as both noninfectious and infectious endophthalmitis, as the presentation is not typical or consistent between cases. Most patients required further vitrectomy surgery, removal of the IOL and/or lensectomy, multiple intravitreal injections, as well as systemic antifungal medications.

Conclusions: Fungal endophthalmitis presents as both a diagnostic and treatment dilemma. Retina surgeons should have this diagnosis in their differential diagnosis when a patient presents with inflammation weeks to months after surgery. The presentation is not always typical of infectious endophthalmitis and the treatment regimen is both arduous and lengthy.

Commercial Relationships: Michael Davis, Sequenom (C), Johnson and Johnson Research and Development (C), Synergetics (C), Allergan (C), Citi Financial Group (C); Kristie Lin, Janssen Pharmaceutical Companies (C), Thrombogenics (C), Sequenom (C);
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Program Number: 1111 Poster Board Number: C0088
Presentation Time: 1:00 PM - 2:45 PM

Anatomical and visual outcome after pars plana vitrectomy in acute postcataract endophthalmitis
Thierry Zhou1, 2, Aurelie Comby1, 2, Nelly Campolmi1, Catherine Creuzot-Garcher, Frederic Rouberol2, Pierre-Loic Cornut2, Karine Palombi1, Gilles Thuret1, Christophe Chiquet1. 1OPHTALMOLOGY, University Hospital, GRENOBLE, France; 2UNIVERSITY, UJF-Grenoble 1, GRENOBLE, France; 3OPHTALMOLOGY, University Hospital, SAINT ETIENNE, France; 4OPHTALMOLOGY, University Hospital, SAINT ETIENNE, France; 5OPHTALMOLOGY, University Hospital, EDOUARD HERriot, Civil Hospices of Lyon, University Lyon I, LYON, France; 6OPHTALMOLOGY, University Hospital, DIJON, France; 7OPHTALMOLOGY, Kleber Center, LYON, France.

Purpose: To report visual and anatomical outcome of patients vitrectomized for acute post bacterial endophthalmitis.

Methods: 123 patients with acute postcataract endophthalmitis and consecutively treated by pars plana vitrectomy (PPV) were included in four academic hospitals (French Institutionnel Endophthalmitis Study (FRIENDS) group). Risk factors of visual outcome and retinal detachment (RD) were analyzed using univariate analysis.

Results: At 6 month follow-up, 49 patients (40%) had a visual acuity (VA) greater than or equal to 20/200, and 84 patients (68%) had VA greater than or equal to 20/200. Baseline clinical factors associated with final VA ≤ 20/100 were VA limited to LP at presentation (OR = 1.6 (1.0-2.3), p = 0.02), hypopyon (OR = 1.4 (1.1-1.7), p = 0.02), fundus visibility at admission (OR = 0.60 (0.5-0.8), p = 0.03), duration of PPV (OR = 0.97 (0.96-0.99), p = 0.007), and identification of virulent bacteria (vs CNS and sterile, OR = 3 (1.9-4.7), p < 0.0001). Ocular complications occurred in 58% of the patients, including phthisis (8%), RD (13%), epiretinal membrane (15%), macular edema (11%), choroidal detachment (5%) and posterior synechia (14%). Risk factors of RD were diabetes (OR = 4.7 (1.4-15.4), p = 0.01), and visualization of retinal vasculitis on the posterior pole (OR = 3.8 (1.1-13.9), p = 0.03) at the time of PPV.

Conclusions: PPV allowed to be beneficial in a majority of the patients. RD remains a major complication, surgical repair of RD can be performed in almost all cases but final anatomical and visual results remains poor, despite updated vitreoretinal techniques.

Commercial Relationships: Thierry Zhou, None; Aurelie Comby, None; Nelly Campolmi, None; Catherine Creuzot-Garcher, None; Frederic Rouberol, None; Pierre-Loic Cornut, None; Karine Palombi, None; Gilles Thuret, None; Christophe Chiquet, None

Program Number: 1112 Poster Board Number: C0090
Presentation Time: 1:00 PM - 2:45 PM

The role of antibiotic prophylaxis to prevent post-injection endophthalmitis

Purpose: To compare the incidence of endophthalmitis following intravitreal injection of anti-vascular endothelial growth factors agents and triamcinolone acetonide with and without post-injection antibiotic prophylaxis.

Methods: Retrospective review of intravitreal injections administered at one large retina practice between January 1, 2009 and October 1, 2012. The total number of injections was determined from billing code records. Injections were performed for a variety of retinal vascular diseases. For the first 32 months of the study period, topical antibiotics were prescribed for 5 to 5 days depending on physicians preference. During the remaining 13 months of the study period, topical antibiotics were not prescribed.

Results: A total of 104870 injections (61182 ranibizumab, 39376 bevacizumab, 4312 triamcinolone acetonide) were given during the study period. Post-injection topical antibiotics were prescribed in 63147 of the injections. Thirty-one cases of endophthalmitis occurred in this group (incidence rate 0.049%). Antibiotics were not given

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following 41723 injections, among which 13 cases of endophthalmitis occurred (incidence rate 0.031%). Incidence of endophthalmitis for patients prescribed topical antibiotics was not significantly different from patients not using antibiotics (p=0.17). No statistically significant difference in incidence of endophthalmitis between the intravitreal medications was identified.

Conclusions: The incidence of endophthalmitis following intravitreal injection is low. Post-injection antibiotic drops do not appear to significantly reduce the risk of developing endophthalmitis.

Commercial Relationships: Philip P. Storey, None; Michael Dollin, None; John D. Pitcher, None; Joseph Voytko, None; Natalie Fang-Yen, None; James Vander, None; Jason Hsu, None; Sunir J. Garg, Lux (F), EyeGate (F), Regeneron (F), Genentech (F), Allergan (C)

Program Number: 1114 Poster Board Number: C0091
Presentation Time: 1:00 PM - 2:45 PM

Incidence of Endophthalmitis after Anti-VEGF Injections and use of Anti-Microbials in the Comparison of AMD Treatments Trials (CATT)

Colin A. McCannel1, Travis Meredith2, Ellen Peskin3, Maureen G. Maguire4, Charles C. Barr5, Berard Doft6, Jonathan L. Prendergast7.

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Purpose: To describe incident cases of endophthalmitis and ascertain whether perioperative topical antimicrobials exerted a protective effect after intravitreal injections of anti-VEGF agents in the Comparison of Age-related Macular Degeneration Treatments Trials (CATT) and the impact of endophthalmitis on visual acuity (VA).

Methods: Through 2 years, patients enrolled in CATT (N=1185) were evaluated every 28 days and treated with intravitreal injection of ranibizumab or bevacizumab according to the assigned dosing regimen (monthly or PRN). Study ophthalmologists examined patients who reported symptoms and initiated treatment immediately upon diagnosis of endophthalmitis. Change in VA from the time of the last treatment injection preceding the onset of endophthalmitis symptoms to the last study visit was calculated for eyes that developed endophthalmitis. Administration and timing of topical prophylactic antimicrobials was at the discretion of the study ophthalmologist. Injections were classified into four groups based on use and timing of topical ocular antimicrobial administration: 1) pre-injection only (n=1301); 2) post-injection only (n=5247); 3) both pre and post injection (n=9961); 4) no antibiotic (n=2000). Comparisons were made for rates of endophthalmitis between groups.

Results: Eleven cases of post-injection endophthalmitis occurred among 18,509 injections (0.06%; [95% CI: 0.03%-0.11%]). Of the 10 eyes with follow-up visual acuity, 5 (50%) eyes returned to VA within 10 letters (range +8 to -9) of their VA prior to injection, and 5 eyes (50%) lost 15 or more letters (range -17 to -63). Event rates for the four antimicrobial treatment groups were: 1) pre-injection-only: 1 case (0.08%); 2) post-injection-only: 3 cases (0.06%); both pre and post injection: 4 cases (0.04%); and 4) no antibiotic: 3 cases (0.15%). Differences in the incidence of endophthalmitis among the groups were not statistically significant (p=0.20).

Conclusions: Endophthalmitis rates in CATT were low and consistent with the results of other large clinical trials of intracocular injections of anti-VEGF agents and triamcinolone. Infections occurred despite topical ocular antimicrobial administration, and risk did not depend on whether or not antimicrobials were used, or on the timing of antimicrobial dosing.

Commercial Relationships: Colin A. McCannel, Alcon (S), Thrombogenics (C), Travis Meredith, None; Ellen Peskin, None; Maureen G. Maguire, Inspire Pharmaceuticals (F), Amakem (F), IDx LLC (F), Merck (C); Charles C. Barr, None; Berard Doft, None; Jonathan L. Prendergast, Genentech (C), Regeneron (C), Thrombogenics (C), Panoptica (C), Ophthotech (B) (I)

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Clinical Trial: NCT00593450

Program Number: 1115 Poster Board Number: C0092
Presentation Time: 1:00 PM - 2:45 PM

Endogenous Endophthalmitis associated with intravenous drug abuse

Shriji Patel, Ronald J. Rescigno, Marco A. Zarbin, Neelakshi Bhagat. Inst. of Ophthalmology & Visual Science, UMDNJ-New Jersey Medical School, Newark, NJ.

Purpose: To describe demographics, characteristics and management of eyes with endogenous endophthalmitis (EE) in intravenous (IV) drug abusers.

Methods: Retrospective chart review of patients with EE that presented to University Hospital (UH), New Jersey Medical School between January 2005 and October 2012.

Results: 34 patients presented with a clinical diagnosis of EE during this time period. 18 patients (53%) had a history of intravenous drug abuse (IVDA) with most cases consisting of IV heroin abuse. Two patients reported concomitant use of heroin with lemon juice. Average age was 43 years (24-61), 13 were males. Both eyes were involved in 3 of 18 patients (total of 21 eyes). Vision on presentation in the affected eye ranged from 20/100 to no light perception; the majority of patients presented with counting fingers vision or worse. All eyes presented with anterior uveitis and vitritis. Detailed examination of the retina could be performed only in 14 of the 21 eyes; 11 showed macular involvement.

All patients were admitted to the hospital for IV antibiotics and/or antifungals as well as further workup; average length of stay was 12 days (4-28 days). 10 of the 18 patients received intravenous antifungals (3 Amphotericin, 7 Voriconazole) during their hospital course for suspected fungal etiology. Only patients with documented history of bacteremia, endocarditis or meningitis (8 of 18) did not receive antifungals. All 18 patients received IV antibiotics, most commonly Vancomycin and Ceftazidime. Certain patients were also on Zosyn, Nafcillin or Rifampin at the discretion of the Infectious Disease service. 16 eyes underwent a vitreous biopsy, four had positive cultures (2 Candida albicans, 2 coagulase negative Staph Aureus). 7 eyes underwent pars plana vitrectomy with intravitreal injections (occurring an average of 3.5 days after presentation). 2 eyes underwent an anterior chamber tap with one positive culture (Corynebacterium).

Final BCVA at last followup ranged from 20/20- to NLP, with most patients having final vision of 20/400 or worse. Four eyes (19%) had vision better than 20/400. Two patients eventually underwent enucleation, one patient passed away from cardiac arrest while in the hospital.

Conclusions: We reviewed 21 eyes of 18 patients with EE and concurrent IVDA over an eight year period; ten patients with fungal EE. Our study shows an extremely poor visual prognosis associated with EE in this setting.

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Commercial Relationships: Shriji Patel, None; Ronald J. Rescigno, None; Marco A. Zarbin, Iridex (C), Novartis (C), Pfizer (C), Calhoun Vision (C), Imagen Biotech (C), UMDNJ (P); Neelaksh Bhat, None

Support: Research to Prevent Blindness, Inc., the New Jersey Lions Eye Research Foundation

Program Number: 1116 Poster Board Number: C0093

Presentation Time: 1:00 PM - 2:45 PM

Acute endophthalmitis post-intravitreal bevacizumab injections wearing surgical masks

Mohamed Haji, Erika Massicotte, Flavio A. Rezende. ophthalmology, university of montréal, Montreal, QC, Canada.

Purpose: To evaluate the outcomes of acute endophthalmitis (AE) post-intravitreal injection of 1.25mg/0.05 ml bevacizumab (IVB) wearing surgical masks for diabetic macular edema (DME) or wet age-related macular degeneration (wAMD)

Methods: This is a retrospective, non-comparative, interventional case series. We reviewed medical records of patients treated for DME or wAMD with IVB from Jun/2010 to Dec/2012. Data collected included age, gender, laterality, number of injections, time from injection to AE diagnosis, microbiological results, initial visual acuity (VA) at AE diagnosis, and final VA. All IVB were done in an outpatient minor procedure room using sterile gloves, sterile lid speculum, 0.5% proparacain drops, 5% betadine drops, and a 1 ml syringe with a 30-gauge needle. Both surgeon and patients were wearing surgical masks. In the first 12 months, prophylactic polysyrpin drops 4 times/day were given for a week; in the last 18 months, no antibiotics (ATB) were given. Pars plana vitrectomy/vitreous tap and injection of vancomycin 1mg/0.1ml and cefazidime 2.25mg/0.1ml were performed to treat all AE cases

Results: Four patients with AE were identified out of 3088 injections of IVB (rate 0.13%). We had 3 females and 1 male, with age range of 68 to 97 years, 2 right eyes and 2 left, and a follow-up range of 3 to 20 months. Two patients were treated for DME and 2 for wAMD. The AE developed after a mean of 8 days (range 4 to 12 days) post-IVB and after a mean of 6 IVB (range 5 to 7 IVB). Three patients developed AE despite prophylactic ATB and 1 had AE with no ATB prophylaxis. Initial visual acuity ranged from 20/40 to 20/70 and at presentation Time: 2:45 PM

Conclusions: The rate of AE post-IVB with both surgeon and patients wearing surgical masks is comparable to that reported in the literature but the microbiologic profile and outcomes seem to differ from reported cases of AE post-IVB without the use of masks and AE secondary to drug compounding contamination

Commercial Relationships: Mohamed Haji, None; Erika Massicotte, None; Flavio A. Rezende, None

Program Number: 1117 Poster Board Number: C0094

Presentation Time: 1:00 PM - 2:45 PM

Crying wolf or a real problem : poisson distribution statistics for rare events applied to endophthalmitis

Sankha Amarako, Jose P. Martinez-Ciriano, René Wubbels, L I. van den Born, Suzanne Yzer, Mirjam E. Van Velthoven, Tom Missotten. ROI, Rotterdam Eye Hospital, Rotterdam, Netherlands.

Purpose: The most feared complication of intravitreal (anti-VEGF) injections is endophthalmitis. An incidence of 1/2000 is reported in the literature. Antiseptic protocols for intravitreal injection vary over the world and start from simple iodine drops and gloves as antiseptic measures to injections in full operating theatre circumstances. Whenever a few cases occur in a relative short time span, a search for related causes is started : date, operator, settings or medication preparation are examined. Unfortunately, unrelated endophthalmitis cases do occur randomly and it is often unclear if additional antiseptic procedures or other measures are mandatory. Poisson distribution statistics are used to determine the significance of increased incidence of unrelated rare events.

Methods: In the Rotterdam eye hospital, 0 endophthalmitis cases in 8500 injections(2011) and 5 cases in 10300 (2012) were observed. The expected rate would haven been 4 (2011) and 5 (2012) based on an incidence of 1/2000 injections in the literature. Poisson distribution statistics were performed to pre-calculate an incidence that should be regarded as a significant rise in incidence and make an upgrade of standard operating procedures mandatory.

Results: For a given incidence of 1/2000, in a cohort of 10.000 injections, 5 endophthalmitis would have been expected. P-values for significant increased observed cases were :

n=0 (p=1.00); n=1(p=0.99); n=2(p=0.96); n=3(p=0.88); n=4 (p=0.74); n=5 (p=0.56); n=6 (p=0.38); n=7(p=0.24); n=8(p=0.13); n=9(p=0.07); n=10(p=0.03); n=11(p=0.01).

Significant p values for other sizes of cohort(c) were : c/1000 (n=2, p=0,01); c/2000 (n=3, p=0,02); c/5000 (n=5, p=0,05); c/20000(n=15, p=0,05); c/50000(n=33, p=0,05)

Conclusions: If no related case can be found in a cluster of endophthalmitis cases, it can be helpful to check the poisson distribution of unrelated rare events, before changing aseptic standard operating procedures, settings (operating theatre) or antibiotic schedules. The ophthalmic community should perhaps set quality standards for the incidence of injection caused endophthalmitis and develop standard operating procedures. Depending on the cohort size, poisson distribution statistics can help set warning points when upgrading of standard operating procedures in mandatory.

Commercial Relationships: Sankha Amarako, None; Jose P. Martinez-Ciriano, None; René Wubbels, None; L I. van den Born, None; Suzanne Yzer, None; Mirjam E. Van Velthoven, None; Tom Missotten, None

Program Number: 1118 Poster Board Number: C0095

Presentation Time: 1:00 PM - 2:45 PM

Meta-Analysis of Infectious Endophthalmitis After Intravitreal Injection of Anti-Vascular Endothelial Growth Factor Agents

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Purpose: To investigate the rate of endophthalmitis after intravitreal injection of anti-vascular endothelial growth factor (VEGF) agents, the spectrum of causative organisms, and associated visual outcomes.

Methods: A literature search was performed of the National Library of Medicine PubMed interface using keywords “endophthalmitis” and “intravitreal” between 01/01/2005 through 05/09/2012 (search date: 05/09/2012). Articles were reviewed and additional studies pertinent to endophthalmitis following intravitreal anti-VEGF injection were identified. Inclusion criteria included article in English, >100 intravitreal anti-VEGF injections, and report of adverse events including endophthalmitis. Endophthalmitis rates, causative organisms, and visual acuity outcomes were analyzed.

Results: Forty-three articles were analyzed. Endophthalmitis occurred following 1973350,535 (0.056% [95% confidence interval [CI], 0.049-0.065%]) intravitreal anti-VEGF injections. The most
common organisms isolated were coagulase-negative staphylococcus (26/68; 38.24% [95% CI, 27.6-50.2%]) and Streptococcus species (20/68; 29.41% [95% CI, 20.0-41.2%]). A final vision within one line of the pre-injection Snellen acuity was achieved by 23.53% of patients with endophthalmitis caused by Streptococcus species, 43.75% of patients with endophthalmitis caused by coagulase-negative staphylococcus, and 64.71% of patients with culture-negative endophthalmitis; 94.12%, 12.50%, and 31.37% of patients, respectively, had a final acuity of 20/400 or worse. **Conclusions:** The reported rate of endophthalmitis following intravitreal anti-VEGF injection is low. Coagulase-negative staphylococcus and Streptococcus species were the most common causative organisms. Streptococcus species is the causative organism of endophthalmitis more frequently following intravitreal anti-VEGF injection than reported following most incisional intracocular surgeries. Among patients with endophthalmitis following intravitreal anti-VEGF injection, endophthalmitis caused by streptococcus is associated with poorer visual outcomes than endophthalmitis caused by coagulase-negative staphylococcus and culture-negative cases. **Commercial Relationships:** John Fileta, None; Ingrid U. Scott, None; Harry W. Flynn, None

**Program Number:** 1119 **Poster Board Number:** C0096 **Presentation Time:** 1:00 PM - 2:45 PM **Pediatric Infectious Endophthalmitis: A Case Series** Bryan P. Jones, Lisa Athwal, Marco A. Zarbin, Paul D. Langer, Neelakshi Bhagat. The Institute of Ophthalmology and Visual Science, UMDNJ - New Jersey Medical School, Newark, NJ. **Purpose:** To describe the etiology, diagnosis, management, and outcomes of pediatric infectious endophthalmitis cases at University Hospital, Newark, NJ over 11 years, 2001-2011. **Methods:** Retrospective series. Data were collected on demographics, presenting clinical findings, management, culture results, and visual and anatomic outcomes. **Results:** Seven cases of infectious pediatric endophthalmitis were identified in six patients. Two patients were male, and four were female. Mean presenting age was 6 years (range 4 weeks to 16 years). The most common etiology was trauma, accounting for 3 out of 7 cases (43%), of which one featured an intraocular foreign body. Two of 7 cases were caused by endogenous bacterial spread (29%), and 2 of 7 were secondary to bleb infection (29%). Patients presented most commonly with symptoms of pain (71%), photophobia (43%), and blurred vision (43%) and signs of vitritis (100%), anterior chamber fibrinous exudates (57%), conjunctival hyperemia (57%), chemosis (71%), and hypopyon (29%). All 3 trauma cases had uveal prolapsed in zone III. None presented with retinal detachment. Only one of three vitreous cultures was positive (33%) and grew Group B Streptococcus. Three cases underwent both pars plana vitrectomy (PPV) and intravitreal antibiotics (43%), and one only intravitreal antibiotics (14%). Best recorded visual acuity after resolution of infection was 20/400 in one patient, counts fingers in another, and no light perception in the remaining 5 eyes. One underwent primary enucleation (14%), one secondary enucleation (14%), and 2 became phthisical (29%). **Conclusions:** Endophthalmitis is a rare but calamitous condition usually resulting in blindness. Our small series finds traumatic open globe injury as the most common cause of infectious endophthalmitis. Despite emergent treatment, patients are frequently left with no light perception in the affected eye. **Commercial Relationships:** Bryan P. Jones, None; Lisa Athwal, None; Marco A. Zarbin, Iridex (C), Novartis (C), Pfizer (C), Calhoun Vision (C), Imagen Biotech (C), UMDNJ (P); Paul D. Langer, None; Neelakshi Bhagat, None

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**Program Number:** 1120 **Poster Board Number:** C0097 **Presentation Time:** 1:00 PM - 2:45 PM **Characterization of Prognostic Factors of Endophthalmitis** Nausheen Abbas, John Huang. Yale New Haven Hospital, New Haven, CT. **Purpose:** To characterize the prognostic factors associated with different etiologies of endophthalmitis in order to tailor therapy for maximal benefit. **Methods:** A retrospective chart review was performed of all patients who presented with endophthalmitis over a period of 5 years. One hundred charts were reviewed and 74 patients were excluded (age <18, pre-existing visual acuity (VA) <20/60, misdiagnosed endophthalmitis and infections treated solely with topical therapy). Data collected included age, gender, presenting visual acuity, final visual acuity, treatment modality (vitrectomy vs. tap/inject) and use of adjuvant oral fluoroquinolones. Univariate analysis of variance was performed on the visual outcomes. **Results:** Of the 26 eyes that were analyzed, etiologies included blebitis, corneal ulcers, cataract surgery, endogenous and intravitreal injections. The biggest difference in terms of visual outcome was seen with treatment modalities. Of the bleb associated infections, 50% of the vitrectomy group had an improvement of VA compared with 25% of the tap/inject group (p=0.633). In the corneal ulcer group, 100% had improved VA with vitrectomy compared with 66% with tap/inject (p=0.576). In the post cataract group, 75% had improved VA with vitrectomy as compared with 100% in the tap/inject group (p=0.685). When stratified according to visual acuity at presentation, all of the groups had a better visual outcome with vitrectomy than with tap and inject. No difference was seen with diabetes or with the addition of oral fluoroquinolones. **Conclusions:** Endophthalmitis is a severe intraocular condition, which can lead to devastating visual loss if not promptly diagnosed and treated. Treatment guidelines set forth in the Endophthalmitis Vitrectomy Study are currently being extrapolated and implemented for etiologies of endophthalmitis other than post-cataract extraction, however every etiology has a different prognostic profile and should be treated as such. In our study, bleb associated and corneal ulcer groups had worse visual outcomes and endogenous and intravitreal groups had better visual outcomes. All of the etiologies (except for cataract) showed better visual outcomes with vitrectomy compared to tap/inject, regardless of initial visual acuity. Our results indicate that a lower threshold for vitrectomy may result in better visual outcomes in certain cases of endophthalmitis. **Commercial Relationships:** Nausheen Abbas, None; John Huang, None

**Program Number:** 1121 **Poster Board Number:** C0098 **Presentation Time:** 1:00 PM - 2:45 PM **Endophthalmitis after open globe trauma** Sebastian P. Lesniak, Alain M. Bauza, Marco A. Zarbin, Paul D. Langer, Neelakshi Bhagat. IOVS - New Jersey Medical School, Newark NJ, Newark, NJ. **Purpose:** To evaluate the demographics, characteristics, and outcomes of endophthalmitis after open globe trauma. **Methods:** Retrospective chart review of patients with endophthalmitis after open globe injuries that presented to University Hospital Newark, between 2001-2010. **Results:** Eighteen patients were identified who were diagnosed with endophthalmitis after open globe trauma between 2001-2010. Fifteen hundred charts were reviewed and 74 patients were excluded (age <18, pre-existing visual acuity <20/60, misdiagnosed endophthalmitis and infections treated solely with topical therapy). Data collected included age, gender, presenting visual acuity, final visual acuity, treatment modality (vitrectomy vs. tap/inject) and use of adjuvant oral fluoroquinolones. Univariate analysis of variance was performed on the visual outcomes. **Commercial Relationships:** Nausheen Abbas, None; John Huang, None

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43.3 years (range, 8-87), and 93% were male. There were 12 accidental injuries, 2 wound dehiscences, and 1 violent assault. Eight injuries were classified as penetrations, 4 as intraocular foreign bodies (IOFB), 2 as ruptures, and 1 was unspecified. There were 10 zone 1 injuries, 4 zone 2, and 1 zone 3 injury. Retinal detachment was diagnosed in 6 cases (40%). Two patients (13.3%) were diagnosed with endophthalmitis on presentation. In 14 cases the mean duration from injury to diagnosis of endophthalmitis was 8.6 days (range 1-42 days). One patient presented with delayed onset, 6 months after open globe trauma. IOFB was diagnosed in 4 cases (26.7%), 3 were metallic and 1 was glass. Three of these 4 IOFB’s were in the posterior chamber. Four eyes (26%) were enuclecated. One patient (6.7%) came in with no-light-perception (NLP) vision and 4 patients (26.7%) ended up NLP. Seven patients (46.7%) underwent pars-plana vitrectomy (PPV) during the initial open globe surgery. Six patients (40%) underwent open globe repair, and subsequently required PPV due to development of endophthalmitis. In 1 case (6.7%) the initial penetrating wound self-sealed, but later required a PPV due to endophthalmitis. In 1 case (6.7%) the second surgery after open globe repair was enucleation. Fourteen cases (93.3%) underwent vitreous biopsy with culture, and were injected with intravitreal antibiotics. The remaining 1 case was enucleated after developing endophthalmitis. All cases received IV antibiotics. Vitreous cultures were negative in 5 cases (33.3%). There were 3 cases (20%) of S. epidermidis, and single cases of the following organisms: MRSA, MSSA, B. cereus, E. vulneris, S. hominis, Candida famata, and Gemella morbillorum. The average presenting visual acuity was 1.787 logMAR, and the average final corrected visual acuity was 1.556 logMAR.

**Conclusions:** Endophthalmitis after open globe trauma remains a serious complication often leading to poor visual outcome, with 26.7% of eyes ending up with NLP vision.

**Commercial Relationships:** Sebastian F. Lesniak, None; Alain M. Bauza, None; Marco A. Zarbin, Iridex (C), Novartis (C), Pfizer (C), Calhoun Vision (C), Imagen Biotech (C), UMDNJ (P); Paul D. Langer, None; Neelakshi Bhagat, None

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**Program Number:** 1122 Poster Board Number: C0099

**Presentation Time:** 1:00 PM - 2:45 PM

**Conjunctival Flora Antibiotic Resistance Patterns After Serial Intravitreal Injections without Post-Injection Topical Antibiotics**

**Purpose:** To determine whether conjunctival flora develop antibiotic resistance after serial intravitreal injections when topical post-injection antibiotic drops are not used.

**Methods:** New patients with neovascular age-related macular degeneration or retinal vein occlusion requiring serial intravitreall injections (≥ 3) were randomized to receive either topical ofloxacin 0.3% and 5% povidone-iodine, or 5% povidone-iodine alone, for pre-injection ocular surface preparation. Conjunctival cultures were performed prior to each injection preparation. Conjunctival flora antibiotic resistance patterns were compared between groups as well as within each group over the course of the study.

**Results:** Twenty-four patients completed the study with 12 patients assigned to each group. Eighty-six cultures were performed with a 76% culture positivity rate. The most frequent organism isolated from positive cultures was coagulase negative staphylococcus (83%). The change in antibiotic resistance between the two groups over the course of the study was not statistically significant (P=0.13).

**Conclusion:** There was no evidence that the incidence of resistance increased within either group over the course of the study.

**Commercial Relationships:** Adam T. Gerstenblith, None; Sunir J. Garg, Lux (E), EyeGate (F), Regeneron (F), Genentech (F), Allergan (C); James Vander, None; Jason Hsu, None

**Support:** Wills Eye Innovations Grant and a J. Arch McNamara Fund Grant.

**Clinical Trial:** NCT01531842

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**Program Number:** 1123 Poster Board Number: C0100

**Presentation Time:** 1:00 PM - 2:45 PM

**Fungal Endophthalmitis Onset Due To Intravitreal Triamcinolone Contaminated by a Compounding Pharmacy**

**Purpose:** A retrospective chart review of the onset and presentation of fungal endophthalmitis was undertaken to assist the ophthalmic, epidemiologic and infectious disease communities in detecting and managing outbreaks from compounding pharmacies. These ophthalmic data may be useful in managing the meningitis outbreak.

**Methods:** A retrospective chart review was performed of 14 patients who received intravitreal injections of preservative-free triamcinolone pre-loaded syringes obtained from Franck’s pharmacy which were subsequently found to be contaminated with the fungus Bipolaris hawaiensis. Sixteen eyes were injected (one twice) with this preservative-free triamcinolone. Two patients received bilateral sequential injections. The data extracted from the charts were: time to onset of signs and symptoms of infection, visual acuity, intraocular pressure, fundus photos, fluorescein angiography, ultrasounds, vitreous culture and biopsy results.

**Results:** Of the sixteen eyes injected, 10 (62%) eventually developed fungal endophthalmitis. The time onset of signs and symptoms ranged from 2 weeks to 7 months, median 3 months. The typical presenting signs and symptoms were painless loss of vision in an eye which was white and quiet appearing except for cell in the anterior chamber or the vitreous. Vitreous biopsy (cyto-spin for hyphae) obtained by pars plana vitrectomy was more sensitive in making the diagnosis of fungal endophthalmitis than vitreous culture or in office “vitreous taps” (including cyto-spin).

**Conclusion:** Fungal endophthalmitis is rare and can have an insidious and much delayed onset. Initially making the diagnosis without the context of a documented “outbreak” is extremely difficult. Endophthalmitis due to Bipolaris hawaiensis, a plant mold, has only been reported twice before. One was in a patient who had a scleral laceration from a rice branch and the other was endogenously in an immuno-compromised patient. Our Bipolaris endophthalmitis cases have many similarities with the Exserohilum meningitis cases. Both are ubiquitous airborne black molds which had contaminated triamcinolone by different compounding pharmacies. The markedly delayed onset of Bipolaris hawaiensis infections is a potentially ominous warning for the patients and doctors involved with the 17,000 patients exposed to Exserohilum meningitis.

**Commercial Relationships:** Kent W. Small, Valeant (C)

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**Program Number:** 1124 Poster Board Number: C0101

**Presentation Time:** 1:00 PM - 2:45 PM

**Endophthalmitis after glaucoma filtering procedure and Glaucoma drainage implants, incidence, outcomes, and management: tertiary care experience Riyadh**
Intravitreal Drug Delivery

Victor A. Neamtu, Surbhi Bansal, Boleslav Kotlyar, Hoon Jung. Ophthalmology, University at Buffalo, Buffalo, NY.

Purpose: To culture and examine possible sources of bacterial contamination of needles from multiple punctures and draws from vials of Bevacizumab (Avastin, Genentech) when preparing intravitreal injections in a staged clinical setting.

Methods: Prospective, case control series with three arms of 92 experiments with bacterial cultures obtained from needles and instruments used in the preparation of Bevacizumab intravitreal injections. Sterile NaCl was used as control. Arm 1 included bacterial cultures of instruments used in routine intravitreal injections (speculum, caliper, forceps, 18 and 30 gauge needles) along with peri-operative medications. Arm 2 included bacterial cultures of needles when used to separately draw Bevacizumab or NaCl employing multiple punctures of each vial with minimal time delay in between draws. Arm 2 also included sources of possible contaminants when deviating from standard local protocol which includes the use of sterile gloves, alcohol swabs to the vial top, and face mask. Arm 3 examined bacterial cultures of needles when multiple punctures were performed at hourly intervals and up to 5 hours from the initial draw, with the Bevacizumab vial being refrigerated in between each draw. All samples were cultured in Thiglycolate broth, where positive contamination was declared when turbidity of the growth medium was observed. The turbid samples were further cultured for identification on standard plates.

Results: Arm 1 showed no growth from sterile instrumentation or peri-operative topical medications (10 cultures, p=1.00). Arm 2 displayed no growth under standard local protocol. However, Arm 2 had growth of alpha-hemolytic streptococci and diphtheroids when the Bevacizumab vial was subjected to sterumination without applying alcohol swab to the vial top (64 cultures, p=0.216). Arm 3 had no growth when time delay draws were performed (18 cultures, p=1.00).

Conclusions: Our study shows relative safety when drawing multiple doses of Bevacizumab for use in intravitreal injection via 18 gauge puncture from one single use vial, either with minimal time delay or with refrigeration of the vial in between serial draws when a standardized technique is used in a staged clinical setting. We observed that exposure to oropharyngeal fomites with deviation from protocol may elevate the risk of bacterial contamination of needles.

Methods and arms

Commercial Relationships: Victor A. Neamtu, None; Surbhi Bansal, None; Boleslav Kotlyar, None; Hoon Jung, None
Transient elevation was recorded in 5 of the 17 eyes (29.4%). None of the patients were diagnosed on routine screening for fugemia. Diffuse anterior and posterior inflammation was the most common finding on examination of affected eyes (66.7%). Hypopyon was noted in 33.3% of affected eyes.

The most common organism cultured by vitreous aspirate or vitrectomy specimen was Aspergillus fumigatus (46.2%) followed by Fusarium oxysporum (15.4%) and Aspergillus glaucus (15.4%). Nonocular cultures were positive in 15.4% of patients. Initial treatment with pars plana vitrectomy (PPV) was performed in 46.7% of eyes. During the course of treatment, 93.3% of eyes received systemic treatment consisting of either oral or intravenous antifungal therapy. 60% of eyes received intravitreal injection of an antifungal agent. 80% of eyes underwent PPV, with or without lensectomy. VA on presentation was >=20/200 in 21.4% of eyes. VA >=20/200 was present in the same 21.4% of eyes at last follow-up. Retinal detachment occurred in 13.3% of eyes. During the course of treatment enucleation was performed in 26.7% of eyes.

Conclusions: In this study of endogenous endophthalmitis caused by molds, Aspergillus fumigatus was the predominant etiology. Common risk factors included recent hospitalization and iatrogenic immunosuppression. The majority of patients in this study underwent PPV during the course of treatment. Endogenous endophthalmitis caused by molds is associated with poor visual acuity outcomes despite early and appropriate management.

Commercial Relationships: Jayanth Sridhar, None; Harry W. Flynn, None; Darlene Miller, None; Thomas A. Albini, Bausch and Lomb (C), Allergan (C), Genentech (F), Eleven Biotherapeutics (C)

205 DME: Clinical Research
Monday, May 06, 2013 8:30 AM-10:15 AM
6E Paper Session
Program #/Board # Range: 1236-1241
Organizing Section: Retina

Program Number: 1236
Presentation Time: 8:30 AM - 8:45 AM
Intraocular Pressure Trends Following Intravitreal Injections of Anti-VEGF Agents for Diabetic Macular Edema
Abdulahal A. Al-Abdullah, Sawsan R. Nowilaty, Nicola G. Ghazi.
Vitreo-retinal, King Khalid Eye Specialist Hospital, Riyadh, Saudi Arabia; *KKESH, Riyadh, Saudi Arabia.
Purpose: To investigate the intraocular pressure (IOP) trends after intravitreal anti-vascular endothelial growth factor (VEGF) agents for diabetic macular edema (DME).
Methods: Retrospective chart review of 162 patients, (28-83 years, median 62), who received intravitreal bevacizumab (86.1% of eyes) and/or ranibizumab (13.9% of eyes) for DME. Data recorded included clinical findings, total number of injections received and IOP at each visit. IOP elevation was defined as an increase above baseline IOP by >5 mmHg or >20%, or an IOP of >24 mmHg on ≥2 consecutive visits or an IOP elevation requiring IOP lowering agents. Return to baseline IOP after two readings without treatment was defined as transient elevation.
Results: A total of 237 eyes of 162 patients were included at the time of this submission. The number of injections per eye ranged from 1-11 over a mean follow up of 16.14 months (range: 1-56; SD: 15.1). IOP elevation was observed in 17 (7.17%) eyes of 16 patients (IOP rise group). Transient elevation was recorded in 5 of the 17 eyes (29.4%). The majority of eyes (13/17 eyes [76%]) showed an IOP elevation above 20% from baseline, ranging from 16 to 32 mmHg (mean 22.41). Although there was no significant difference in the baseline IOPs between the IOP rise group (mean 15.76; SD=3.18) vs. the rest of the eyes (mean 17.34 (SD= 3.48), p= 0.071), final IOP was significantly higher in the IOP rise group (mean 18.65 vs.16.81, p = 0.047). None of the eyes required surgery, laser therapy, or systemic medications for IOP control. Only one eye required topical IOP lowering agents. Using univariate analysis, the total number of injections was higher in the IOP rise group (mean 4.76, SD 1.78) vs. 2.90, SD 2.09; p= 0.001, and a shorter interval between injections was significantly associated with IOP elevation (mean 3.89 months, SD 3.02) vs. 8.18, SD 8.93; p< 0.001. Logistic regression analysis disclosed the total number of injections as the only variable significantly associated with post-injection IOP elevation (p= 0.012; 95% CI:1.06-1.64; Odds ratio: 1.32).
Conclusions: Our results suggest that IOP elevation following intravitreal anti-VEGF injections occurs in DME patients at a rate comparable to that reported for AMD patients. Eyes requiring a higher number of injections with shorter intervals between injections appear to be at increased risk.
Commercial Relationships: Abdulahal A. Al-Abdullah, None; Sawsan R. Nowilaty, None; Nicola G. Ghazi, None
studies are needed to understand whether macular morphological parameters in patients with diabetes without DME are associated with future risk of developing clinical DME, and reveal the clinical implication of these findings.

**Commercial Relationships:** Marko Sasaki, None; Motoko Kawashima, Santen Pharmaceutical Co., Ltd (F); Ryo Kawasaiti, None; Miho Kawai, None; Atsuro Uchida, None; Takashi Koto, None; Hajime Shinoda, None; Kazuo Tsubota, AcuFocus, Inc (C), Allergan (F), Bausch Lomb Surgical (C), Functional visual acuity meter (P), JINS (P), Kissei (F), Kowa (F), Santen, Inc. (F), Otsuka (F), Pfizer (C), Thea (C), Echo Denki (P), Nidek (F), Ophtec (F), Wakasa Seikatsu (F), CEP Technology (P); Jie Wang, None; Yoko Ozawa, Wakasa Seikatsu Co., Ltd. (F), NOVARTIS Pharmaceutical Co., Ltd. (F), Senju Pharmaceutical Co., Ltd. (F)

**Program Number:** 1238

**Presentation Time:** 9:00 AM - 9:15 AM

**Evaluating SAVE, a novel grading protocol for the treatment of diabetic macular edema**

Sonja G. Prager, Matthias Bolz, Gabor Deak, Andreas Polleireisz, Berthold Pemp, Katharina Kriechbaum, Christoph D. Scholda, Ursula Schmidt-Erfurth. Ophthalmology and Optometry, Medical University of Vienna, Vienna, Austria.

**Purpose:** To adopt a new grading scale (SAVE protocol) based on morphologic characteristics in spectral domain optical coherence tomography (SDOCT) and fluorescein angiography (FA) for the follow up of patients treated with intravitreal injections for diabetic macular edema (DME).

**Methods:** Monthly acquired OCT scans and quarterly acquired FAs obtained during the study period of 12 months in 3 prospective clinical trials of the diabetic retinopathy research group (DRRG) Vienna were graded in regard to morphologic characteristics. The grading protocol abbreviated “SAVE” evaluates the presence of subretinal fluid (“S”), the edema expansion in the ETDRS grid (area, “A”), vitreous-retinal abnormalities (“V”), as well as the source of leakage (edema type, “E”).

**Results:** 586 OCTs and 247 FAs of 50 patients (mean age 61 (±10.2) years, 22 female) receiving treatment for center involving DME were evaluated: 20 patients received three initial injections with 2.5mg bevacizumab followed by monthly PRN treatment, 20 patients received initially 8mg triamcinolone intravitreally followed by quarterly PRN treatment, and 10 patients received a loading dose of three injections with 0.5mg ranibizumab followed by monthly PRN treatment. Treatment response was similar in all treatment groups showing early resolution of subretinal fluid and dissolving macular edema from initially 509(±125) microns at the center subfield to 325(±105) microns after 12 months. At baseline retinal thickening was prevalent in 7 ETDRS subfields and regressed to 3 subfields at month 12. Vitreomacular abnormalities were present in 11 patients, in 3 cases they were not visible at baseline but only became apparent after regression of CME. In FA primarily focal or primarily diffuse edema pattern were graded in 22 and 28 patients respectively, with ischemic areas detected in 42 subjects.

**Conclusions:** SD OCT and FA provide more information than currently used for DME classification or treatment algorithms. The SAVE grading scale defines the basic characteristics of DME in a detailed, but evident approach that can be easily integrated in daily clinical practice. Future studies are needed to evaluate treatment decisions based on the SAVE protocol.

**Commercial Relationships:** Sonja G. Prager, None; Matthias Bolz, None; Gabor Deak, None; Andreas Polleireisz, None; Berthold Pemp, None; Katharina Kriechbaum, None; Christoph D. Scholda, None; Ursula Schmidt-Erfurth, Alcon (C), Bayer Healthcare (C), Novartis (C)

**Clinical Trial:** NCT00682539

**Program Number:** 1239

**Presentation Time:** 9:15 AM - 9:30 AM

**Double Masked Trial Demonstrates Superiority Of Combined Ranibizumab Plus Laser Versus Laser In Patients With Diabetic Macular Edema With Or Without Proliferative Diabetic Retinopathy**

Chris P. Lohmann, Jessica Voegeler, Sandra Liakopoulos, Peter M. Wiedemann, Georg Spital, Gabriele E. Lang. 1 Dept of Ophthalmology, Klinikum rechts der Isar, Technical University, Munich, Germany; 2 Clinical Research Speciality Medicine Ophthalmology, Novartis Pharma GmbH, Nuernberg, Germany; 3 Cologne Image Reading Cent, Dept of Ophthalmology, Cologne, Germany; 4 Dept of Ophthalmology, University of Leipzig, Leipzig, Germany; 5 Dept of Ophthalmology, St Franziskus Hospital, Muenster, Germany; 6 Dept of Ophthalmology, University of Ulm, Ulm, Germany.

**Purpose:** Diabetic Macular Edema (DME) and proliferative diabetic retinopathy (PDR) are common consequences of diabetic retinopathy. Anti-VEGF therapy alone or combined with laser showed convincing results in DME, while outcome in patients with PDR remains unclear.

**Methods:** In the RELATION study, a multicenter, 12-months, two-armed, double-masked, parallel-group, active controlled clinical trial, patients with visual impairment die to DME were randomized 2:1 to ranibizumab in combination with focal/grid laser photocoagulation (combined group) or focal/grid laser photocoagulation combined with sham injections (laser group) with a follow-up of up to 12 months. After initial treatment starting at baseline with laser and 4 monthly ranibizumab/sham injections, treatment was given as needed (PRN). Visual acuity (VA) was tested with ETDRS charts by certified VA-assessors. Anatomical changes were graded by central reading center assessing OCT (time Or spectral domain), fluorescence angiography (FLA) and fundus photography (FP). A subgroup of patients with concomitant PDR was included receiving additional panretinal laser photocoagulation (PRP) at baseline, then treatment as randomized.

**Results:** Of 128 patients, 85 were randomized to the combined group and 43 to the laser group. BCVA in the combined group was significantly better than BCVA in the laser group at final follow-up (mean change from baseline +6.5 vs +1.4 ETDRS letters, p=0.001, LOCF method). 80% of Centers used SD-OCT instruments. The reduction of total retinal volume within 6 mm ETDRS grid mm3 was significantly higher in the combination group than in the laser group [mean change from baseline -1.174 vs -0.501 mm3, FAS, LOCF]. 27 patients had PDR at baseline (20 in combined and 7 in laser group). Presence of PDR had no significant effect on BCVA outcome. eight (40%) patients with PDR in the combined group but none of the PDR patients in the laser group showed regression of PDR during follow-up. The adverse Event profile was similar to previous studies in NPDR and PDR patients.

**Conclusions:** Results of this clinical trial show that combined therapy of ranibizumab and laser yielded better outcomes on BCVA and CRT than laser monotherapy in eyes with DME, also in eyes with PDR. Combination of laser with ranibizumab may result in regression of PDR.

**Commercial Relationships:** Chris P. Lohmann, None; Jessica Voegeler, Novartis Pharma Gmbh (E); Sandra Liakopoulos, Novartis (F), Novartis (C), Heidelberg Engineering (R), Novartis (R); Peter M. Wiedemann, Novartis (F), Bayer (F), Novartis (R), Bayer
Ranibizumab for Diabetic Macular Edema, compared to anti-VEGF mono-therapy.

Methods: A consecutive series of 76 eyes with DME were included and randomized into 3 groups: 1. Ranibizumab monotherapy (n=27; using an observation and retreatment paradigm for anti-VEGF therapy that is compliant with the European Public Assessment Report (EPAR, European Medicines Agency) for ranibizumab); 2. Three consecutive monthly ranibizumab injections followed by navigated laser therapy, then application of the observation and retreatment paradigm as in group “1” (n=15); 3. Monthly ranibizumab injection until central retinal thickness (CRT) was reduced to 450µm (Spectralis OCT) then navigated laser therapy followed by the application of the observation and retreatment paradigm as in group “1” (n=34). Subjects were followed monthly (best corrected Visual acuity (BCVA); CRT) for 12 month, to assess the number of anti-VEGF injections required to maintain stable clinical improvement.

Results: After 12 month BCVA increased and in all three investigated groups significantly (group 1: 6.3 ±6.77; group 2: 7.1 ±8.22; group 3: 7.4 ±7.53 letters). To achieve these results, after an upload of three consecutive monthly applied ranibizumab injections, ranibizumab mono-therapy group (group 1) needed 5.2 ± 3.2 injections. In contrast, group 2 and 3 needed significantly less ranibizumab injections (0.5 ± 0.8 and 0.8 ± 1.1, p=0.001).

Conclusions: In this study, additional navigated laser therapy applied after 3 initial anti-VEGF injections in DME patients was effective in preserving visual gains, comparable to anti-VEGF mono-therapy. In addition, navigated macular laser reduced the number of injections needed significantly.

Commercial Relationships: Sarah Cserhati, None; Raffael Liegl, None; Michael W. Ulbig, Novartis (R), Bayer (C), Pfizer (C), Allergan (R), Bausch & Lomb (R), Alimera (R); Christos Haritoglou, None; Anselm Kampik, None; Aljoscha S. Neubauer, None; Marcus Kern, Allergan (R), Novartis (R), OD-OS (C), Optos (C)

Program Number: 1241
Presentation Time: 9:45 AM - 10:00 AM

206 CNV: Clinical and Translational Research
Monday, May 06, 2013 8:30 AM-10:15 AM
6C Paper Session
Program #/Board # Range: 1242-1247
Organizing Section: Retina

Program Number: 1242
Presentation Time: 8:30 AM - 8:45 AM

Suppression of experimental choroidal neovascularization by curcumin in mice
Ping Xie, Qinghua Liu, Songtao Yuan, Qing Yang, Weiwei Zhang, Ophthalmology Department, The First Affiliated Hospital with NanJing Medical University, NanJing, China.

Purpose: To investigate the effects of curcumin on the development of experimental choroidal neovascularization (CNV) with underlying cellular and molecular mechanisms.

Methods: C57BL/6N mice were pretreated with intraperitoneal injections of curcumin daily for 3 days prior to laser-induced CNV,
and the drug treatments were continued until the end of the study. The CNV area was analyzed by fluorescein-labeled dextran angiography of retinal pigment epithelium (RPE)-choroid flat mounts on day 7 and 14, and CNV leakage was evaluated by fluorescein angiography (FA) on day 14 after laser photocoagulation. The infiltration of F4/80 positive macrophages and GR-1 positive granulocytes were evaluated by immunohistochemistry on RPE-choroid flat mounts on day 3. Their expression in RPE-choroid complex was quantified by real-time PCR (F4/80) and Western blotting (GR-1) on day 3. RPE-choroid levels of vascular endothelial growth factor (VEGF), tumor necrosis factor (TNF)-α, monocyte chemotactic protein (MCP)-1, and intercellular adhesion molecule (ICAM)-1 were examined by ELISA on day 3. Double immunostaining of F4/80 and VEGF was performed on cryo-sections of CNV lesions on day 3. The expression of nuclear factor (NF)-κB and hypoxia-inducible factor (HIF)−1α in the RPE-choroid was determined by Western blotting.

**Results:** Curcumin-treated mice had significantly less CNV area (P<0.05) and CNV leakage (P<0.001) than vehicle-treated mice. Curcumin treatment led to significant inhibition of F4/80 positive macrophages(P<0.05) and GR-1 positive granulocytes infiltration (P<0.05). VEGF mainly expressed in F4/80 positive macrophages in laser injury sites, which was suppressed by curcumin treatment (P<0.01). Curcumin inhibited the RPE-choroid levels of TNF-α (P<0.05), MCP-1 (P<0.05) and ICAM-1 (P<0.05), and suppressed the activation of NF-κB in nuclear extracts (P<0.05) and the activation of HIF−1α (P<0.05).

**Conclusions:** Curcumin treatment led to the suppression of CNV development together with inflammatory and angiogenic processes including NF-κB and HIF−1α activation, the up-regulation of inflammatory and angiogenic cytokines, and infiltrating macrophages and granulocytes. This provides molecular and cellular evidence of the validity of curcumin supplementation as a therapeutic strategy for the suppression of age-related macular degeneration (AMD)-associated CNV.
drug exposure in the CNV model compared to the normal animals. Therefore, extrapolation of ocular PK obtained in normal animals to CNV animals for the purpose of PKPD data analysis should be performed with caution.

**Conclusions:** These findings demonstrate that miR-24 represses ocular angiogenesis by simultaneously regulating multiple components in the actin cytoskeleton pathways. Manipulation of actin cytoskeleton pathways by miR-24 may represent an attractive therapeutic solution for treatment of wet AMD and other vascular diseases.

**Commercial Relationships:** Qinbo Zhou, None; Ashwath Jayagopal, None; Shusheng Wang, UT Southwestern Medical Center (P)

**Program Number:** 1245
**Presentation Time:** 9:15 AM - 9:30 AM

**Impact of Ranibizumab on Patient-Reported Visual Functioning in Myopic Choroidal Neovascularization:** 3- and 6-Month Results

**Purpose:** To examine the effects of 0.5 mg ranibizumab given for 6 months on visual functioning among patients with myopic choroidal neovascularization (CNV).

**Methods:** In a phase 3, multi-country study, patients were randomized to: at least two monthly ranibizumab injections with subsequent retreatment based on visual acuity criteria (stabilization group, n = 106); at least one ranibizumab injection with subsequent retreatment based on optical coherent tomography or fluorescein angiography features (disease activity group, n = 116); or verteporfin photodynamic therapy (vPDT, n = 55). From month 3, patients assigned to vPDT could receive ranibizumab. The National Eye Institute Visual Function Questionnaire-25 (NEI VFQ-25) was administered in the local language at baseline, 3 months and 6 months to measure patient-reported visual functioning. Initial results from an exploratory analysis (including descriptive p-values) are reported using last observation carried forward analysis.

**Results:** The mean baseline NEI VFQ-25 composite score was 69.3, 71.0 and 71.9 in the stabilization, disease activity and vPDT groups, respectively. At month 3, the mean increase from baseline in NEI VFQ-25 composite score was greater in the stabilization (5.3 points, p < 0.05) and disease activity (4.3 points, p < 0.05) groups than in the vPDT group (0.3 points). At month 6, the mean increase from baseline in the composite score was 6.3 and 5.1 points in each ranibizumab group, respectively. In the subscales of near activities and mental health, some greater improvements were observed with ranibizumab (both groups) than with vPDT. At month 3, the mean increase from baseline in near activities score was 11.5 points (p < 0.01) and 5.3 points (p = 0.138) in the stabilization and disease activity groups compared with 0.9 points in the vPDT group. Mental health scores increased by 7.4 points (p < 0.05) and 4.9 points (p < 0.05) and decreased by 1.8 points in these groups, respectively. At month 6, the increase from baseline was sustained at 10.0 and 6.5 points for near activities and 10.3 and 8.9 points for mental health in

**Commercial Relationships:** Jie Shen, Allergan (E); Chandrasekar Durairaj, Allergan (E); Ton Lin, Allergan Inc (E); Yan Liu, None; James A. Burke, Allergan, Inc (E)

**Program Number:** 1244
**Presentation Time:** 9:00 AM - 9:15 AM

**Functional study of microRNA-24 in ocular angiogenesis**

**Purpose:** Actin cytoskeleton is critical for cell motility and proliferation, both of which are important for angiogenesis. MicroRNAs (miRNAs or miRs) are important posttranscriptional regulators of gene expression, and are emerging as pivotal modulators of vascular development and disease. Currently, miRNAs are rapidly advanced as novel therapeutic targets for several diseases. How miRNAs regulate actin cytoskeleton dynamics in endothelial cells (ECs) and angiogenesis is still unclear. Our recent studies have shown that miR-23 and miR-27 in miR-23–27–24 family are required for proper angiogenesis and choroidal neovascularization (CNV). Here we test the hypothesis that miR-24 regulates ocular angiogenesis through modulating actin dynamics in ECs by targeting multiple components downstream of Rho signaling.

**Methods:** In vitro Matrigel assay, time-lapse living cell imaging, novel transgenic mouse model, laser injury AMD model, and in vivo miRNA mimic delivery methods were used to dissect the function of miR-24 in angiogenesis, ocular vascular development and laser-induced CNV.

**Results:** In vitro and in vivo results provide comprehensive evidence that miR-24 plays an important role in ocular angiogenesis by regulating multiple critical components in actin cytoskeleton dynamics. Overexpression of miR-24 in ECs blocked stress fiber and lamellipodia formation, represses ECs migration, proliferation and tube formation in vitro. Overexpression of miR-24 inhibited EC cell tube formation in Matrigel and angiogenic vessel sprouting in an ex vivo aortic ring assay. We also generated miR-24 transgenic mice and found that the development of superficial vascular plexus is delayed upon miR-24 overexpression in mice. Moreover, the adult miR-24 transgenic mice also lack the deep layers of vascular plexus. Consistently, therapeutic subretinal delivery of miR-24 mimics potently repressed laser-induced CNV in vivo. Mechanistically, miR-24 represses angiogenesis by regulating PAK-LIMK-Cofilin pathway. Knockdown of miR-24 target gene LIMK2 or PAK4 inhibited stress fiber formation and tube formation in vitro, mimicking miR-24 overexpression phenotype.

**Commercial Relationships:** Jie Shen, Allergan (E); Chandrasekar Durairaj, Allergan (E); Ton Lin, Allergan Inc (E); Yan Liu, None; James A. Burke, Allergan, Inc (E)

**Program Number:** 1244
**Presentation Time:** 9:00 AM - 9:15 AM

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the stabilization and disease activity groups, respectively.

**Conclusions:** The improvement in patient-reported visual functioning in patients with myopic CNV was greater for some NEI VFQ-25 subscales at 3 months with ranibizumab than with vPDT. These improvements were sustained at 6 months.

**Commercial Relationships:** Kyoko Ohno-Matsui, None; Nikolle Tan, Novartis (C), Novartis (R), Novartis (S), Bayer (C), Bayer (R), Bayer (S), Allergan (R), Allergan (S); Tien Y. Wong, Allergan (C), Bayer (C), Novartis (C), Pfizer (C), GSK (F), Roche (F); Tatsuro Ishibashi, None; Jennifer Petriello, Novartis Pharmaceuticals (E); Neil M. Bressler, Abbott Medical Optics, Inc (F), Allimera Sciences (F), Allergan (F), Bausch & Lomb, Inc (F), Bayer (F), Carl Zeiss Meditec, Inc (F), ForSight Labs, LLC (F), Genentech, Inc (F), Genzyme Corporation (F), Lumenis, Inc (F), Notal Vlson (F), Novartis Pharma AG (F), Pfizer, Inc (F), Regeneron Pharmaceuticals, Inc (F), Roche (F), Thrombogencis (F); Claudia Leteneux, Novartis Pharma AG (E)

**Clinical Trial:** NCT01217944

**Program Number:** 1246
**Presentation Time:** 9:30 AM - 9:45 AM

**Activated Histoplasmosis Scars**

James C. Folk, Matthew A. Cunningham, Michael D. Abramoff, Elliott H. Sohn. Ophthalmology & Visual Sciences, Univ of Iowa, Iowa City, IA.

**Purpose:** We present an OCT finding in patients with the presumed ocular histoplasmosis syndrome, POHS, which probably represents either inflammation or very early choroidal neovascularization, CNV. Granular hyper-reflective material overlies a previous histo scar or inactive membrane. When active, the material obliterates or obscures the outer nuclear layer, external limiting membrane, photoreceptor layers and RPE and, in severe cases, pushes the outer plexiform layer forward. The material may also extend into the choroid. After resolution, the material may: 1. Disappear completely with reconstitution of all of the layers on OCT. 2. Form an atrophic scar with displacement posteriorly of the middle retinal layers, or 3. form a small lump covered anteriorly by the photoreceptor inner segment line and loss of only the outer photoreceptor and RPE layers.

**Methods:** In order to determine the frequency of this sign, we reviewed the spectral domain OCTs of our previous 50 patients with POHS

**Results:** 78 eyes of 50 patients had an atrophic scar, active CNV or inactive CNV (without fluid) in the macula. Fibrotic scars or CNV with fluid were seen in 21 eyes; inactive atrophic scars with variable loss of the RPE were seen in 39 eyes; and the hyper-reflective material was seen in 18 eyes of 15 patients. No intraretinal or subretinal fluid was seen in these 18 eyes. All but 3 patients had symptoms of blurring or metamorphopsia that correlated with the location of the finding. Fifteen of the 18 eyes were treated with anti-VEGF agents. The material resolved in 14 and in the 15th resolved after additional intravitreal Kenalog. Of the three eyes that were not treated immediately, two went on to a CNV with fluid and one improved with observation.

**Conclusions:** POHS patients with early symptoms often show hyper-reflective granular material around a previous scar. These changes appear to presage the development of choroidal neovascularization. Arguments as to whether this material represents new blood vessels that are not yet causing fluid accumulation or inflammation prior to new vessel formation will be presented.

**Commercial Relationships:** James C. Folk, None; Matthew A. Cunningham, None; Michael D. Abramoff, IDx LLC (E), IDx LLC (I), University of Iowa (P); Elliott H. Sohn, None

**Program Number:** 1247
**Presentation Time:** 9:45 AM - 10:00 AM

**Twelve-month efficacy and safety of ranibizumab 0.5 mg(RBZ) versus verteporfin photodynamic therapy(vPDT) in the treatment of visual impairment(VI) due to choroidal neovascularization(CNV) secondary to pathologic myopia(PM)**

Francesco Bandello, Ophthalmology, Univ Vita Salute-Saint Inst San Raffaele, Milan, Italy.

**Purpose:** PM is the leading cause of CNV causing visual impairment in individuals ≤50 years. This is the first randomized controlled study reporting the 12 month(M) efficacy and safety of two different dosing regimens of RBZ vs vPDT in the treatment of VI due to CNV secondary to PM.

**Methods:** A 12M, phase III, multicenter, double-masked, active controlled study. Patients(n=277) were randomized 2:2:1 to Group(G)1(n=106) with RBZ treatment on Day1, M1, individualized treatment as needed(pro re nata(PRN) as of M2 based on visual acuity(VA) stability, G2(n=116) with RBZ treatment on Day1, PRN as of M1 based on disease activity, and G3(n=55) with vPDT on Day1 and thereafter at investigator discretion(minimum quarterly interval) with RBZ as of M3. Primary endpoint: RBZ superiority to vPDT based on mean average best-corrected visual acuity(BCUVA) change from baseline(BSL) to M1-3. Secondary endpoints: inferiority of G2 vs G1 based on mean average BCVA change from BSL to M1-6(key), mean change in BCVA from BSL to M12, patients gaining ≥10 letters, and safety over 12M.

**Results:** 267(96.4%) patients completed 12M. BSL characteristics: mean age(years) 54(G1), 56.1(G2), 57.4(G3); females(75.5%); and mean VA 55.4(G1), 55.8(G2), and 54.7(G3). Both RBZ groups were superior to vPDT in improving mean average BCVA change from BSL to M1-3(+10.5[G1], +10.6[G2] vs +2.2 letters[G3]; both p<0.00001), primary endpoint met. G2 was non-inferior to G1 based on mean average BCVA change from BSL to M1-6(+11.7[G2] vs +11.9[G1] letters; p<0.00001). Mean BCVA change at M12: +13.8(G1), +14.4(G2), +9.3(G3, after M3 with RBZ) letters. At M12: 69.5%(G1), 69.0%(G2), and 49.1%(G3, after M3 with RBZ) of patients gained ≥10 letters. Mean RBZ injections(Day1-M11): 4.6(G1), and 3.5(G2). No reports of endophthalmitis, deaths; no new ocular/nonocular safety findings with RBZ over 12M.

**Conclusions:** RBZ treatment based on VA stability or disease activity criteria demonstrated superior BCVA gain vs vPDT at M3. Mean RBZ injections over 12M: 4.6(G1) and 3.5(G2). No new safety findings were identified in patients with VI due to CNV secondary to PM.

**Mean BCVA change:** Day1-M12
### ARVO 2013 Annual Meeting Abstracts by Scientific Section/Group – Retina

<table>
<thead>
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<th>Safety set*, Preferred term, n (%)</th>
<th>Group 1 (n = 106)</th>
<th>Group 2 (n = 116)</th>
<th>Group 3 (n = 53)</th>
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</table>

### Results:

**Local neutralization of Il17a via intravitreal injection of AAV2.sIl17R significantly ameliorated retinal degeneration in DKO/rd8 mice.** Protection was likely conferred from a decrease in MAPK activity. Based on similarities in disease pathogenesis between these mice and AMD, we believe this pathway should be considered in the treatment of AMD.

**Conclusions:** Local neutralization of Il17a via intravitreal injection of AAV2.sIl17R significantly ameliorated retinal degeneration in DKO/rd8 mice. Protection was likely conferred from a decrease in MAPK activity. Based on similarities in disease pathogenesis between these mice and AMD, we believe this pathway should be considered in the treatment of AMD.

### Clinical Trial: NCT01217944

### 242 AMD: Translational Research

**Program #:Board # Range**: 1713-1718

**Organizing Section:** Retina

**Program Number:** 1713

**Presentation Time:** 11:00 AM - 11:15 AM

**Interleukin-17 neutralization ameliorates retinal degeneration in Cx3cr1-/-/Ccl2-/-/Crb1rd8 mice**

By funduscopv, 26/40 (65%) of sIL17R-treated eyes showed improvement, 12/40 (30%) were similar to EV-treated eyes, and 2/40 (5%) were worse. By histology, 12/15 (80%) of sIL17R-treated eyes showed improvement whereas just 3/15 (20%) worsened. A2E was significantly lower in sIL17R-treated eyes compared to EV eyes, which was confirmed by TEM. Treated eyes had healthier inner and outer photoreceptor segments as well as healthier RPE cells. The sIL17R treatment reduced expression of Il17rc in the retina relative to EV controls. Treatment also resulted in inhibition of signal transduction via the MAPKs p38 and Erk1/2 but had no effect on Akt activity.

**Conclusions:** Local neutralization of Il17a via intravitreal injection of AAV2.sIL17R significantly ameliorated retinal degeneration in DKO/rd8 mice. Protection was likely conferred from a decrease in MAPK activity. Based on similarities in disease pathogenesis between these mice and AMD, we believe this pathway should be considered in the treatment of AMD.

### Commercial Relationships:

- **Daniel Ardeljan**: None; **Yujuan Wang**: None; **Mones S. Abu-Asab**: None; **Jingsheng Tuo**: None; **Chengrong Yu**: None; **Gary White**: Genzyme Corporation (E); **Sami Wadsworth**: Genzyme (E); **Abraham Scaria**: Genzyme Corporation (F), Genzyme Corporation (P); **Chi-Chao Chan**: None

**Presenting Authors:**


**Program Number:** 1714

**Presentation Time:** 11:15 AM - 11:30 AM

**Oral administration of Apolipoprotein A-I mimetic peptide D-4F reduces lipid accumulation in murine Bruch’s membrane (BrM)**

**Martin Rudolf**, **Armin Mohi**, **Zouhair Aherrahrou**, **Salvatore Grisanti**, **Yoko Miura**

**Department of Ophthalmology**, **University of Luebeck**, **Luebeck**, **Germany**; **Institute for Integrative and Experimental Genomics**, **University of Luebeck**, **Luebeck**, **Germany**; **Institute of Biomedical Optics**, **University of Luebeck**, **Luebeck**, **Germany**

**Purpose:** Neutral lipid accumulation in BrM is a major age change in the eye and an important factor for the development of age-related macular degeneration (AMD). ApolipoproteinA-I mimetic peptides like D-4F, primarily developed to remove lipids from atherosclerotic lesions, demonstrated already a significant reduction of BrM lipids after intravitreal injection (Rudolf et al., IOVS 2010, 51: Abstract 2984). Here we report the effect of oral administered D-4F on murine BrM lipid deposits and atherosclerotic aorta lesions in an established atherosclerosis mouse model.

**Methods:** Forty 11 months old ApoEnull mice received D-4F orally with their daily drinking water (50 µg/ml). The animals were sacrificed at 4 different time points after treatment start (4, 8, 12, and 16 weeks) and serum level of HDLC, LDLC and triglyceride were determined. As controls ten animals received only regular water and were sacrificed at treatment start (baseline). All eyes were enucleated, processed to BrM whole mounts, stained with the fluorescent dye PFO/D4-GFP for esterified cholesterol, and evaluated for the BrM lipid content semiquantitatively. Atherosclerotic lesion size at the aortic valves was stained using Oil Red O and quantified.

**Results:** Mice treated daily with orally available D-4F demonstrated significant lipid deposit reduction in BrM first after 12 weeks (-

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Effect of Aspirin on CNV size and size of laser spot in mouse model of CNV

Commercial Relationships: Sunali Goyal, None; Valeriy V. Lyzogubov, None; Puran S. Bora, None; Nalini S. Bora, None; Sami H. Uwaydat, None

Support: This work was supported by Lions of Arkansas Foundation, Inc and Pat & Willard Walker Eye Research Center, Jones Eye Institute, Little Rock, AR.

Program Number: 1716
Presentation Time: 11:45 AM - 12:00 PM
Eyedrop application of CLT-005, a Stat3 inhibitor, is efficacious in animal models of Wet and Dry Age-related Macular Degeneration


1-Charleston, Oklahoma City, OK; 2-SKS Ocular, Great Neck, NY.

Purpose: Activation of Stat3 in the posterior segment is associated with neovascular and inflammatory processes. We assessed the safety, opthalmic distribution, and efficacy of CLT-005, a selective small molecule inhibitor of Stat3, after topical eyedrop administration to rabbit and rodent animal models.

Methods: A custom emulsion consisting of 1% CLT-005 was prepared and dosed daily at QID (9am, 12pm, 3pm, 6pm) for all experiments throughout the study duration. Dutch Belted rabbits were scored daily for tolerability/irritation, and the RPE/choroid was isolated for LC-MS/MS quantification of CLT-005 at Day 5. Brown Norway rats were induced by thermal laser to produce choroidal neovascular lesions on Day 1, and in-vivo fluorescence angiography was used to quantify lesion area on Day 22. The CEP Dry-AMD model (under license from SKS Ocular) was induced by immunization of C57Bl/6 mice with Carboxyethylpyrrole-Mouse Serum Albumin (CEP-MSA). At day 60, contrast sensitivity was evaluated with optokinetic tracking at a spatial frequency of 0.064 cycles/degree.

Results: Topical application of CLT-005 achieved mean drug levels in the RPE/Choroid of >2000 ng/g and did not result in any measurable hypermia, chemosis, or discharge. In the laser-CN model, treatment with topical CLT-005 or oral CLT-005 at 500 mg/kg in a soybean oil vehicle significantly reduced lesion size and late-stage leakage from lesions. In the CEP Dry-AMD model at Day 60, mean contrast sensitivity was significantly reduced to 0.0512 in CEP-MSA immunized mice as compared to 0.0841 in normal naïve controls. Daily eyedrop application of 1% CLT-005 prevented the loss of contrast sensitivity in CEP-MSA immunized mice and the mean was 0.0842, as compared to 0.054 in the vehicle control group. CLT-005 also significantly reduced inflammation in the posterior segment of CEP-MSA animals.

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Conclusions: Eyedrop application of 1% CLT-005 delivers therapeutic amounts of drug to the RPE/choroid which can reduce neovascularization in the laser CNV model of wet AMD. Inhibition of Stat3 by CLT-005 also prevented the dramatic loss of contrast sensitivity in the CEP Dry-AMD model. These data support future clinical studies of topical CLT-005 as a standalone therapy or in conjunction with other intravitreal-based therapies to treat various forms of Age-related Macular Degeneration and Geographic Atrophy.

Commercial Relationships: Rafał Farjo, Charlesson LLC (E), EyeCRO LLC (E); Didier J. Nuno, Charlesson LLC (E), EyeCRO LLC (E); Alexander B. Quiambao, Charlesson LLC (E), EyeCRO, LLC (E); Phillip A. Vanlandingham, Charlesson LLC (E), EyeCRO (E); Fadee Mondalek, Charlesson LLC (E), EyeCRO (E); Eric Phelp, Charlesson LLC (E), EyeCRO (E); Glenn Stoller, Lpath (C), Regeneron (F), Lpath (P), SKS (I); Drew Wassel, Charlesson LLC (E), EyeCRO (E)

Support: EY018989

Program Number: 1718
Presentation Time: 12:15 PM - 12:30 PM
Intraocular Delivery of Ciliary Neurotrophic Factor (CNTF) by Encapsulated Cell Technology Implants Restores Cone Function and Day Vision in Dogs with CNGB3-Achromatopsia
Andras M. Komaromy1, 2, Kristin L. Koehl1, Christine Harman1, Pam Heatherton1, Konrad Kauper1, Gustavo D. Aguirre2, Weng Tao1, 2

Purpose: We have previously demonstrated in dogs with CNGB3-auchromatopsia that intravitreal bolus injection of CNTF (1) resulted in transient restoration of cone function and day vision, and (2) optimized long-term cone functional response to AAV-mediated gene augmentation therapy. The objective of this study was to determine if sustained intravitreal delivery of CNTF by encapsulated cell technology (ECT) could reverse the disease phenotype of CNGB3-auchromatopsia in dogs long-term.

Methods: Dogs homozygous for the D262N missense mutation in CNGB3 were unilaterally implanted with CNTF-secreting, encapsulated cell implants. The pre-implant CNTF secretion rate was 15 ng/day. The animals were 3 months (n=2) and 27 months (n=1) of age and were day blind with no recordable cone ERG prior to surgery. Following implant placement, the dogs were examined weekly by standard full-field electroretinography under general anesthesia and visual behavioral testing in an obstacle avoidance course.

Results: In the operated eyes, day vision and cone function were partially restored by 1 week following CNTF-implant placement. The amplitudes of single and flicker cone ERG responses were small (~5-10% of normal) but were maintained for at least 5 weeks thus far. Scotopic ERG responses were reduced in 2 of the 3 implanted eyes to on full-length C3 was assayed by immunoprecipitation and Western blotting. Binding to tissue-bound C3 activation products was examined in CNV lesions in vitro (flatmounts of RPE/choroid) and in vivo (after tail vein injection of FITC-labeled mAb).

Results: (1) Three mAbs preferentially bound to the iC3b, C3dg, and C3d fragments, without binding to or interacting with C3 or C3b. (2) One of the mAbs (C3d29) identified tissue-bound C3 activation products in CNV lesions by immunohistochemistry in wildtype (WT) mice. (3) Staining was abolished or attenuated in CNV of fB-deficient mice or WT mice treated with an inhibitor of the complement alternative pathway. (4) FITC-C3d29, bound to CNV lesions could be imaged in vivo 24 hours after the injection by Micron III retinoscopy, when compared to a nonspecific FITC-labeled mAb.

Commercial Relationships: Taasam Al-Awadi, KEA Life Sciences (E), KEA Life Sciences, Inc. (F), KEA Life Sciences (P); Balbina G. Al-Maily, KEA Life Sciences (E), KEA Life Sciences, Inc. (F), KEA Life Sciences (P)

Support: NIH grant EY019320, a Department for Veterans Affairs merit award RX000444, Foundation Fighting Blindness, the Beckman Initiative for Macular Research, and Research to Prevent Blindness.

In vivo imaging of complement activation in mouse choroidal neovascularization using a novel monoclonal antibody against the C3 activation fragment C3d
Baerbel Rohrer1, 2, 3, Alex S. Woodell1, 2, 3, Liudmila Kulik1, Beth Coughlin1, Gloriana Schnabolk1, Joshua M. Thurman1, 3, Michael Holers1, 3
1Pharmacology and Experimental Therapeutics, University of Colorado (P); 2University of Colorado (P); 3Alexion Therapeutics (C), Alexion Pharmaceuticals, Inc. (P); 3Alexion Pharmaceuticals, Inc. (P)

Purpose: Uncontrolled activation of the alternative complement pathway is thought to be associated with age-related macular degeneration. During activation of the complement cascade complement C3 protein is hydrolyzed resulting in the generation and fixation of C3 activation fragments on affected tissues. Previously, we have shown that in mouse laser-induced choroidal neovascularization (CNV), C3 fragments are present in the CNV lesions and can be used as addressable ligands for targeted therapeutics to reduce CNV. Here we examined the potential use of novel anti-C3d antibodies to detect complement activation in vivo in mouse CNV.

Methods: C3-deficient mice were immunized with human C3d protein. Monoclonal antibodies (mAb) were screened by ELISA, and their ability to bind to epitopes on C3d that are not present or exposed

Conclusions: Antibodies specific to tissue-bound C3 activation fragments can be used to visualize sites of complement activation. This technique may be employed in the future for diagnostic purposes and to monitor effects of therapeutic agents.

Commercial Relationships: Baerbel Rohrer, WO/2007/1149567 (P), Colorado University, CU3015H (P), 61/317,185 (P); Alex S. Woodell, None; Liudmila Kulik, University of Colorado (P); Beth Coughlin, None; Gloriana Schnabolk, None; Joshua M. Thurman, Alexion Pharmaceuticals, Inc. (C), Alexion Pharmaceuticals, Inc. (P); Michael Holers, Alexion Therapeutics (F), Alexion Therapeutics (C), Alexion Therapeutics (P)

Support: NIH grant EY019320, a Department for Veterans Affairs merit award RX000444, Foundation Fighting Blindness, the Beckman Initiative for Macular Research, and Research to Prevent Blindness.

Day 60

Contrast Sensitivity

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<30% of amplitudes recorded in the non-operated fellow eyes. These ERG data were comparable to our observations following single intravitreal bolus injection of 12 μg CNTF.

**Conclusions:** Sustained intravitreal delivery of CNTF by ECT rescues cone function and day vision in CNGB3-achromatopsia. It remains to be shown if this therapeutic effect can be sustained long-term and if ECT can be combined with AAV-mediated cone-directed gene augmentation to optimize treatment.

**Commercial Relationships:** Andras M. Komaromy, None; Kristin L. Koehl, None; Christine Harman, None; Pam Heatherton, None; Konrad Kauper, Neurotech Pharmaceuticals (E); Gustavo D. Aguirre, None; Weng Tao, Neurotech (E)

**Support:** NIH Grants EY019304, EY017549, EY006855, P30EY001583, FFB

243 DR: Factors and Function

Monday, May 06, 2013 11:00 AM-12:45 PM
6E Paper Session
Program #/Board # Range: 1719-1725
Organizing Section: Retina

**Program Number:** 1719
**Presentation Time:** 11:00 AM - 11:15 AM

**Patterns of Progression in Diabetic Retinopathy. Correlation between phenotypes and genotypes**

Sandrina Nunes1, 2, Conceicao F. Lobo1, 2, Luisa Ribeiro1, 2, Isabel Pires1, 2, Rui Bernardes1, 2, Telmo Miranda1, 2, Maria J. Simões1, 2, Carlos Faro3, Jose G. Cunha-Vaz3, 2, AIBILI, Coimbra, Portugal; 1SMUC, University of Coimbra, Coimbra, Portugal; 2BIOCANT, Coimbra, Portugal.

**Purpose:** To establish a correlation between phenotypes of non-proliferative diabetic retinopathy (NPDR) progression (phenotypes A, B and C) and different candidate genes in type 2 diabetic patients.

**Methods:** A population of 307 diabetic patients with NPDR, followed-up during a 2 years prospective study was classified in 3 different phenotypes of DR progression based on non-invasive methods, Color Fundus Photography (CFP) to assess microaneurysm turnover (MAT) and Optical Coherence Tomography (OCT) to measure Retinal Thickness (RT). Phenotype A was considered for MAT<9 & Normal RT; Phenotype B for MAT=9 & Increased RT; and Phenotype C for MAFR>9 & Normal or Increased RT. Twenty one (21) patients/eyes developed during the 2-year study clinically significant macular edema (CSME), 14 from Phenotype C, 5 from Phenotype B and 2 from Phenotype A. Eleven genes were selected from a list of candidate genes (ACE, AGER, AKR1B1, ICAM1, MTHFR, NOS1, NOS3, PPARGCA1, TGFBI, TNF-a, and VEGFA) and their distribution were analyzed for the 3 different phenotypes.

**Results:** The distribution for the 3 phenotypes was respectively 54.1%, 23.4% and 22.5%. Statistically significant differences between phenotypes were found for ACE (rs34241302, rs4317 and rs4318, P<0.05) and NOS1 (rs1552228, P=0.012). When considering patients that developed CSME, statistically significant differences were found for ACE (rs1720737, rs35865660, rs4317 and rs4318, P=0.016), for NOS1 (rs41340250 and rs9658481, P=0.001), and MTHFR (rs7533315, P=0.029).

**Conclusions:** ACE, NOS1 and MTHFR were found to be associated with different phenotypes of DR progression and development of CSME. The identification of these phenotypes-genotypes correlations opens new perspectives for the management and the treatment of DR in type-2 diabetic patients.

249 DR: Factors and Function

Monday, May 06, 2013 11:30 AM-11:45 AM

**Commercial Relationships:** Sandrina Nunes, None; Conceicao F. Lobo, None; Luisa Ribeiro, None; Isabel Pires, None; Rui Bernardes, None; Telmo Miranda, None; Maria J. Simões, None; Carlos Faro, None; Jose G. Cunha-Vaz, Allergan (C), Pfizer (C), Novartis (C), Alimera Sciences (C), Roche (C), Fovea Pharmaceuticals (C), Gene Signal (C)

**Support:** PTDC/SAU-OSM/103226/2008 COMPETE (FCOMP-01-0124-FEDER-011347)

**Clinical Trial:** NCT01228981

**Program Number:** 1720
**Presentation Time:** 11:15 AM - 11:30 AM

**Neuroretinal Function and Retinal Vessel Changes over One Year Are Altered by Long-Term Blood Glucose Change in Adolescent Type 1 Diabetes**

Marcus A. Bearse, Michal Laron, Ann Chang, Kevin Bronson-Castain, Brian E. Wolff, Glen Y. Ozawa, Shirin Barez, Marilyn E. Schneck, Anthony J. Adams. School of Optometry, University of California, Berkeley, CA.

**Purpose:** To examine how change in long-term blood glucose concentration and aging affect neuroretinal function and retinal vascular caliber over one year in adolescents with type 1 diabetes and adolescents without diabetes.

**Methods:** We examined the right eyes of 82 adolescents with type 1 diabetes and no retinopathy (patient group), and 34 healthy adolescents without diabetes (control group). All subjects were examined twice, with the exams separated by 1.1 +/- 0.2 years in each group. All subjects were 13 - 21 years old at exam 1, the patient group was 15.4 +/- 1.7 years old, and the control group was 18.1 +/- 2.7 years old. Digital fundus photographs taken at both exams were graded by a retina expert to verify the absence of retinopathy. At each exam, we measured HbA1c to determine long-term blood glucose levels, and recorded dilated photopic multifocal electroretinogram (mERG) from the central 45 degrees. Average mERG implicit time (IT) of each recording was calculated. Arteriole caliber (AC) and venule caliber (VC) were measured from digital optic disc photographs using IVAN software. Change was calculated as (change = exam 2 - exam 1). Linear regression analysis was used to assess associations between factors.

**Results:** IT change was positively correlated with HbA1c change in the patient group (P=0.030) but not in the control group (P=0.403). (Exam 1 HbA1c was 9.1 +/- 1.6% in the patient group.) We examined whether change in age might be a contributing factor. IT change and age change were not correlated in the patient group (P=0.942), but they were positively correlated in the control group (P<0.004). Next, we examined retinal vessel calibers. IT change was marginally, negatively correlated with AC change (P=0.044) in the control group but not in the patient group (P=0.299). IT change and VC change were not correlated in either group (both P>0.229).

**Conclusions:** Change in neuroretinal function is correlated with change in long-term blood glucose concentration over one year in adolescents with type 1 diabetes and no retinopathy. This relationship appears to override the associations between neuroretinal function change and changes in age and arteriole caliber that we observed in healthy adolescents without diabetes.

**Commercial Relationships:** Marcus A. Bearse, None; Michal Laron, None; Ann Chang, None; Kevin Bronson-Castain, None; Brian E. Wolff, None; Glen Y. Ozawa, None; Shirin Barez, None; Marilyn E. Schneck, None; Anthony J. Adams, None

**Support:** JDRF Grant 8-2008-823 to MAB

**Program Number:** 1721
**Presentation Time:** 11:30 AM - 11:45 AM

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Correlation of Number of Microaneuysms with Retinal Thickness
Beng Beng Ong, Jason Arora, Amy Hammond-Kenny, Jennifer Doyle, Shahrnaz Izadi, Christine A. Kiire, Victor Chong
Oxford Eye Hospital, Oxford, United Kingdom; *Oxford University, Oxford, United Kingdom.

Purpose: Recent evidence suggests that neuronal loss plays a key role in the development of diabetic retinopathy. As microaneuysms are the initial hallmark of diabetic retinopathy, we sought to correlate the number of microaneuysms with retinal thickness in patients with early diabetic retinopathy.

Methods: 80 patients with microaneuysms within 1 disc diameter of the fovea in at least one eye were recruited. Fundus photography and Heidelberg Spectralis Spectral Domain Optical Coherence Topography (SD-OCT) were carried out in each patient. The number of microaneuysms within 3 mm of the fovea were manually counted by 2 independent observers. If there was a significant discrepancy then a third observer would do a re-count. The average of the 2 observers, or the re-count were used for the analysis. The retinal area analyzed was divided into 4 sections: superior, temporal, inferior and nasal. These were analyzed separately in each eye by non-linear regression analysis using a negative binomial method.

Results: The total number of microaneuysms in the 4 quadrants was 474, 792, 418, and 262 in the superior, temporal, inferior, and nasal quadrants respectively. The average sectorial thickness on SD-OCT was 318, 314, 310 and 332 in the superior, temporal, inferior, and nasal quadrants respectively. In all analyzed sectors of each eye, the number of microaneuysms was found to be statistically significantly higher with thinner retina. The best fit model for the number of microaneuysms in the right eye was: -10.26 + 0.03 x thickness (p<0.0001), -.832 + 0.03 x thickness (p<0.0001), -.433 + 0.015 x thickness (p<0.003) & -.474 + 0.013 x thickness (p<0.003) in the superior, temporal, inferior, and nasal quadrants respectively. The best fit model for the number of microaneuysms in the left eye was: -6.87 + 0.023 x thickness (p<0.006), -.841 + 0.031 x thickness (p<0.001), -13.6 + 0.044 x thickness (p<0.0001) & -.988 + 0.03 x thickness (p<0.0001) in the superior, temporal, inferior, and nasal quadrants respectively.

Conclusions: We have found a significant correlation between higher numbers of microaneuysms and lower retinal thickness, even after accounting for regional differences in microaneuysm distribution. This is consistent with our hypothesis that neuronal loss might play a role in the pathogenesis of microaneuysms. Our results also support the previously reported finding that the temporal retina has the highest number of microaneuysms.

Commercial Relationships: Beng Beng Ong, None; Jason Arora, None; Amy Hammond-Kenny, None; Jennifer Doyle, None; Shahrnaz Izadi, None; Christine A. Kiire, None; Victor Chong, Novartis (C), Bayer (C), Allergan (C), Pfizer (F), Novartis (F), Alimera Science (C), QuanTel (R)

Program Number: 1722
Presentation Time: 11:45 AM - 12:00 PM

AGE products disrupt RPE barrier function in vitro and in vivo
Mohammad Dahrourj, Yueying Liu, Craig E. Crosson, Zsolt Ablonczy
Ophthalmology, Medical Univ of South Carolina, Charleston, SC.

Purpose: Advanced glycation end-products (AGEs), form during aging, are increased in diabetic patients, and have been correlated with the progression of diabetic retinopathy. However their effect on RPE function is not fully understood. To investigate how AGE products influence RPE function, the effect of glycated-albumin (Glyc-alb) on human RPE monolayers barrier function and subretinal fluid reabsorption in vivo were evaluated.

Methods: Transepithelial electrical resistance (TEER) measurements were used to assess the permeability of confluent ARPE-19 and human fetal RPE monolayers. Cells were treated apically with 100 µg/mL albumin or Glyc-alb in the absence or presence of ZM323881 (10 nM), a VEGF-R2 inhibitor. Monolayer TEER was monitored for up to 6 hours post drug-administration. ELISA assays were used to measure VEGF secretion. The rate of reabsorption of subretinal blebs in rabbits was used to evaluate the RPE function in vivo. Albumin or Glyc-alb (1 mg/mL) was injected into the vitreous and subretinal blebs (1-5µL PBS) were created 48 hours later. Rate of bleb reabsorption was measured using high resolution OCT. In selected experiments, ZM323881 (1 µM) was co-injected with Glyc-alb.

Results: Although albumin did not significantly alter TEER, Glyc-alb induced a 20% reduction in TEER. Pretreatment with ZM323881 reversed the effect of Glyc-alb on TEER. Additionally, Glyc-alb caused a significant increase in the rate of VEGF secretion into the apical media from 27.5 to 39.7 pg.mL-1.hr-1. In rabbits, the baseline rate for fluid reabsorption was 8.2 ± 0.6 µL.cm-2.hr-1. The intravitreal injection of albumin did not significantly alter fluid reabsorption; however intravitreal injection of Glyc-alb significantly decreased this rate of reabsorption to 2.2 ± 0.4 µL.cm-2.hr-1. Administration of ZM323881 reversed the effect of Glyc-alb on subretinal fluid reabsorption (5.15 ± 0.6 µL.cm-2.hr-1).

Conclusions: Our data show that Glyc-alb was effective in disrupting RPE function in vitro and in vivo and this response can contribute to the development of retinal edema. The ability of ZM323881 to reverse this response provides evidence that these AGE-induced effects are dependent on VEGF secretion and VEGF-R2 activation. These data provide new information on the cellular mechanisms involved in the development of diabetic macular edema, as well as identifying new therapeutic targets.

Commercial Relationships: Mohammad Dahrourj, None; Yueying Liu, None; Craig E. Crosson, Alimera Sciences (C), Lexicon Pharmaceuticals, Inc (R); Zsolt Ablonczy, None
Support: NIH EY021368; EY019065 and Research to Prevent Blindness, NY

Program Number: 1723
Presentation Time: 12:00 PM - 12:15 PM

Biomarkers of Retina Macrogliosis Activation in the Aqueous of Human Diabetics
Eduardo Midenra, Marianna Berton, Silvia Bini, Alessandra Micera, Graziana Esposito, Stela Vujosevic
Ophthalmology, University of Padova, Padova, Italy; GB Bietti Foundation, IRCCS, Roma, Italy.

Purpose: To identify early biomarkers of retina macrogliosis activation in diabetic patients without and with nonproliferative diabetic retinopathy.

Methods: 22 diabetic subjects with mild or moderate non-proliferative diabetic retinopathy (NPDR) were enrolled and 12 healthy subjects served as controls. All eyes had cataract of the same grade acording to LOCS classification. Twelve diabetic patients had no signs of diabetic macular edema (DR-noDME), and 10 had DME (DR-DME). Aqueous humor was sampled in all eyes using a 30 gauge needle through a peripheral clear cornea approach, before cataract extraction. Each subject underwent full ophthalmic examination and Spectral Domain Optical Coherence Tomography (SD-OCT) before aqueous humor sampling. Each sample was analyzed to quantify: glial fibrillary acidic protein (GFAP), aquaporine 1 (AQP1) and AQP4 as biomarkers of retinal macrogliosis activity, by ELISA. ANOVA analysis followed by Tukey-Kramer post-hoc test was applied.

Results: There was not significant difference in the age among the...
Peripheral Diabetic Retinal Lesions Identified on Ultrawide Field (UWF) Imaging May Predict 3-Year Diabetic Retinopathy Progression

**Method:*** Macular MAs were assessed on 1x1.2° AOSLO images (2.5µm resolution limit) for dimension, wall reflectivity, lumen clot, and perfusion pattern. Images were montaged with wider field fundus photos to register MA location. Eyes underwent SDOCT (Spectralis: 2.5µm resolution limited to ETDRS fields (far peripheral lesions) were noted. DR severity on subsequent dilated exams performed by retina specialists, and mean A1c values over the preceding 1 and 2 years were recorded.

**Results:** A1c at 1 and 2 years prior to imaging was available in 75% (152) and 77% (158) of subjects. Median number of prior A1c results in diabetic eyes versus controls. When DR-noDME eyes and DR-DME eyes were separatedly evaluated, there was a significant decrease in GFAP, AQP1 and AQP4 about 24 folds increase in diabetic patients versus controls. When DR-noDME eyes and DR-DME eyes were separately evaluated, there was a significant decrease in GFAP, AQP1 e AQP4 in DR-DME eyes versus DR-noDME eyes, (Tukey Kramer post hoc p<0.05). GFAP and AQP1 showed even a slight, non significant, fold decrease versus controls. AQP4/AQP1 concentration showed weak and non significant correlation (Tu=0.21, p=0.3) between these biomarkers, despite increasing trend.

**Conclusions:** GFAP, AQP1 and AQP4 are known as biomarkers of retinal macroglia activity. All these biomarkers are significantly increased in human eyes with diabetes, confirming that retinal glia is a key actor in this disorder. The decrease of these biomarkers In eyes with DME probably represents a sign of Müller cells degeneration.

**Commercial Relationships:** Jennifer K. Sun, Boston Micromachines (F), Abbott Laboratories (C), Novartis (C), Genentech (F); Jan Lammer, None; Sonja G. Prager, None; Michael M. Lin, None; Michael C. Cheney, None; Paolo S. Silva, Optos plc (F); Stephen A. Burns, None; Lloyd P. Aiello, Genentech (C), Genzyme (C), Thrombo genesis (C), Ophthotech (C), Calvista (C), Pfizer (C), Proteostasis (C), Abbott (C), Vantia (C), Optos, plc (F)

**Support:** Eleanor Chesterman Beaton Childcare Ambassador Program Foundation Grant, JDRF 17-2011-359, NIDDK 5 P30 DK036836-24 P&F Grant, Massachusetts Lions Eye Research Fund
Conclusions: In this cohort of patients followed at a single center over 3 years, baseline DR severity and A1C were the greatest predictors of progression, emphasizing the importance of accurate DR assessment and glycemic control. In eyes with NPDR, presence of far peripheral DR lesions may predict subsequent DR progression independent of baseline DR severity and glycemic control.

Commercial Relationships: Paolo S. Silva, Optos plc (F); Jerry Cavallerano, None; Jennifer K. Sun, Boston Micromachines (F), Abbott Laboratories (C), Novartis (C), Genentech (F); Lloyd M. Aiello, None; Lloyd P. Aiello, Genentech (C), Genzyme (C), Thrombogenetics (C), Ophtotech (C), Kalvista (C), Pfizer (C), Proteostasis (C), Abbott (C), Vantia (C), Optos, plc (F)

Support: Optos plc

275 Vitreoretinal Surgery I

Monday, May 06, 2013 2:45 PM-4:30 PM
6C Paper Session
Program #/Board # Range: 2142-2148
Organizing Section: Retina

Program Number: 2142
Presentation Time: 2:45 PM - 3:00 PM

Long-term Safety of Vitrectomy for Patients with Floaters
Christianne A. Wa1,2, Kenneth M. Yee1,2, Laura C. Huang1,2, Alfredo A. Sadun1,2, J Sebag1,2,3, Neuro-Ophthalmology, USC/Doheny Eye Institute, Los Angeles, CA; 2VMR Institute, Huntington Beach, CA; 3University of Miami School of Medicine, Miami, FL.

Purpose: Floaters are curable by vitrectomy, but retinal tears/ detachments and cataract formation are concerns. It is hypothesized that performing vitrectomy with 25G instruments and not inducing a PVD intra-operatively will lower the incidence of retinal tears (previously reported 30%; Tan et al, AJO 2011). It is further hypothesized that not inducing PVD and also leaving the anterior vitreous intact will lower the incidence of post-vitrectomy cataract formation.

Methods: A retrospective chart review was performed for consecutive cases of therapeutic 25G vitrectomy for floaters. Eyes that had injections or previous vitrectomy or scleral buckle were excluded. PVD was not induced during surgery and the anterior vitreous was left intact in phakic eyes. 66 eyes in 52 patients (age = 63 ± 12 years) were included; 36/66 (54.5%) eyes were phakic. The average duration of coping was 30 months. The etiology of floaters was PVD in 44/66 (67%), myopia in 19/66 (28%), asteroid hyalosis in 8/66 (12%) and old blood in 2/66 (3%) eyes. Retinopexy for retinal breaks occurring at the time of PVD was performed in 16 eyes (36% of all eyes with PVD; 24% of all eyes), a minimum of 3 months prior to vitrectomy. The mean follow-up was 12.3 months (range: 3-50 months). Main outcome measures were the incidence of retinal tears/ detachments and cataract formation requiring surgery.

Results: Floater symptoms resolved in 65 of 66 eyes (98.5%). Over a period of 3 months to 4 years, no patients (0/66; 0%) developed retinal breaks, hemorrhage, infection, or glaucoma. More specifically, retinal breaks/ detachments did not develop in the 22 patients without PVD pre-operatively (0/22 vs 9/30 (30%); Tan et al, AJO 2011; Fisher’s exact t-test P < 0.007). Only 7/36 (19%) phakic eyes developed cataracts requiring surgery, an average of 16.5 months post-vitrectomy (7/36 vs 18/36 (50%); Tan et al, AJO 2011; Fisher’s exact t-test P < 0.02).

Conclusions: Vitrectomy using small-gauge instruments without PVD induction reduced retinal tear incidence from 30% to 0% (P < 0.007). Not inducing PVD and leaving the anterior vitreous intact lowered the incidence of post-vitrectomy cataract surgery from 50% to 19% (P < 0.02).

Treatment symptomatic floaters by 25G vitrectomy without inducing PVD or removing the anterior vitreous can be safe and still effective, eliminating iatrogenic retinal tears/ detachments and minimizing the need for cataract surgery.

Commercial Relationships: Christianne A. Wa, None; Kenneth M. Yee, None; Laura C. Huang, None; Alfredo A. Sadun, None; J Sebag, ThromboGenics (C), ThromboGenics (I)

Support: VMR Consulting, Inc.

Program Number: 2143
Presentation Time: 3:00 PM - 3:15 PM

Prospective study of vitrectomy for floaters: improvement in contrast sensitivity and standardized VFQ testing
Kenneth M. Yee1,2, Laura C. Huang1,2, Christianne A. Wa1,2, Alfredo A. Sadun1,2, J Sebag1,2,3, VMR Institute, Huntington Beach, CA; 2Neuro-Ophthalmology, USC/Doheny Eye Institute, Los Angeles, CA; 3University of Miami School of Medicine, Miami, FL.

Purpose: Patients often report that floaters can have a significant impact on vision, but the exact mechanism is unknown. Contrast sensitivity function (CSF) and patient well-being were evaluated prospectively in patients with floaters treated by vitrectomy with the hypothesis that patients with bothersome floaters have a reduction in CSF that can be normalized by vitrectomy.

Methods: CSF was prospectively studied by computer-based Freiburg Acuity Contrast Testing [Weber index: %W = (Lummax - Lummin)/ Lummax] in 38 eyes of 22 patients. Patients with floaters (N = 8; 51±23 years) were tested before vitreotomy and results were compared to age-matched controls (N=30; 53 ± 15 years). Minimally-invasive, sutureless 25 G vitrectomy was performed. Patient well-being was quantified pre-operatively in 16 subjects with the validated NEI visual function questionnaire-39 (VFQ-39) using the composite index of all 39 questions, as well as four other sub-indices [mental health, role difficulties, general vision and near vision]. CSF measurements and VFQ evaluations were repeated post-operatively at 1 week and 1 month as outcome measures.

Results: Pre-operatively, patients with floaters had 54.4% attenuation in CSF (5.39 ± 2.55 %W) compared to controls (2.93 ± 1.2 %W; P < 0.003). Post-operative CSF normalized at 1 week (2.44 ± 1.87 %W; P < 0.019) and 1 month (2.26 ± 1.29 %W; P < 0.016).

By VFQ testing, mental health, role difficulties, general vision, and near vision improved 83.8% (P<0.01), 69.4% (P < 0.016), 54.9% (P<0.004), 41.2% (P<0.034), respectively, with a composite VFQ-39 improvement of 29.5% (P < 0.006) at 1 month post-operatively.

Conclusions: Profound CSF diminution establishes a clear basis for significant dissatisfaction in patients with floaters as demonstrated by standardized VFQ testing. Vitrectomy dramatically normalized CSF in patients with floaters and may explain the observed improvement in patient well-being as determined by VFQ testing. Assessing patients with objective measures of contrast sensitivity and standardized quality of life questionnaires may provide useful guides for patient selection when considering vitrectomy for floaters.

Commercial Relationships: Kenneth M. Yee, None; Laura C. Huang, None; Christianne A. Wa, None; Alfredo A. Sadun, None; J Sebag, ThromboGenics (C), ThromboGenics (I)

Support: VMR Consulting

Program Number: 2144
Presentation Time: 3:15 PM - 3:30 PM

Prospective study of vitrectomy for floaters: improvement in contrast sensitivity and standardized VFQ testing

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Hydroxyl Free-Radical Formation during Vitrectomy

Nathan Ravi1,2, Paul D. Hamilton2,3. Ophthalmology and Energy, Environmental and Chemical Engineering, Washington University, St Louis, MO; Ophthalmology Research, VA Health Care System, St Louis, MO.

**Purpose:** We are examining the formation of hydroxyl free-radicals (OHFR) in natural and artificial hydrogels during vitrectomy and expanding our knowledge of polymer and macromolecular sciences to the natural vitreous by evaluating the possibility of free-radical production as a mechanism of tissue damage during the vitrectomy.

**Methods:** Collagen gels and synthetic hydrogels [copolymer acrylamide/10 % sodium acrylate] were used as vitreous phantoms during vitrectomy [ProCare Plus Vitrectomy System, Vision Care Devices] with a cut rate per minute of 3000 in the presence of a fiber-optic light source. This procedure was repeated up to ten times then the hydrogel was analyzed for OHFR formation; see Korotkova, [Int. J. Mol. Sci. 12, 401-409; 2011] where non-fluorescent terephthalic acid H2-TA is hydroxylated by OHFR to give the fluorophor TA-OH. The reaction in hydrogels was compared to and quantified by the Fenton reaction of iron and hydrogen peroxide free-radical production (Fe2+ + H2O2→Fe3+ + 2OHFR→2TA-OH).

**Results:** Measurable quantities of OHFR were produced during the hydrogel cutting procedure, which was proportional to the number of times the gel was passed through the vitrectomy cutter, see figure. The difference in the level of free-radical production is likely dependent on the concentration of material in the gels with the OHFR levels corresponding to ~0.5 (1cut)- 4.0 uM (10 cuts) in the Am copolymer gel.

**Conclusions:** Currently, increased partial pressure of oxygen, in the absence of the natural vitreous, is implicated in the pathogenesis of the increased incidence of nuclear sclerotic cataract and open angle glaucoma after vitrectomy [Beebe, Phil. Trans. R. Soc. B, 366, 1293-1300, 2011]. Mechanical disruption of polymers and macromolecules is known to generate free-radicals. It is possible that sufficient oxygen free-radicals are generated during vitrectomy to indiscriminately react with cellular components and cause their dysfunction depending on the redox buffer capacity (RBC) of cell and tissues. A combination of free-radical production along with the age-related decrease in RBC of tissues could offer an alternate hypothesis to formation of cataract post-vitrectomy.

Fluorescent detection of the production of hydroxyl free-radicals by the Fenton reaction with the hydroxylation of terephthalic acid.

Fluorescent detection of the formation of hydroxyl free-radicals by the cutting of hydrogels with vitrectomy unit.

Commercial Relationships: Nathan Ravi. None; Paul D. Hamilton. None

Support: This research was supported by the Grace Nelson Lacy Glaucoma Foundation Award to Dr. Nathan Ravi, Washington University, Research to Prevent Blindness, Inc., NIH Core Grant (P30 EY 02687) and the St. Louis VA Health Care System.

Program Number: 2145

Presentation Time: 3:30 PM - 3:45 PM

Thermodynamics of vitreoretinal surgery in human eyes and implication of changes in rheology of endotamponades

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**Purpose:** To report the fluctuations in temperature occurring inside the human eye during vitreoretinal surgery and to investigate the effect of such fluctuations in temperature on intraocular tamponades.

**Methods:** Intraocular temperature was recorded in continuous during the entire vitrectomy in 16 eyes of 16 patients with idiopathic or diabetic epiretinal membrane. Temperature was monitored through a custom made thermoprobe. Time points of particular interest during the vitrectomy for statistical analysis were: a) baseline (inflow off - outflow off), b) beginning of the vitrectomy, c) end of vitrectomy (inflow on - outflow on), d) during the epiretinal procedures (inflow on - outflow off), e) under air infusion, f) under oil, g) under endolaser treatment. The effect of the recorded temperature variations in vivo was investigated in vitro on rheology of intraocular tamponades. We calculated the changes in the kinematic shear viscosity of 1000cS and 5000 cS silicone oil (SO) at the different temperatures using a Ubbelhode viscometer. Interactions between different kinds of PFCL [perfluoro-n-octane (PFO) or perfluorodecaline (PFD)] and HSO (either alkane or ether) were also studied in vitro by incubating fluids for 7 days at 36°C and removed at different temperatures.

**Results:** The mean temperature in the AC and on the nasal retinal side was 23.8 (SD 1.6) °C and 32.7 (SD 1.2) °C respectively. The mean vitreous temperature at baseline, before opening the infusion, was 34.2 (SD 1.1) °C. The mean temperature at the beginning and end of the vitrectomy was 27.1°C (SD 1.1) and 24.4 (SD 1.0) °C respectively. The fluctuations in temperature were statistically different between the time points during the vitrectomy (P<0.001). Kinematic viscosity of SO shows a decrease of 188 cSt for the 1000 cS and of 866 cSt for the 5000 cS SO increasing the temperature from 22 to 32 °C. In vitro, interactions between PFCL-HSO led to the formation of hyper-viscous solutions with significative decrease in...
aspiration time at 36°C versus 22°C in group (P = 0.003).

**Conclusions:** Vitreoretinal surgery induces significant fluctuation in temperature in human eye. The rheology properties of intraocular tamponades is affected by such variations. Keeping the temperature stable around 30°C we could reduce shear SO viscosity and we could also dissolve the sticky oil formation induced by the interaction between PFCL-HSO.

**Commercial Relationships:**
- Mario R. Romano, Bausch and Lomb (C); Vito Romano, None; Riccardo Vinciguerra, None; Jose L. Vallejo-garcia, None; Ciro Costagliola, None; Paolo Vinciguerra, SOOFT Italia (C), Oculus Optikgerate GmbH (C), NIDEK, Japan (C), Schwind (C)

**Program Number:** 2146
**Presentation Time:** 3:45 PM - 4:00 PM

Assessment of Microarchitectural Changes During Vitrectomy Surgery for Vitreomacular Traction Syndrome Utilizing Intraoperative Optical Coherence Tomography

**Purpose:** To assess the microarchitectural changes that occur during surgery for vitreomacular traction (VMT) utilizing intraoperative optical coherence tomography (iOCT).

**Methods:** Retrospective case series of eyes undergoing pars plana vitrectomy (PPV) for VMT with concurrent iOCT was collected. A microscope-mounted portable spectral domain OCT system (Bioptigen) was used for intraoperative imaging with a standard acquisition protocol (e.g., preincision, following hyaloid elevation). IRB approval was obtained. Qualitative and quantitative assessment of the retinal microarchitectural features was performed.

**Results:** Eleven eyes of 11 patients were included with a mean preoperative visual acuity (VA) of 20/72 and improving to 20/46 postoperatively (p = 0.04). No surgical complications were noted. For 2/11 eyes, the preincision iOCT scans showed interval development of subclinical full-thickness macular holes (FTMH). Following hyaloid elevation, one eye showed definitive FTMH formation and an additional eye showed possible FTMH. In all four of these eyes (4/11, 36%), iOCT impacted the surgical procedure to address the subclinical findings (e.g., internal limiting membrane peeling, gas tamponade). Other microarchitectural changes noted with iOCT following hyaloid elevation included increased inner segment-outer segment (IS-OS) disruption and increased subretinal hyporeflectivity with expansion of the distance between the RPE and outer retina (e.g., IS-OS, cone outer segment tips).

**Conclusions:** Intramuscular imaging utilizing iOCT during VMT can impact surgical planning through the detection of subclinical changes (e.g., small FTMH formation). Architectural changes occur following surgical maneuvers that are particularly noted in the outer retina. The functional significance of these changes is currently unknown.

**Program Number:** 2147
**Presentation Time:** 4:00 PM - 4:15 PM

Time Interval Before Re-operation Influences Visual Outcomes in Repeat Macular Hole and Macular Pucker Surgery

**Purpose:** Vitrectomy with membrane peel sometimes has poor visual outcome, usually following re-operations. To determine the role of timing between the primary procedure and re-operation in

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Persistent/recurrent macular pucker (MP) and macular hole (MH), the final vision and histopathologic analyses of excised membranes were correlated with the time interval between operations. Tissue obtained at surgery was analyzed to seek elements of inner retina adherent to the excised membrane, which was hypothesized to be the cause of poor post-operative vision.

Methods: Eyes with a history of prior vitreoretinal surgery, retinal detachment, vein occlusion, wet age-related macular degeneration or diabetic retinopathy were excluded. Ten pseudophakic eyes undergoing re-operation for MH or MP were evaluated using Snellen visual acuity (VA) as an outcome measure. 25G vitrectomy was performed in all cases. Chromodissection with doubly-diluted indocyanine green dye was performed in all primary MH surgeries and in all re-operations for MH and MP. VA was correlated with immunohistochemistry for neurofilament and transmission electron microscopy of excised tissue in 6/10 cases.

Results: VA improved by >3 lines in 6 cases and worsened by >3 lines in 3 cases. All 6/6 (100%) cases with ≥6 month interval before re-operation had VA improvement (>3 lines), while 3/4 (75%) with <6 month interval had VA worsening (>3 lines; P = 0.03). The average post-operative logMAR VA was 1.59 ± 1.07 (20/800) for <6 months inter-operation interval, with positive neurofilament staining and retinal cell debris present on the peeled membrane in 2/2 eyes. Waiting ≥6 months before re-operating resulted in logMAR VA of 0.42 ± 0.25 (20/50) (P = 0.03) and no evidence of neurofilament staining or retinal elements on the peeled membranes (0/4 eyes).

Conclusions: If repeat vitrectomy with membrane peeling is performed too early, there may not be adequate time for Müller cells to re-form a layer of endplates over the denuded retinal nerve fiber layer, exposing it to damage during the second operation with resultant poor vision. Waiting more than 6 months before re-operating for MH or MP may allow enough time to re-form normal tissue planes, enabling a better surgical plane of dissection at re-operation, which seems to be associated with significantly less inner retinal damage and superior final vision.

Commercial Relationships: Billy X. Pan, None; Kenneth M. Yee, None; Fred N. Ross-Cisneros, Edison Pharmaceutical, Inc. (F); Alfredo A. Sadun, None; J Sebag, ThromboGenics (C), ThromboGenics (I)

Support: Research to Prevent Blindness, Keck School of Medicine of the University of Southern California Dean’s Research Scholarship, and National Institutes of Health Grant EY03040

Program Number: 2148
Presentation Time: 4:15 PM - 4:30 PM
The Value of Routine Preoperative Medical Testing Before Vitreoretinal Surgery

Ajay Shalwala1, Richard Y. Hwang1, Ariana K. Tabing2, Stephen J. Kim1. 1Vanderbilt Eye Institute, Nashville, TN; 2Vanderbilt University School of Medicine, Nashville, TN.

Purpose: Screening medical tests are performed on patients in preparation for vitreoretinal surgery, but the benefit of routine testing is uncertain. This study aims to determine the predictive value of routine medical testing for post-operative systemic adverse events.

Methods: Medical charts of 2103 patients ages 17 or greater who underwent vitreoretinal surgery between January 2002 and November 2011 at Vanderbilt University in Nashville, Tennessee were reviewed for baseline comorbidities, pre-operative testing, and adverse events occurring at the time of or within 30 days of surgery. Charts were excluded if there were less than 7 days of documented follow-up. Logistic regression analysis was performed to correlate adverse events with pre-operative testing and baseline comorbidities.

Results: Of 2033 included patients, 83 experienced adverse events, with 9 patients having multiple events. Of 95 total adverse events observed, 66 (69%) occurred in the first 24 hours post-operatively, while the remaining 29 (31%) occurred between post-operative days 1 and 30. The most common adverse events were bradycardia (22 events) and desaturation (19 events). Presence of coronary artery disease, chronic renal failure, chronic liver disease, and history of cerebrovascular accident all independently predicted adverse events (p < 0.05), while age, race, diabetes, COPD, smoking history, asthma, and systemic malignancy were not associated. Pre-operative renal function testing (blood urea nitrogen and creatinine) appeared to reduce the risk of adverse events (p < 0.05) while general anesthesia increased the risk compared to local anesthesia (p < 0.001).

Conclusions: The incidence of adverse events following vitreoretinal surgery in this series was 4.1%. General anesthesia and the presence of specific comorbidities increased the risk of adverse events while pre-operative renal function testing appeared to be protective. This information may allow more selective testing for those individuals at greatest risk for adverse systemic events after vitreoretinal surgery and consequently reduce the burden of routine testing in those individuals at low risk.

Commercial Relationships: Ajay Shalwala, None; Richard Y. Hwang, None; Ariana K. Tabing, None; Stephen J. Kim, None

Support: Research to Prevent Blindness unrestricted grant to Vanderbilt Eye Institute

290 DME
Monday, May 06, 2013 2:45 PM-4:30 PM
Exhibit Hall Poster Session
Program #/Board # Range: C0064-C0118
Organizing Section: Retina

Program Number: 2363 Poster Board Number: C0064
Presentation Time: 2:45 PM - 4:30 PM

Effect of Focal Laser and anti-VEGF Therapy on Choroidal Thickness in Diabetic Macular Edema as measured by Enhanced-Depth Imaging Optical Coherence Tomography

Varsha Manjunath1, Glenn Yiu2, Stephanie J. Chiu2, Sandra Stinnett1, Sina Farsi2, Tamer H. Mahmoud1, 1Ophthalmology, Duke University Eye Center, Durham, NC; 2Biomedical Engineering, Duke University, Durham, NC.

Purpose: To evaluate choroidal thickness (CT) as measured by enhanced-depth imaging optical coherence tomography (EDI-OCT) in patients with untreated diabetic macular edema (DME), and after focal laser or anti-vascular endothelial growth factor (VEGF) therapy.

Methods: This is a retrospective cross-sectional study of 172 eyes from 98 consecutive diabetic patients (51 male, 47 female; mean age 60.2) with and without DME who had Heidelberg Spectralis EDI-OCT at the Duke Eye Center from October 2011 to October 2012. Semi-automated segmentation of the choroid was performed and CT was measured at the fovea. Stepwise multivariable linear regression was performed to evaluate the association of CT with age, type of diabetic retinopathy (NPDR vs. PDR), HbA1c, visual acuity, and refractive error. Subfoveal CT was compared between eyes with untreated DME (n=35) and without DME (n=60) using a general linear model to adjust for age. Among eyes with DME, choroidal thickness after focal laser (n=27), intravitreal anti-VEGF injections (n=7), or both treatments (n=13) were compared with untreated DME (n=35). Finally, the relationship between subfoveal CT and central foveal thickness (CFT) and macular volume (MV) was assessed.

Results: Subfoveal CT in all eyes correlated most with age (β−
Microperimetry-Guided Micropulsed Laser Photo Stimulation for the Treatment of Diabetic Macular Edema

Renato Peroni
1, 2, Jose A. Cardillo
3, 4, Alessandro J. Dare
2, Rodrigo Jorge
1, 2
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Purpose: All current laser therapies are still in great need of an accurate treatment protocol. New strategies have been developed for laser treatments that minimize the choriotretral damage, but very little attention is given to the real fixation point at the time of the photocoagulation. The purpose of this investigation is to suggest an optimized delivery technique where in addition to the central fovea an additional area of 500 microns from the center of the new fixation point is preserved from treatment as well or treated only with micropulse laser.

Methods: Twenty eyes of 16 patients with DME were treated using a yellow micropulse laser (577 nm) and sparing the 500 micron from the center of the fovea and the 500 microns from the center of the new fixation point as defined by fundus microperimetry. The mean retinal sensitivity within the central 10 degrees and the fixation point were measured with a fundus-related microperimeter, MP1, ETDRS-best corrected visual acuity (BCVA), optical coherence tomography-determined central macular thickness (CMT), and fluorescein angiography (FA) were performed before, 1, 3 and 6 months after a single treatment.

Results: Central macular thickness decreased by an average of 199 μm. At 6 months main change in visual acuity was 4 letters better. Mean retinal sensitivity improved (P<0.005) at 3 and 6 months. Laser lesions were not clinically observed by any means.

Conclusions: Among the usual variables that determine the success of any laser therapy approach, the sparing of the fixation point when localized outside of the anatomical fovea has emerged as a new, important variable to consider in preventing a possible negative therapeutic effect.

Commercial Relationships: Renato Peroni, None; Jose A. Cardillo, None; Alessandro J. Dare, None; Rodrigo Jorge, None.

Program Number: 2366 Poster Board Number: C0067
Presentation Time: 2:45 PM - 4:30 PM

Bevacizumab suppresses retinal blood flow to reduce macular thickness in diffuse diabetic macular edema

Masahiko Shimura
1, Sho Watarai
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Purpose: To evaluate dynamic changes of retinal blood flow (RBF) and choroidal blood flow (CBF) after an intravitreal injection of bevacizumab (IVB) in patients with diffuse diabetic macular edema (DDME).

Methods: Fourteen eyes of 10 patients with DDME without any previous treatments received 1.25mg/0.05ml IVB. RBF and CBF were assessed with mean blur rate (MBR) measured by laser speckle flowgraphy (LSFG) of the optic disc and fovea before and after 1, 4 and 12 weeks of IVB. Central macular thickness (CMT) measured by optical coherence tomography and best-corrected visual acuity (VA) using a logMAR chart was also evaluated during the clinical course.

Results: After IVB, RBF was reduced to 78.2±9.6% at 1 week, 79.6±7.6% at 4 weeks and 87.8±7.4% at 12 weeks, while CBF was...
Purpose: To investigate macular thickness and visual acuity changes after intravitreal injection of micronized triamcinolone acetonide (mTA) or bevacizumab (B) at the end of phacoemulsification in naïve eyes with cataract and diabetic macular edema (DME)

Methods: One hundred naïve eyes with cataract and diabetic macular edema were randomly assigned to receive at the end of phacoemulsification 4mg of mTA (Vitreal S, SooItalia) or 0.5 mg of B (Avastin, Roche). Comprehensive ophthalmic evaluation was performed preoperatively and at 1, 4, 12 and 24 weeks postoperatively. Main outcome measures included central macular thickness (CMT) and best-corrected ETDRS visual acuity (BCVA).

Results: All the patients completed the 24-week study visit. The 2 group did not show significant preoperative differences in CMT (p>0.05) and BCVA (p>0.05). Mean CMT decreased significantly at the end of follow-up in mTA group (p<0.05), but not in B group (p>0.05). Mean BCVA increased significantly in both groups versus baseline (p<0.05). The BCVA gain was greater in mTA group than B group. Intraocular pressure increased only in 4% patients in mTA group. No other complications were recorded.

Conclusions: There preliminary data showed that intravitreal mTA is more effective than intravitreal B in management of DME in eyes undergoing cataract phacoemulsification. Further studies with longer follow up are required.

Oxygenation of retinal vessels before and after laser therapy in sight threatening diabetic macular edema

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Purpose: Laser therapy for macular edema is used to stabilise visual acuity, a direct indicator of retinal function. We aim to identify the short term effects of macular laser therapy on oxygenation of retinal vessels in diabetic macular edema (DME). To assess if a reduction of maculopathy affects oxygenation at the centre of the retina.

Methods: Patients were recruited to a single centre, open label, prospective, cohort study, to measure retinal oxygen levels in sight threatening diabetic maculopathy. Ethical approval was obtained by an independent committee and consent was obtained from recruited patients. Retinal images of the macula in 22 patients with unilateral DME were obtained using Oxymap technology. The patients were treated with retinal laser photocoagulation in the affected eye.

Oxygenation levels of the retina in the affected eye was compared to the concurrent eye before and after laser. Patients were followed up monthly with repeat Oxymap scans for a period of 4 months, when final images were taken. These were analysed and set against parameters such as visual acuity and retinal thickness. Patients with bilateral DME and other co-morbidities were excluded from the study.

Results: Data was collected from 22 patients at baseline, 16 male and 6 female. In 60% of cases the left eye had laser therapy, and in 40% the right eye. Age of cohort ranged between 29 to 81years. Average central retinal thickness (CRT) in the affected eye at baseline was 302µm, with average normal thickness of 259µm. After 4 months CRT in the treated eye reduced to 260µm.

Macular arteriole oxygen (MAO) saturation of the healthy eye was 92.4±3%, with mean venous oxygenation (MVO) of 57±6%. Whereas the eye with DME had average baseline MAO of 93±4% and MVO of 65±4% pre-laser. Post laser MAO increased 96%±4 and MVO to 66±3%.

Conclusions: Results show that initially MVO increases greatly due to DME, but post laser CRT reduced over the 4 months in the effected eye. We also found MAO improved post laser.

It is postulated that diabetic retinopathy affects oxygen metabolism. Due to an auto regulatory response the eye shunts oxygen away from ischemic areas of the retina to larger vessels, thus in DME oxygenation increases in venous circulation. Laser therapy reserves this change and increased oxygenation causes vessel constriction, lower intravascular pressure and reduced edema by sterlings law.

Oxygenation levels of the retina in the affected eye was compared to the concurrent eye before and after laser. Patients were followed up monthly with repeat Oxymap scans for a period of 4 months, when final images were taken. These were analysed and set against parameters such as visual acuity and retinal thickness.
performed by 3 reviewers. Following focus groups, study participants completed a 90-day diary detailing out-of-pocket (OOP) expenses and recorded time they and their caregivers spent on diabetes- or vision-care-related activities.

**Results:** There were 8 participants total (4 current drivers and 4 former drivers who had stopped driving due to DME-associated vision loss). Noteworthy themes included the secretive elements of managing diabetes while conforming to commercial driver’s license requirements and degraded driving performance directly attributable to DME. Examples included manipulating testing to ensure diabetes-negative results, avoiding treatment to prevent detection, driving with monocular vision and the challenges of glare or poor lighting conditions with reduced vision. Mean total annualized OOP costs for diabetes- and DME-related care was $4743 (Figure 1). The greatest contributor to total OOP costs was the purchase of equipment (eg vision aides). Not included in these totals are direct medical costs for one catastrophic diabetes-related event for 2 separate participants: 1) a toe amputation with systemic infection and 2) kidney failure. Mean annualized time for diabetes- or vision-care-related activities was 36 hrs for patients and 92 hrs for caregivers.

**Conclusions:** Diabetes and DME create significant economic burden for truck drivers. Current commercial driver’s license requirements (eg those that prohibit insulin use) may encourage behaviors that can jeopardize the health of the patient and potentially lead to high-cost events. Healthcare providers may want to consider these issues as they develop programs to improve outcomes among diabetes patients.

![Image](image_url)

**Figure 1. Mean annualized out-of-pocket patient costs related to diabetes and DME-related care.**

**Commercial Relationships:** 
Sunil S. Patel, Alcon (F), Allergan (F), Alimera (F), Genentech (F), Pfizer (F), Ophthotech (F), Regeneron (F), Allergan (C), Genentech (C), Ophthotech (C); Colleen Peters, Pfizer (F), Genentech (F); Kristen L. Garcia, None; Angela Jaimies, None; Bryce Miller, Genentech, Inc (E); Steven M. Kymes, None; Adam Turpcu, Genentech (E)

**Support:** Genentech

**Program Number:** 2370 Poster Board Number: C0071

**Presentation Time:** 2:45 PM - 4:30 PM

**Spectral-Domain Optical Coherence Tomography Parameters Associated with Baseline Vision in Diabetic Cystoid Macular Edema**

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**Purpose:** to study spectral-domain optical coherence tomography (SD-OCT) parameters that may be associated with baseline visual acuity in eyes with center-involved diabetic cystoid macular edema (DCME)

**Methods:** The analysis included eyes with new onset center-involved DCME that had to have had a macular SD-OCT and fluorescein angiography (FA) at presentation. The baseline OCT scans were analyzed for the extent of retinal involvement by the cystoid change and its location with respect to the center. Both inner and outer retinal parameters were assessed. Eyes with clinical and angiographic evidence of lipid and ischemic maculopathy and those with poor quality OCT were excluded. Statistical analysis correlating the various OCT variables with baseline logMAR visual acuity was performed.

**Results:** Forty-nine eyes of 35 patients were analyzed. Twenty-five patients (71.4%) were males and 10 (28.6%) were females with a mean (±SD) age of 57.22 (±10.4) years (range 29 - 78 years). The baseline Log MAR visual acuity, central macular thickness (CMT) and central foveal thickness (CFT) ranged from 0.3 to 1.2; mean (±SD) = 0.53 (±0.23) (20/40 to 20/30 Snellen equivalent range), 315 to 738 microns; mean (±SD) = 462.3 (±106.1) microns and 153 to 735 microns; mean (±SD) = 442.3 (±137.5) microns respectively. Pearson correlation test showed that the only OCT parameters associated with the baseline visual acuity were the chord length of involvement of the photoreceptor IS/OS junction within the central subfield (CSF) (p=0.001), the thickness of the residual photoreceptor outer segments within the CSF (p=0.002), and the size of the largest cystoid space within the CSF (p=0.037).

**Conclusions:** In DCME, baseline visual acuity appears to correlate strongly with the status of the photoreceptor outer segments and to a lesser extent with the degree of cystoid change in the CSF. These findings may help explain the impact of specific morphological changes on visual acuity in eyes with center-involved DCME.

**Commercial Relationships:** Abdulrahman M. Alfaran, None; Ahmed Mousa, None; Nicola G. Ghazi, None

**Support:** KING SAUD UNIVERSITY

**Program Number:** 2371 Poster Board Number: C0072

**Presentation Time:** 2:45 PM - 4:30 PM

**Diabetic Macular Edema Treatment with Bevacizumab vs. Ranibizumab: A Micropereimetry Study**

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**Purpose:** To compare macular sensitivity in patients with diabetic macular edema (DME) treated with intravitreal Bevacizumab (IVB) vs Ranibizumab (IVR) using micropereimetry.

**Methods:** Forty-eight patients (63 eyes) with center-involved DME were randomly assigned to receive either 1.5 mg/0.06 cc IVB or 0.5 mg/0.06 cc IVR. Injections were performed at baseline and monthly if central subfield thickness (CSFT) measured by spectral domain optical coherence tomography (SDOCT) was 275 μm or higher. Evaluations were done monthly, including SDOCT and best-corrected visual acuity (BCVA). Micropereimetry (MAIA - CenterVue) was performed before, 3, 6, 9 and 12 months of follow up, to determine the fixation stability (95 % bivariate contour ellipse area - BCEA), and the sensitivity threshold (ST) on 37 test points: a central point, and 3 concentric rings: 1, 3 and 5 degrees from the fixation location, with 12 test points each.

**Results:** Forty-three patients (61 eyes; IVB n=32; IVR n=29) completed the 12 months follow-up. Significant improvement was observed for BCVA and CSFT within each of the two study groups at all study visits compared to baseline (p<0.05). BCEA was comparable in IVB: 20.2 ± 5.1 and IVR: 23.3 ± 4.8 at baseline (P=0.3334), and no significant improvement was observed for BCEA
during follow-up. On the other hand, ST at central ring significantly improved (P<0.05) in all study visits, going from 16.6 ± 1.0 dB, and 15.1 ± 1.0 dB at baseline, to 19.1±1.1 dB and 18.1 ± 1.2 dB at 12 months, for IVB and IVR respectively. The ST improvement was significant at 12 months, but not in all study visits for the external rings 3 and 4 for IVB and IVR. There was no difference for ST improvement between IVB and IVR during follow-up.

Conclusions: Fundus-related microperimetry showed a significant increase in central retinal sensitivity for IVB and IVR in DME, particularly for the internal (1 degree) microperimetry ring. IVB and IVR were not significantly different improving central retinal sensitivity up to 12 months follow-up.

Commercial Relationships: Antonio Bruno Nepomuceno, None; Felipe P. Almeida, None; Andre Messias, None; Erika Takaki, None; Jefferson A. Ribeiro, None; Jose A. Cardillo, None; Ingrid U. Scott, None; Rodrigo Jorge, None

Support: FAPESP
Clinical Trial: NCT01487629

Program Number: 2372 Poster Board Number: C0073
Presentation Time: 2:45 PM - 4:30 PM

Autoregulation of retinal vessel diameter in diabetic macular edema is not altered by intravitreal ranibizumab


Purpose: In patients with diabetic macular edema the autoregulatory response of retinal vessel diameter before and three times after intravitreal injections of ranibizumab was investigated

Methods: 30 eyes of 30 patients aged 60±11years (mean ± SD) (M/F: 14/16) participated in this prospective study. Inclusion criterion: clinically significant diabetic macular edema. Treatment: three intravitreal injections of ranibizumab at intervals of four weeks. Examination time points: before first (TP1), second (TP2), third (TP3) injection and three months after the first one (TP4).

Parameters: Systemic blood pressure, retinal vessel diameter by still images: central retinal artery (CRAE) and vein equivalent (CRVE) (Visualis, Imedos, Germany) and change in vessel diameter in response to flicker stimulation (Dynamic Vessel Analysis, Imedos, Germany): 50s baseline recording followed by online measurement during 20s flicker stimulation (push-pull interruption of fundus illumination) and 80s online measurement in an arteriolar and venular vessel segment. Three recording cycles were averaged. Statistics: Analysis of variance (ANOVA) for repeated measurements or Friedman-test, Student t-test for paired samples, Bonferroni-Holm correction (SPSS 17). Target figures: Diameter change of retinal arterioles and venoles. Level of significance: alpha=5%.

Results: Systolic blood pressure BP: 160±18(mmHg,arith.mean±s), diastolic BP: 86±11. No significant change TP1-TP4 (p=0.10).

CRAE in µm: TP1: 182±23, TP2: 172±22, TP3: 174±27, TP4: 171±22 (ANOVA: p=0.02). CRVE TP1: 216±25, TP2: 213±25, TP3: 215±24, TP4: 211±24 (ANOVA: p=0.12). Flicker response, dilation, %: Arterioles TP1: -4.80.1,20.5,7; venoles TP1: -0.90.2,6.5,7.2. No significant change TP1-TP4 (Friedman-test): arterioles: p=0.13, venoles: p=0.15. The differences of the flicker response TP2-TP1, TP3-TP1, TP4-TP1 didn’t differ significantly from zero (p>0.10).

Conclusions: The CRAE may be significantly lower from TP2-TP4 compared to TP1 before the first injection of ranibizumab. This observation is consistent with earlier findings in the literature. The CRVE, however, doesn’t show a significant change. The median flicker response in arterioles and venoles is remarkably lower compared to healthy subjects and shows no significant change after ranibizumab treatment.

Dilation of arterioles

Dilation of venoles

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(BCVA) at 36 months/LOCF was analysed using multivariate linear regression adjusting for baseline characteristics. 

**Results:** In both ranibizumab- and laser only-initially treated patients (n=166 and n=74 respectively), the baseline characteristic most strongly correlated (Inversely) with change in BCVA was baseline VA (p=0.0002 and p=0.0001 respectively). Older age, duration of both diabetes and DME were also significantly correlated with 36-month BCVA in ranibizumab-treated patients only (p=0.045, 0.013, and 0.045 respectively). Shorter duration periods for diabetes and also for DME were associated with better clinical responses to ranibizumab treatment. In patients initially treated with laser, but not in patients commenced on either of the ranibizumab regimens, baseline central retinal thickness correlated positively with change in BCVA (p=0.0063).

**Conclusions:** Baseline BCVA was a strong predictor of BCVA changes over 36 months, so that patients with poorer VA achieved greater gains than those with better baseline vision. Other correlates varied by treatment modality, consistent with differing modes of action between ranibizumab and laser photocoagulation. Better responses in patients with more recently diagnosed DME highlights the need for prompt therapy.

**Commercial Relationships:** Paul Mitchell, Novartis (R), Bayer (R); Victor Chong, Novartis (C), Bayer (C), Allergan (P), Pfizer (F), Novartis (F), Alimera Science (C), Quantel (R)

**Clinical Trial:** NCT00687804

**Program Number:** 2374 Poster Board Number: C0075
**Presentation Time:** 2:45 PM - 4:30 PM

**Effect of combined treatment of diabetic macular edema on macular ischemia**

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**Purpose:** To evaluate the effect of treatment on macular ischemia in patients with diabetic macular edema.

**Methods:** Twenty-seven eyes from 15 patients diagnosed of diabetic macular edema were included in the study. A comprehensive ophthalmologic examination was performed. All patients underwent a digital high-resolution fluorescein angiography with a laser confocal ophthalmoscope (SPECTRALIS HRA2+OCT), followed by a Spectral-Domain OCT examination with active eye tracking at the beginning and at the conclusion of the study. Patients were treated either with intravitreal injections of bevacizumab, with focal laser or with a combination of both. The mean follow-up period was 15 months. The ischemia was quantified with a computer-assisted image analysis software. Data from one eye of each patient were assessed with the T-test for paired samples.

**Results:** Of the eyes treated, 27% received only intravitreal injections of bevacizumab, 20% only focal laser and 53% a combination of both. The mean number of injections for each eye treated with bevacizumab was 2.25. In all three treatment groups, there was no significant change observed in macular ischemia (p=0.201, p=0.213, p=0.688). In all three groups, the visual acuity (VA) did not change significantly (p=0.215, p=0.523, p=0.810). The mean foveal thickness (FT) decreased statistically significantly in the groups that received treatment with intravitreal injections of bevacizumab, alone or combined with focal laser, but not in the focal laser-alone group (p=0.05, p=0.05, p=0.427).

**Conclusions:** The macular ischemia was not altered after repeated intravitreal injections of bevacizumab, focal laser treatment or a combination of both.

**Commercial Relationships:** Alexandros Deligiannidis, None; Jose Lorenzo Carrero, None; Ines Perez Flores, None; Theodore Paraskevopoulos, None; Pilar Bolivar Montesa, None

**Program Number:** 2375 Poster Board Number: C0076
**Presentation Time:** 2:45 PM - 4:30 PM

**Reduced Energy Macular Laser Phototherapy for the Treatment of Diabetic Macular Edema**

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**Purpose:** Exploiting optimized parameters and treatment guidelines will be the key to progress macular photocoagulation for an ultimate tissue injury minimization and vision restoration. The purpose of this investigation is to determine the anatomical and functional outcome of this suggested optimized treatment technique consisting of confluent (high density) and barely visible photocoagulation lesions in patients with diabetic macular edema (DME).

**Methods:** Twenty-eight eyes of 21 patients with DME were treated using a yellow diode laser (577 nm) clinically adjusted to show barely visible photocoagulation lesions at 20 ms exposure time. The mean retinal sensitivity within the central 10 degrees measured with a fundus-related microperimeter, MP1, ETDRS-best corrected visual acuity (BCVA), optical coherence tomography-determined central macular thickness (CMT), and fluorescein angiography (FA) were performed before, 1, 3 and 6 months after a single treatment.

**Results:** Central macular thickness decreased by an average of 277 μm. At 6 months main change in visual acuity was 5 letters better. Mean macular sensitivity improved (P<0.005) at 3 and 6 months. Laser lesions were not clinically observed, but detected on the early phase of the FA examination.

**Conclusions:** An extensive destruction of retinal tissue with laser burns may not be necessary to achieve an effective laser therapy. In the effort to minimize the side effects while maintaining the efficacy, short pulsed and low energy laser delivery targeting a barely visible lesion endpoint may characterize a more selective alternative to the present standard of care.

**Commercial Relationships:** Alexandro J. Dare, None; Jose A. Cardillo, None; Rodrigo Jorge, None; Rubens Belfort, CNPQ (F), FAPESP (F), ALCON (C), ALLERGAN (R), BAYER (R), NOVABAY (R), ALCON (R); Michel E. Farah, None

**Program Number:** 2376 Poster Board Number: C0077
**Presentation Time:** 2:45 PM - 4:30 PM

**Relevance of inner versus outer retinal thickness in diabetic macular edema in the RELATION study**

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**Purpose:** To analyze the correlation between inner and outer retinal thickness on Optical Coherence Tomography (OCT) with visual acuity (VA) and fluorescein angiography (FA) parameters, and the response to treatment in diabetic macular edema (DME).

**Methods:** OCT volume scans and FA images from the RELATION study were analyzed by certified reading center graders. In the multicenter, double masked clinical trial 128 patients with visual impairment due to DME were randomized 2:1 to ranibizumab in combination with focal/grid laser photocoagulation (combined group)
or focal/grid laser photocoagulation combined with sham injections (laser group) with a follow-up of up to 12 months. Manual quantitative OCT analysis was performed and mean central retinal thickness (CRT) was calculated for the neurosensory retina, the outer retina (outer nuclear layer and photoreceptors) and the inner retina (inner limiting membrane to outer retina). Thickness values were correlated with ETDRS VA, severity of macular ischemia and type of DME on FA.

**Results:** OCT volume scans of 109 patients were available for analysis (spectral and time domain OCT). At baseline, VA showed significant correlations with CRT for neurosensory retina (R=0.44, p<0.001), inner retina (R=0.22, p<0.05) and outer retina (R=0.28, p<0.01). Eyes with greater inner retinal thickness values at baseline had lower VA values at last follow-up (R=0.32, p<0.001), whereas outer retinal thickness appeared to have no significant prognostic value. Eyes with fluorescein leakage predominantly due to telangiectasia showed greater inner retinal thickness values than eyes with leakage predominantly due to microaneurysms (p<0.01). Outer retinal thickness values showed no difference between groups. There was no difference regarding severity of macular ischemia. Eyes in the combination group showed significantly stronger decrease in inner retinal thickness than eyes in the laser group (R=0.34, p<0.001), but no significant difference in reduction of outer retinal thickness values.

**Conclusions:** CRT values for the inner and the outer retina show differences regarding the type of DME on FA, VA outcome as well as the response to treatment. Subanalysis of various retinal layers on OCT may be relevant as outcome parameters in DME clinical trials.

**Commercial Relationships:** Tina Ristau, Novartis (F); Jessica Voegeler, Novartis Pharma GmbH (E); Gabriele E. Lang, Novartis (F), Novartis (R), Novartis (C), Alcon (C), Allergen (C); Sandra Liakopoulos, Novartis (F), Novartis (C), Heidelberg Engineering (R), Novartis (R).

**Clinical Trial:** NCT01131585

**Program Number:** 2377 Poster Board Number: C0078
**Presentation Time:** 2:45 PM - 4:30 PM

**Photocoagulation for peripheral nonperfusion-areas to prevent the recurrence of diabetic macular edema after single intra-arterial injection of bevacizumab**

*Yoshihiro Takamura, Takeshi Tomomatsu, Takehiro Matsumura, Yuji Takihara, Masaru Inatani.* Ophthalmology, University of Fukui, Ehimeji Yoshida, Japan.

**Purpose:** Although intra-arterial injection of bevacizumab (IVB) is strong tool to treat diabetic macular edema (DME), multiple injections are necessary to maintain its therapeutic effect. Randomized prospective study was carried out to investigate whether the photocoagulation (PC) for peripheral ischemic area has effect to prevent the recurrence of DME after IVB.

**Methods:** Patients with DME were randomized to receive 1.25mg IVB (IVB group) and IVB with combination of peripheral PC for ischemic retina determined by fluorescein angiography (IVB+PC group). At 2 weeks before IVB, grid/focal PC was performed in both groups. Every month after IVB up to 6 months, best corrected visual acuity (BCVA) and central retinal thickness (CRT) determined by optical coherence tomography were measured.

**Results:** Forty-one eyes of 41 patients (68.8±4.6 years) were participated and eyes were randomized to IVB group (n=20) and IVB+PC group (n=21). At the treatment of grid/focal PC and IVB, there was no significant difference in BCVA and CRT between the groups. At 1 month after IVB, both groups exhibited significant decrease in CRT. Decreased CRT in IVB+PC group was maintained thereafter, while CRT in IVB group turned to decrease. The average of CRT in IVB+PC group was significantly smaller than that of IVB group at 3 months and thereafter (p<0.05; unpaired Student’s t-test).

**Conclusions:** The combination of photocoagulation for peripheral nonperfusion-area with grid/focal PC and IVB treatments provided benefit for patients with DME to prevent the recurrence of residual edema.

**Commercial Relationships:** Yoshihiro Takamura, None; Takeshi Tomomatsu, None; Takehiro Matsumura, None; Yuji Takihara, None; Masaru Inatani, None

**Clinical Trial:** UMIN000007566

**Program Number:** 2378 Poster Board Number: C0079
**Presentation Time:** 2:45 PM - 4:30 PM

**Outcomes of Focal Laser Photocoagulation for Diabetic Macular Edema (DME) at Los Angeles County (LAC+USC) Medical Center**


**Purpose:** To report outcomes of focal laser photocoagulation for clinically significant macular edema (CSME) among diabetics at the LAC+USC eye clinic, a predominantly underinsured, Hispanic patient population

**Methods:** IRB approval was obtained. Retrospective chart review was performed on patients who received focal/grid laser photocoagulation for CSME, as defined by the ETDRS, from Sept 1, 2010 to March 31, 2011 at the LAC+USC Eye Clinic. The primary outcome measures were: (1) improvement in visual acuity by 1 line or more (similar to measured reported in ETDRS Report 1), and (2) reduction in OCT central subfield foveal thickness by 50 microns or more at 2-4 months. Baseline and follow-up parameters were collected from sociodemographic and clinical chart data, lab results, and OCT data.

**Results:** Of 177 eyes that received laser over the 6-month study period: 72 were excluded because of poor quality OCT or lack of follow-up, and 105 had complete follow-up data at 2-4 months. 70% of the LA County study population (with baseline visual acuity worse than 20/40 and mild to moderate diabetic retinopathy) experienced improved visual acuity by 1 line or better at 2-4 months after receiving focal laser. This is compared to 40% of the ETDRS population, with the same baseline parameters, who experienced at least 1 line of improvement in vision at 1 year. Like the ETDRS, there was no significant difference in the mean log MAR visual acuity before and after laser (0.56 post-focal, as compared to 0.57 pre-focal; p=0.8). The mean foveal central subfield thickness (CST) improved from 356 microns to 329 microns after laser (p=0.006), and 40% experienced reduction of CST by 50 microns or more. Of all the sociodemographic and clinical variables collected, the only univariate predictor of visual acuity improvement by 1 line or more was having total cholesterol of less than 200 (odds ratio 5.69 [1.50-21.4]; p=0.01). In contrast, subfoveal hard exudates (OR 7.41 [1.19-46.2]; p=0.03) predicted visual acuity outcome worse than 20/40.

**Conclusions:** Our patient population had a favorable response to focal laser treatment, compared to historical white populations, at least at shorter follow-up. Focal laser remains an efficacious treatment option for DME, especially in patients with limited follow-up capabilities and in lower resource settings.
Monotherapy For Mild to Moderate Diabetic Macular Edema
Subthreshold Micropulse Diode Laser Photocoagulation

Stela Vujosevic1, Ferdinando Martini1, Enrica Convento1, Evelyn Longhin2, Elisabetta Pilotto2, Edouard Medina2. 1Department of Ophthalmology, University of Padova, Padova, Italy; 2Fondazione GB Bietti-IRCCS, Roma, Italy.

Purpose: To evaluate the safety and efficacy of subthreshold micropulse diode laser as monotherapy for mild to moderate diabetic macular edema.

Methods: This was a retrospective chart review of 11 patients with mild to moderate, non-ischemic, non-tractional diabetic macular edema observed on clinical exam and confirmed by spectral domain optical coherence tomography (SD-OCT). All patients had visual field loss due to diabetic macular edema and were not candidates for photodynamic therapy.

Results: The average visual acuity improved by a mean of 9.2 letters (p<0.05) and 7.4 letters (p<0.05) in the treated (IR-MPL) and Y-MPL groups, respectively. At 1 year, 67% of treated eyes maintained at least 20/40 visual acuity. SD-OCT showed significant improvement in mean central retinal thickness, volume, and area in both treatment groups at 1 year.

Conclusions: Subthreshold micropulse diode laser appears to be safe and effective as monotherapy for mild to moderate diabetic macular edema.

Commercial Relationships: Stela Vujosevic, None; Ferdinando Martini, None; Enrica Convento, None; Evelyn Longhin, None; Elisabetta Pilotto, None; Edouard Medina, None.

Program Number: 2381 Post Board Number: C0082
Presentation Time: 2:45 PM - 4:30 PM
optical coherence tomography with a central macular thickness of less than 400 microns. Best-corrected visual acuity (BCVA) ranged from 20/30 to 20/80. None of the patients had received treatment for diabetic retinopathy in the previous six months. Subthreshold micropulse diode laser (577 nm) was performed with a 5% duty cycle and power ranging from 80-160 mW with a spot size of 100 microns. Best-corrected visual acuity (BCVA) and central macular thickness were compared at baseline and at 4 months. Careful documentation was performed to look for appearance of new focal scars during the follow up visits.

**Results:** The preoperative best-corrected visual acuity and central macular thickness ranged from 20/30 to 20/80 and 285 +/- 82 microns respectively. At 4 months, visual acuity was gained or maintained within 1 line in 8 of the 11 patients (72.7%). The central macular thickness improved to 274 +/- 76 microns in 9 of the 11 patients (81.8%). No new laser scars were detected in any patient.

**Conclusions:** Subthreshold micropulse diode laser appears to be safe and effective in controlling mild to moderate diabetic macular edema. The absence of detectable focal scars theoretically allows safe retreatment if necessary, while preserving macular function. Combination with anti VEGF therapy might be a valuable option in cases of severe and diffuse diabetic macular edema. Further studies with larger patient groups are needed in the future.

**Commercial Relationships:** Rohit Adyanthaya, None; Gabriela Zavala, None; Victor H. Gonzalez, Genetech (C), Regeneron (C), Pfizer (C), Valiant (C), Alimera (C)

**Program Number:** 2382 **Poster Board Number:** C0083

**Presentation Time:** 2:45 PM - 4:30 PM

**Tissue sparing micropulse laser for the treatment of diabetic macular oedema**

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**Purpose:** Tissue sparing micropulse retinal laser can be used for the treatment of diabetic macular oedema. It allows the tissue to cool between laser pulses, minimizing tissue damage. Treatment risks are reduced, with increased patient comfort than with conventional continuous-wave laser treatment. This prospective non-comparative case series studied the effectiveness of micopulse laser in the treatment of diabetic macular oedema.

**Methods:** This was a non-comparative case series. 36 eyes of 23 patients received micropulse laser for clinically significant macular oedema. A 810nm laser was used for all treatments (Iridex, Mountainview, CA)

The settings used for macular treatment were 100 μm x 950 miliwatts x 5% duty cycle x 300 milliseconds. the laser was applied in a dense contiguous pattern over the edematous area based on OCT. An indirect Area Centralis (Volk Optical, Mentor, OH) contact lens was used for all treatments.

Parameters measured included visual acuity, central macular thickness, central 1 mm OCT volume, central 6 mm OCT volume, fundus autofluorescence. Patients received treatment on an “as required” basis at regular review.

**Results:** Mean Visual acuity improved from 0.78 to 0.84 after laser. Mean central 1mm and 6mm OCT volume remained stable following treatment. Central 1mm volume was 0.231mm³ before and 0.238mm³ after laser treatment. Mean central 6mm OCT volume was 7.975mm³ before and 7.965mm³ after laser. Central macula thickness remained stable at 296μm before and 298μm after laser. There was no evidence of RPE damage seen on fundus autofluorescence.

**Conclusions:** Tissue sparing micropulse laser has a beneficial long-term effect on maintenance of visual acuity and resolution of diabetic macula oedema. The treatment was associated with no chorioretinal damage.
loss of vision in 36% of cases. The median VA gain was 5 ETDRS letters [-15 to 21] at 2 months and 3 letters [-11 to 27] at 4 months. A gain of more than 10 letters was observed in 27% of cases at 2 months and 24% at 4 months. Eight eyes (21%) developed a transient IOP increase 2 months after injection, which was successfully managed with medical treatment.

Conclusions: At 2 months, I-Dex treatment allowed systematic anatomic improvement in all patients, and functional improvement in more than half cases, with good safety. However, recurrence of edema was observed in 76% of cases at 4 months, leading to re-treatment in more than one third of cases.

Commercial Relationships: Sophie BONNIN, None; Benedicte M. Dupas, Novartis (C); Julien Perol, None; Ali Erginyay, Novartis (R), Bayer (R), Alimera (C); Ramin Tadayoni, Alcon (C), Novartis (C), Allergan (C), DORC (R), Bausch + Lomb (R), FCI-Zeiss (C), Takeda (R), Alimera (R), Bayer (C); Pascale Massin, Novartis (C), Allergan (C), Fovea Pharmaceutical (C), Fournier Abbott (C)

Program Number: 2384 Poster Board Number: C0085
Presentation Time: 2:45 PM - 4:30 PM
Dexamethasone Intravitreal Implant at the Time of Cataract Surgery in Patients with Diabetic Macular Edema
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Purpose: It is well known that the presence of chronic and persistent diabetic macular edema (DME) can vanish the visual benefits of phacoemulsification (PE) in these patients. Nevertheless cataract extraction can be necessary both to maintain residual visual function and for a correct follow up of retinopathy. The use of dexamethasone intravitreal implant (Dex-I) at the time of surgery has an elevate rationale in these patients due to its combined high anti-inflammatory and anti-VEGF properties together with its long lasting effect and absence of systemic side effects. We here report the functional and anatomical results of a combined surgical procedure of Dex-I and PE in 7 patients with cataract and chronic DME followed for six months after surgery.

Methods: Seven consecutive type-2 diabetic patients with cystoid chronic DME and advanced nuclear cataract (N3-5 at LOCS-III chart) underwent PE. Dex-I was injected as the first surgical maneuver and than PE and IOL implantation proceeded as usual. Postop topical therapy for the first month included combined steroid/antibiotic and combined acetazolamide/B-blocker eye drops. Follow up visits were scheduled at one week and than monthly for 6 months. We measured variations in foveal thickness (FT) and macular thickness (MT) at SD-OCT, changes in ETDRS visual acuity (VA) and intraocular pressure (IOP).

Results: Mean preop FT was 344μ (range 278-489), preop visual acuity was 18 letters (range 5-26) and mean IOP 17mmHg (range 14-19). Mean preop glicated haemoglobin (HbA1c) was 7.2% (range 6.2-9.8). No complications were registered during or after the surgical procedure. During follow up, mean FT decreased by 122μ (range 81-213) at 1W, 137μ (76-198) at M1, remained unchanged at M2/M3 and than at M4 the gain reduced to 56μ (12-109) to progressively return to preop values at M5 and M6 (final mean FT 356μ). Mean VA change was +5 letters at 1W (range -1+13), +8 (range +2+/+12) at 1M, +11/13 (range +1+/+16) at M2-3.4-5, and +9 (range +3+/+8) at M6. IOP remained ≤23mmHg in all patients (hypotensive eye drops maintained until M6 in 3 patients)

Conclusions: In this small case series, Dex-I avoided worsening of chronic DME after cataract extraction and also improved foveal thickness for up to 4-5 months. Dex-I appears to be a good surgical adjuvant in these cases, but larger studies are necessary to confirm these data.

Commercial Relationships: Elena Gusson, None; Giacomo Panozzo, None; Stefano Casati, None

Program Number: 2385 Poster Board Number: C0086
Presentation Time: 2:45 PM - 4:30 PM
Dexamethasone Intravitreal Implant for Diabetic Macular Edema
Giacomo Panozzo1, Elena Gusson1, Stefano Casati2.
1Ophthalmology, Bussolengo Public Hospital, Verona, Italy; 2Ophthalmology, Verona University of Medicine, Verona, Italy.

Purpose: To evaluate the anatomical and functional efficacy of a single injection of dexamethasone intravitreal implant 0.7mg (Ozurdex, Allergan) for diabetic macular edema (DME).

Methods: We administered a single dose of dexamethasone intravitreal implant in 18 eyes of 18 consecutive patients with type 2 diabetes and cystoid macular edema. Of these 18 eyes, 10 eyes (Group 1) had DME refractory to previous intravitreal anti-VEGF treatment (plus focal laser in 3 eyes), and 8 eyes received dexamethasone implant as a first line therapy (Group 2). Follow up was scheduled 1 week after injection and than monthly for four months. We measured variations in foveal thickness (FT) and macular volume (MV) at SD-OCT, changes in ETDRS visual acuity, intraocular pressure and lens opacity (LOCS chart III) in phakic eyes. Patients were further divided in two sub-groups based on glycated haemoglobin (HbA1c) ≥ 8.5%.

Results: Changes in FT and MV between preop and follow up visits were statistically similar in both Groups. Mean FT decreased by 142μ (36.9%) at 1W, 154 μ (40%) at M1, and remained than stable at M2 and M3. At M4 this gain reduced to 104μ (27%) in patients with HbA1c < 8.5%, and only to 21μ (5.4%) in patients with HbA1c > 8.5%. In Group 1 mean preop VA was 23 letters and increased by 3 letters (13%) at 1W, 12 letters (52.2%) at M1 remaining stable until M4, when decreased by 2 letters (-10%) from initial values, independently from HbA1c. In Group 2, VA improved from 41 letters at baseline to 50 (21.9%) at 1W, to 56 (36.6%) at M1, 59 (43.9%) at M2 and M3, and than at M4 returned to 42 (+2,4%) in patients with HbA1c > 8.5% and remained at 51 (+24,4%) if HbA1c < 8.5%. No differences in lens opacity were registered in phakic eyes. Intraocular pressure remained ≤ 23mmHg in all eyes (11 patients required topical ipotensive therapy).

Conclusions: In this small case series, a single dexamethasone intravitreal injection was effective in reducing DME and improving VA for up to 4 months both in naïve and refractory DME. Better glycemic control influenced the duration but not the amount of the results. Further studies are necessary to confirm these data.

Commercial Relationships: Giacomo Panozzo, None; Elena Gusson, None; Stefano Casati, None

Program Number: 2386 Poster Board Number: C0087
Presentation Time: 2:45 PM - 4:30 PM
Intravitreal Dexamethasone Implant in Patients with Refractory Diabetic Macular Edema
Pietro Frascio, Francesca Allavena, Massimo Nicolò, Serena Telani, Carlo E. Traverso, Clinica Oculistica, Genova, Italy.

Purpose: To evaluate the effects of dexamethasone intravitreal implant in eyes with refractory diabetic macular edema (DME).

Methods: In this retrospective interventional study, 4 patients with decreased visual acuity, as a result of DME refractory to treatments with anti-VEGF and/or laser photoagulation, received a dexamethasone intravitreal implant 0.7 mg. Main outcome measures included changes in best-corrected visual acuity (BCVA) and central

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retinal thickness (CRT).

**Results:** Six eyes of 4 patients (3 males, 1 female; mean age 70.7 years) were included in the analysis. The mean duration of DME was 36 months (range 24-48). All patients had undergone previous treatments for DME with intravitreal injections of anti-vascular endothelial growth factor, and/or laser photocoagulation before entering this study. At baseline, the mean BCVA was 0.73 logMAR, and the mean CRT was 475.2. The mean BCVA improved to 0.43 logMAR (p = 0.04), 0.41 logMAR (p = 0.04), 0.41 logMAR (p = 0.04), 0.53 logMAR (p = 0.1), 0.41 logMAR (p = 0.04) and 0.53 logMAR (p = 0.1) at 1, 2, 3, 6, 9 and 12 months of follow-up respectively. The mean CRT improved to 361.5 (p = 0.003), 322.7 (p = 0.004), 326.0 (p = 0.02), 349.5 (p = 0.01), 312.8 (p = 0.002) and 314.3 (p = 0.02) after 1, 2, 3, 6, 9 and 12 months of follow-up respectively. Two eyes were retreated at month 6 and 1 eye at month 9. One eye developed a transient intraocular pressure (IOP) increase 1 month after injection, which was successfully managed with topical IOP-lowering medication.

**Conclusions:** Our data show that in eyes with refractory DME, a dexamethasone intravitreal implant produced a statistically significant improvement in BCVA and CRT and may represent a novel therapeutic option.

**Commercial Relationships:** Pietro Frascio, None; Francesca Allavena, None; Massimo Nicolò, None; Serena Telani, None; Carlo E. Traverso, None

**Program Number:** 2387 **Poster Board Number:** C0088 **Presentation Time:** 2:45 PM - 4:30 PM

**Multicenter OZURDex Assessment for Diabetic Macular Edema: MOZART Study**

**Silvia Soares,1 Christian Hajjar,1 Eric Parrat,1 Pierre Yves Merite,4 Stephan Pommier,2 Franck Meyer,2 Olivier Prost-Magnin,2 Frederic Matonti,5 Sebastien Guigon2.**

1Ophthalmology, Centre Hospitalier Henri Duffaut, Avignon, France; 2Ophthalmology, P 1.5 Collective, Basse-Terre, France; 3Ophthalmology, P 1.5 Collective, Baie-Mehault, France; 4Ophthalmology, P 1.5 Collective, Aix en Provence, France; 5Ophthalmology, P 1.5 Collective, Isle sur Sorgue, France; 6Ophthalmology, P 1.5 Collective, Dijon, France; 7Ophthalmology, P 1.5 Collective, Avignon, France; 8Ophthalmology, P 1.5 Collective, Marseille, France.

**Purpose:** To evaluate the efficiency and safety of Ozurdex (intravitreal implant of 0.7mg dexamethasone) in visual impairment due to diabetic macular edema (DME).

**Methods:** This was a retrospective, multicenter, non-comparative study. 69 eyes of 59 patients with DME (17% type 1 diabetes mellitus, 83% type 2 diabetes mellitus) followed for at least 6 months (follow-up 8.8 months) were included in 5 French eye clinics (P 1.5 collective). We monitored 2 systemic parameters: blood pressure and glycemic balance. Best-corrected visual acuity (BCVA), central retinal thickness (CRT, Spectralis OCT), intraocular pressure (IOP) and cataract progression are studied at baseline and then at 1, 2, 4 and 6 months.

**Results:** The mean age of patients was 65 years. Diabetic mellitus evolved for 15 years on average. The mean systolic blood pressure was 138 mmHg and the mean HbA1c was 7.2%. 17 patients (24%) were naive to any macular treatment. At baseline the mean CRT was 540 mm; the average CRT decrease was 188 mm at Month 1 (M1), 235 mm at Month 2 (M2), 117 mm at Month 4 (M4), 77 mm at Month 6 (M6). The initial BCVA letter score was 54.4 letters ETDRS; mean improvement from baseline BCVA was 2.1 letters at M1, 5.4 at M2, 2.4 at M4 and 1.6 at M6. For naive patients this gain was increased: 5.8 letters at M1, 6.7 at M2, 8.7 at M4 and 6.7 at M6. During the follow-up 28% of patients had a BCVA >20/40 (73 letters), for only 6% at the baseline. A gain greater than 15 letters was found in 28% of patients; a loss greater than 15 letters was found in 6% of patients. The mean rate injections was 1.2 at 6 months with an average of 4.9 months for re-injection. The mean initial PIO was 15 mmHg; ocular hypertension greater than 25 mmHg, managed by topical treatment, was observed in 7% of patients. 4% of progression of cataract, 1.5% of vitreous hemorrhage and none endophthalmitis were reported.

**Conclusions:** Dexamethasone has an anatomical and functional effectiveness in the treatment of DME. Outcomes for naive patients suggest that the duration of diabetes mellitus and previous treatments are negative factors of recovery. Side effects are rare and manageable. OZURDEX seems to be a treatment for visual impairment due to DME with a favorable safety profile. Patient follow-up must be adapted to the duration of action of the product with a consultation before M2 to detect any high intraocular pressure and before M4 to detect DME recurrence.

**Commercial Relationships:** Silvia Soares, None; Christian Hajjar, None; Eric Parrat, None; Pierre Yves Merite, None; Frederic Pommier, None; Franck Meyer, None; Olivier Prost-Magnin, None; Frederic Matonti, Allergan (C), Alcon (R), Théa (R), Topcon (R); Sebastien Guigon, None

**Program Number:** 2388 **Poster Board Number:** C0089 **Presentation Time:** 2:45 PM - 4:30 PM

**Real-life use of ranibizumab in the treatment of diabetic macular edema: results on visual acuity at month 6 in a French Phase IV study (LUDIC study)**

**Pascale Massin,1 Laurent Kodjikian,2 Marie Laure Lelez,2 Ali Erginay3, Stéphane Quéré2, Véronique Schneider,2.**

1Ophthalmology, Hôpital Lariboisière, Paris, France; 2Ophthalmology, Hôpital de la Croix Rousse, Lyon, France; 3Ophthalmology, Hôpital Bretonneau, Tours, France; 4Research Departement, Novartis Pharma, Reuil Malamaison, France.

**Purpose:** To describe the visual acuity (VA) results from a prospective interventional phase IV study designed to investigate efficacy in real-life use of ranibizumab in diabetic macular edema (DME), and compare it with that observed in RESTORE, a key development study.

**Methods:** LUDIC is an open-label single-arm study. Patients recruited at 46 centers were given three monthly injections of ranibizumab and retreated if necessary in strict application of the current Summary of Product Characteristics (SmPC). In contrast with the development studies, no exclusion criteria related to prior treatment for DME were imposed.

**Results:** Between February and December 2011, 350 patients were enrolled. At baseline mean age was 63.7 years, diabetes had been diagnosed for 18 years and DME had been diagnosed for 2.2 years (mean values). Mean baseline VA was 57.0 ± 10.3 letters, versus 64.7 letters in RESTORE. 48.1% of patients had been treated by laser photocoagulation during the preceding 12 months and 19.7% had been treated with IVT anti-VEGF. The proportion of patients demonstrating a 10 letters gain from baseline after 6 months of IVT ranibizumab treatment (primary endpoint) was 39.9%, versus 34.8% in RESTORE. The mean change in VA from baseline after 6 months was 7.1 ± 10.2 ETDRS letters (6.7 ± 7.3 in RESTORE at 6 months). The correlation coefficient between gain in VA after 3 consecutive injections and VA at M6 was 0.6678 (p<0.0001). The mean number of injections needed to achieve a VA gain ≥10 letters was 2.3 ± 1.3 injections; the mean number required to achieve stable VA (variation <3 letters) for three consecutive visits was 3.9 ± 1.0.

**Conclusions:** This phase IV study conducted in a real world setting
showed VA gains comparable to those observed in the pivotal study RESTORE despite lower VA at baseline and including patients with a broader range of medical histories pretreatments. This confirms the effectiveness of the individualised treatment regimen as recommended in the Lucentis® SmPC and the relevance of the RESTORE study.

**Commercial Relationships:** Pascale Massin, Novartis (C), Allergan (C), Fovea Pharmaceutical (C), Fournier Abbott (C); Laurent Kodjikan, None; Marie Laure Lelez, None; Ali Erginay, Novartis (R), Bayer (R), Alimera (C); Stéphane Quéré, Novartis Pharma SAS (E); Véronique Schneider, Novartis (E)

**Support:** NOVARTIS PHARMA Support

**Clinical Trial:** NCT 01315275

**Program Number:** 2389 Poster Board Number: C0090

**Beneficial Effects of Intravitreal Fasudil in Diabetic Macular Edema**

Ali Hafezi-Moghadam¹, Ramin Nourinia², Souska Zandi³, Shintaro Nakao⁴, Hamid Ahmadi⁵.¹ Radiology, Harvard Medical School, Boston, MA; ²Ophthalmology, Labbafinejad Medical Center, Tehran, Islamic Republic of Iran.

**Purpose:** New treatments of diabetic macular edema (DME) are highly desired in cases that are refractory to anti-VEGF treatment. Recently, the key role of the ROCK pathway in diabetic retinopathy was elucidated. Here, we investigate the efficacy of intravitreal fasudil, a potent pan ROCK inhibitor, together with bevacizumab in anatomical and visual outcomes of patients with DME resistant to previous treatments.

**Methods:** This prospective interventional small case series included 5 patients (59-76 years), who had persistent DME after macular laser photocoagulation and multiple intravitreal bevacizumab (IVB) injections (2.8±1.3). Fasudil (0.025 mg/0.05 ml, Asahi Kasei Pharma, Japan) and Avastin (1.25mg/0.05ml, Roche, Switzerland) were injected at two separate sites. Anterior chamber paracentesis was performed. Best Corrected Visual Acuity (BCVA), central macular thickness (CMT) by OCT (SD-OCT Cirrus, Zeiss, Germany), and electroretinograph (ERG, Roland Consult, Germany) were recorded before and 6 weeks after the injections.

**Results:** The mean BCVA before intervention, 0.82±0.34 logMAR, significantly improved to 0.34±0.26 logMAR (P<0.05), six weeks after combined treatment. Mean CMT (409±74µm) significantly decreased (314±29µm) six weeks after treatment (P<0.05), while ERG showed no sign of toxicity.

**Conclusions:** These results may pave the way for the use of fasudil in treatment of DME cases refractory to current therapies.

**Commercial Relationships:** Ali Hafezi-Moghadam, None; Ramin Nourinia, None; Souska Zandi, None; Shintaro Nakao, None; Hamid Ahmadi, None

**Support:** NIH, AHA, MPOB

**Program Number:** 2390 Poster Board Number: C0091

**The LUCIDATE study: a randomized clinical trial to evaluate the long-term functional and anatomical effects of repeated ranibizumab therapy compared with laser in diabetic macular edema**

Oliver Comyn, Tunde Peto, Catey Bunce, Magella M. Neveu, Graham E. Holder, Praveen J. Patel, Catherine A. Egan, James W. Bainbridge, Philip G. Hykin. NIHR Biomedical Research Centre at Moorfields Eye Hospital and University College London Institute of Ophthalmology, London, United Kingdom.

**Purpose:** To determine the effect of repeated ranibizumab treatment on retinal function and morphology associated with diabetic macular edema (DME) and to identify factors that may be associated with a favourable treatment response.

**Methods:** Randomized controlled trial. 36 subjects with center-involving DME; BCVA 55-79 ETDRS letters, OCT central retinal thickness >300 µm and moderate macular ischemia only were randomized 2:1 to receive ranibizumab 0.5 mg (3 initial 4-weekly injections then pm retreatment) or modified ETDRS laser (at baseline and every 12 weeks if CSME present). Criteria included a foveal avascular zone (FAZ) <1000 µm and perifoveal capillary loss less than severe. Subjects underwent best-corrected ETDRS visual acuity, fluorescein angiography; Spectralis OCT; Nidek MP1 microprecision; ChromaTest color contrast sensitivity; and pattern, full-field and multifocal electroretinography at baseline, 12, 24 and 48 weeks (primary endpoint for exploratory outcomes). Masked graders evaluated angiographic images for FAZ characteristics and OCT scans for the presence of retinal fluid, hyperreflective foci, outer retinal disruption and vitreomacular interface abnormalities.

**Results:** 33 patients completed 48 weeks follow up. Ranibizumab-treated subjects gained 6.0 ETDRS letters while laser subjects lost 0.9 letters (p=0.008). FAZ area increased from baseline to 48 weeks in ranibizumab-treated subjects by 0.113±0.124 mm² and by 0.153±0.078 mm² in laser treated subjects (p=0.34). At 48 weeks, external limiting membrane was more likely to be present than interrupted in the ranibizumab group than the laser group (45% vs 0%, p=0.013). Retinal sensitivity improved in the central 4° by 3.2 dB in the ranibizumab group and by 1.9 dB in the laser group. Tritan color contrast threshold improved from 81% to 70% (ranibizumab) and from 89% to 86% (laser). PERG P50 amplitude decreased in laser-treated subjects by 10.7% at 48 weeks and remained constant for ranibizumab-treated subjects. Other electrophysiological parameters showed no significant changes.

**Conclusions:** This exploratory study has shown a trend towards greater improvements in visual function with ranibizumab therapy than with laser for DME, without evidence of increased macular ischemia. These findings can be used to inform the design of larger clinical trials.

**Commercial Relationships:** Oliver Comyn, Novartis (F), Novartis (R); Tunde Peto, None; Catey Bunce, None; Magella M. Neveu, None; Graham E. Holder, Servier (C); Praveen J. Patel, Allergan (R), Bayer (C), Novartis UK (C), Heidelberg UK (R), Topcon UK (R), Thrombogenics (C); Catherine A. Egan, Bayer (S), Oculogics (S), Novartis (S), Allergan (S), Novartis (F); James W. Bainbridge, Novartis (F), Alimera (C), Gene Signal (C), Advanced Cell Technology (F), Targeted Genetics (P), Oxford Biomedica (C), GSK (F); Philip G. Hykin, Bayer (C), NOVARTIS (C), ALLERGAN (C), BAYER (R), NOVARTIS (R), ALLERGAN (F), NOVARTIS (F)

**Support:** NIHR Moorfields Biomedical Research Centre; Novartis Pharmaceuticals (UK) Ltd.

**Clinical Trial:** NCT01223612

**Program Number:** 2391 Poster Board Number: C0092

**Bevacizumab and Ranibizumab in the treatment of diabetic macular oedema: Can results from clinical trials be reproduced in the National Health Service?**

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Purpose: To assess the reproducibility of clinical trials on the treatment of DMO with anti-VEGF modalities in the National Health Service in the United Kingdom.

Methods: A retrospective case note analysis of patients treated with Bevacizumab or Ranibizumab for DMO at two west London hospitals. Minimum 12month follow up. Treated between 2008-2012.

Outcome measures:
1. Difference in ETDRS best-corrected visual acuity (BCVA) at Baseline and 12 months.
2. Mean change in BCVA
3. Proportion gaining at least 15 letters, 0-15 letters and 0-10 letters
4. Change in central macular thickness.

Results: 91 patients were treated with Bevacizumab and 15 with Ranibizumab that met the diagnostic and follow up inclusion criteria. The Bevacizumab group showed 7 ETDRS letter gain with a mean change in CMT of -104 µm. 70% of patients responded to treatment with 22% gaining ≥ 15 letters and 48.4% gaining between 0-10 letters. In the Ranibizumab group a 4 ETDRS letter gain with a mean change in CMT of -64 µm was obtained. 40% of patients responded to treatment with 13% gaining ≥ 15 letters and 27% gaining 0-10 letters. There were no adverse events reported in either group.

Conclusions: Although both anti-VEGF modalities improved visual acuity the degree of improvement was inferior to that seen in the recently published clinical trials. In our study the results for Bevacizumab were superior to Ranibizumab.

Commercial Relationships: Nicholas Brennan, None; Maxwell P. Treacy, None; Conor Ramsden, None; Nicholas Lee, novartis (R)

Program Number: 2392 Poster Board Number: C0093
Presentation Time: 2:45 PM - 4:30 PM

Visual Outcomes Following Bevacizumab Treatment in Diabetic Macular Edema

Jluiwi almasaud1, Abdulrahman M. Alfaran2, Ahmed Mousa2, Nicola G. Ghazi1. 1King khaled eye special hospital, Riyadh, Saudi Arabia; 2King saud university, Riyadh, Saudi Arabia.

Purpose: To study the visual outcomes following intravitreal bevacizumab treatment for eyes with center-involved diabetic macular edema (CIDME).

Methods: A retrospective study of 1000 eyes with CIDME that received intravitreal bevacizumab as their main treatment at the King Khaled Eye Specialist Hospital. At each follow up visit, a full ophthalmic evaluation was performed. Fluorescein angiography was obtained as per physician’s preference. Statistical analysis comparing the final and baseline visual acuity was performed.

Results: Forty-nine eyes of 35 patients were analyzed at the time of this writing. Twenty-five patients (71.4%) were males and 10 (28.6%) were females with a mean age of 57.22 years (range 29 - 78 years; SD= 10.4). The baseline log MAR visual acuity ranged from 0.3 to 1.2 (mean ± SD= 0.53 ± 0.23) (20/40 to 20/300 Snellen equivalent range). The mean duration of follow-up was 13.6 months (range 6 - 36 months; SD= 7.6). Nineteen eyes (38.8%) had at least two lines of Snellen visual acuity improvement at final follow up.

Conclusions: Bevacizumab may improve vision in a substantial proportion of patients with CIDME. It may be an alternative to ranibizumab as a first line therapy for this condition.

Commercial Relationships: Jluiwi almasaud, None; Abdulrahman M. Alfaran, None; Ahmed Mousa, None; Nicola G. Ghazi, None

Program Number: 2393 Poster Board Number: C0094
Presentation Time: 2:45 PM - 4:30 PM
**Results:** Data from 739 patients were available for analysis. Through 24 months of treatment the percentages of study eyes in the absent category increased from 20.9% to 36.5% in the sham arm and from 22.1% to 60.7% and 23.6% to 61.2% in the ranibizumab 0.3 and 0.5 mg arms respectively. The resolution of DME was not paralleled by an increase in HE. Decrease in percentage of study eyes in the HE present category was evident after 6 months in the ranibizumab arms. At baseline, there was no correlation between VA and presence of HE in the central subfield in any treatment arm. Post-baseline, there was no consistent correlation between presence of HE in the central subfield and VA change over time.

**Conclusions:** In this exploratory analysis, ranibizumab appears to result in a reduction in the distribution of HE in patients with DME. However, baseline VA was not associated with the presence of HE, nor was the therapeutic benefit of ranibizumab on visual acuity clearly associated with the presence or absence of HE in the central subfield. Additionally, contrary to prior expectations, the presence and area of HE did not increase as DME resolved (both in the ranibizumab or sham groups).

**Commercial Relationships:** Michael S. Ip, Eye Technology Ltd. (C), Genentech, Inc. (C), NioX (C), Notal Vision (C), QLT Phototherapeutics, Inc. (C), Regeneron (C), Sirion (C), Allergan, Inc (F), Regeneron (F); Amitha Domalpally, None; Dafeng Chen, Genentech/Roche (F), Genentech/Roche (C); Jason S. Ehrlich, Genentech (E), Roche (I)

**Support:** Genentech, Inc.

**Clinical Trial:** NCT00473330 and NCT00473382

**Program Number:** 2395 **Poster Board Number:** C0096

**Presentation Time:** 2:45 PM - 4:30 PM

**Ranibizumab for the treatment of diabetic macular edema in patients treated with Bevacizumab**

**Gisela Velez,** Ophthalmology, Univ of Massachusetts Med School, Worcester, MA; 3Central Massachusetts Retina and Uveitis Center, Worcester, MA.

**Purpose:** Anti-VEGF agents have been shown to be effective in the treatment and management of diabetic macular edema. The CATT study has shown that Ranibizumab (Lucentis) and Bevacizumab (Avastin), are similarly effective for the treatment of exudative macular degeneration. The purpose of our study is to determine whether or not there is an advantage to the use of Ranibizumab over Bevacizumab; in the management and treatment of diabetic macular edema.

**Methods:** The records of all patients treated with anti-VEGF agents for diabetic macular edema were reviewed. 25 eyes (of 16 patients) were identified which had been treated first with Bevacizumab (1.25 mg), then switched to Ranibizumab (0.3 mg). Visual acuity was measured by Snellen chart and retinal thickness was measured using Cirrus OCT. All eyes were treated at monthly intervals.

**Results:** All eyes treated with Bevacizumab showed an improvement in visual acuity, with a reduction in retinal thickening on OCT. On average, each eye received a total of 8 intravitreal Bevacizumab injections before switching to Ranibizumab. All of the eyes had persistent thickening on OCT after treatment with Bevacizumab. After Bevacizumab, each eye received an average of 6 Ranibizumab treatments. Although Ranibizumab injections did not result in a significant improvement in VA, there was an observed decrease in retinal thickness as measured by OCT, in patients switched from Bevacizumab to Ranibizumab.

**Conclusions:** Although Ranibizumab can result in better anatomical results, Bevacizumab is equally effective and results in VA improvement. Bevacizumab is therefore a viable alternative to Ranibizumab for the treatment of diabetic macular edema.
Fluorescein angiography: DME at baseline

OCT spectral domain: DME at baseline

Commercial Relationships: Cazet-Superville Agathe, None; Michèle Boissonnot, None; Nicolas Leveziel, None
Clinical Trial: 2010-02397224

Program Number: 2397 Poster Board Number: C0098
Presentation Time: 2:45 PM - 4:30 PM

Pegaptanib in the treatment of ischemic diabetic macular edema

Purpose: Pegaptanib has been shown to be an effective treatment in patients with diabetic macular edema (DME). In the original trial, however, patients with ischemia were excluded from the study. In this prospective, Phase IV, single-arm clinical trial, we have treated patients with ischemic DME.

Methods: Ischemia was defined as a 30% increase in the area of the foveal avascular zone (FAZ) at 45 seconds on a fundus fluorescein angiogram (FFA). Participants were also required to have diffuse, fovea-involving DME with a central subfield thickness (CST) >300 microns on Heidelberg spectral domain optical coherence tomography. Five intravitreal Pegaptanib injections were given 6 weeks apart, with a final visit 6 weeks after the fifth injection. The primary study outcome was change in the size of the FAZ at 45 seconds on FFA. This was measured using Adobe Photoshop on a standardised image size. Secondary study outcomes were changes in best corrected visual acuity (BCVA) and CST over the 6 visits. Participants were subdivided into those with minimal/moderate ischemia (n=16, FAZ area <1000 pixels) and those with more severe ischemia (n=14, FAZ area >1000 pixels).

Results: There were 30 participants. Mean age was 66.5 years (range 43-89 years) and the male:female ratio was 2:1. Three patients were unable to complete the full course of treatment: one due to a drop in BCVA of >30 letters, another due to bowel ischemia and another chose to discontinue treatment after 3 injections. The final results for these participants were carried forward for the purpose of this analysis. The overall mean FAZ area changed from 964 pixels at baseline to 937 pixels at Visit 6 (p=0.771). In the minimal/moderate ischemia group the mean FAZ area increased from 441 pixels at baseline to 538 pixels at Visit 6 (p=0.335). In the more ischemic group mean FAZ area decreased from 1562 pixels to 1500 pixels (p=0.624). Overall mean BCVA increased from 47.8 letters to 49.7 letters (p=0.476) and mean CST decreased from 491 microns to 451 microns (p=0.128). Analysis of the mean BCVA of those who completed the full course of treatment shows an increase from 49.2 letters at baseline to 53.9 letters at Visit 6 (p = 0.046).

Conclusions: In our study intravitreal injection of Pegaptanib did not significantly alter the size of the FAZ in patients with varying degrees of ischemia and DME. In addition it did not lead to a statistically significant improvement in BCVA or CST.

Commercial Relationships: Christine A. Kiire, None; Rupal Morjaria, None; Robert M. Purbrick, None; Spyridon Charisis, None; Sami Habal, None; Victor Chong, Novartis (C), Bayer (C), Allergan (C), Pfizer (F), Novartis (F), Alimera Science (C), Quantel (R)
Support: Funded by Pfizer.
Clinical Trial: NCT01175070

Program Number: 2398 Poster Board Number: C0099
Presentation Time: 2:45 PM - 4:30 PM

Comparison of Bevacizumab and Ranibizumab on Central Sub-Foveal Thickness and Visual Acuity in Diabetic Macular Edema
Loren S. Jack1, 2, Charles R. Blake2. Ophthalmology, University of South Carolina/Palmetto Health, Columbia, SC; Ophthalmology, William Jennings Bryan Dorn Veterans Administration Memorial Center, Columbia, SC.

Purpose: Compare the response of the first injection of ranibizumab and bevacizumab in diabetic macular edema in patients without and after focal macular laser to determine the sample size needed to be able to either accept or reject the null hypothesis. The only prior study that directly compared ranibizumab to bevacizumab included only 29 patients.

Methods: 48 eyes at the Williams Jennings Bryce Dorn VAMC in Columbia, SC were identified which had received injections of either bevacizumab or ranibizumab for diabetic macular edema from 1/01/08 - 03/31/12. Pre- and post-treatment central sub-foveal thickness, visual acuity, and when focal macular laser was applied were obtained.

The mean and standard deviation of change of the central macular thickness of ranibizumab and bevacizumab without focal laser targeting injections given between 01/01/08 - 10/31/11 were compared by Student’s T-test. Exclusion criteria: exudative ARMD, vein occlusion, intravitreal or periocular injection within a year.

Results: There was a statistical difference in the pre-treatment central sub-foveal thickness of the ranibizumab without focal group when compared to the ranibizumab after focal group with the later being more edematous (p=0.02). There was no statistical difference between the ranibizumab without focal and bevacizumab without focal (p=0.24). There was no statistical difference between ranibizumab after focal and bevacizumab after focal (p=0.28). There was no statistical difference between ranibizumab without focal and ranibizumab after focal (p=0.57). There was no statistical difference between bevacizumab without focal and bevacizumab after focal (p=0.51).
Conclusions: Although statistical differences were not detected between any treatment groups, linear regression analysis for the ranibizumab groups, both without and after focal, followed a trend toward greater effectiveness when compared to both bevacizumab groups. This study suggests that there may be a difference in the mean reduction of central sub-foveal thickness of ranibizumab when compared to bevacizumab. More importantly, this study gives us information regarding reasonable means and standard deviations required to determine an adequate sample size. Based on these findings, approximately 45 patients per group are required to have sufficient power to either accept or reject the null hypothesis.

Commercial Relationships: Loren S. Jack, None; Charles R. Blake, None

Program Number: 2399 Poster Board Number: C0100
Presentation Time: 2:45 PM - 4:30 PM

Impaired Vascular Endothelial Function in Patients with Diabetic Macular Edema

Purpose: The retinal vascular endothelial dysfunction may play a role in the breakdown of the blood-retinal barrier and leakage of plasma from retinal vessels and capillaries, resulting in diabetic macular edema (DME). To determine if the vascular endothelial function is involved in the pathogenesis of DME, we measured brachial artery flow-mediated vasodilation (FMD) in patients with diabetes.

Methods: Twenty-three patients with type 2 diabetes mellitus (DM) and nonproliferative diabetic retinopathy were enrolled. Based on optical coherence tomography and fluorescein angiography findings, the patients were divided into 2 groups: the DME(+) group (n=12; mean age, 65.9 ± 7.6 years) and the DME(-) group (n=11; mean age, 64.1 ± 10.3 years). We evaluated the logarithm of the minimum angle of resolution (logMAR VA) and central macular thickness (CMT). Using high-resolution ultrasonographic imaging, we evaluated the FMD by measuring changes in the brachial artery diameter during reperfusion after arterial occlusion.

Results: The mean CMTs ± standard deviations (SDs) were 410.2 ± 131.1 μm and 229.9 ± 33.5 μm in DME(+) and DME(-) groups, respectively. The mean logMAR VAs ± SDs were 0.42 ± 0.38 and 0.10 ± 0.07 respectively. There were significant differences in the CMT and logMAR VA between the two groups (p<0.001 for both comparisons). The group-averaged FMD values were significantly lower in the DME(+) group (3.1 ± 1.5%) compared with the DME(-) group (5.4 ± 2.7%, p = 0.035). In the DME(+) group, the FMD value was not significantly correlated with the CMT and logMAR VA.

Conclusions: The current results showed that the FMD in patients with DME with type 2 DM was lower than in patients without DME, suggesting that impaired systemic vascular endothelial function might be associated with the pathogenesis of DME.

Commercial Relationships: Kengo Takahashi, None; Taiji Nagaoka, None; Akihiro Ishibazawa, None; Kenji Sogawa, None; Akitoshi Yoshida, None

Program Number: 2400 Poster Board Number: C0101
Presentation Time: 2:45 PM - 4:30 PM

Association between Diabetic Macular Edema and Chronic Kidney Disease in Patients with Type 2 Diabetes

Purpose: To investigate the association between diabetic macular edema (DME) and chronic kidney disease (CKD) in type 2 diabetic mellitus patients.

Methods: Sixty-one eyes of 61 patients with clinically relevant DME were analyzed using optical coherence tomography (OCT) and fluorescein angiography (FA). The features of DME were classified from OCT and FA findings. The presence of CKD was defined as persistent proteinuria or an estimated glomerular filtration rate below 60 ml/min/1.73 m². The central macular thickness (CMT) and logarithm of the minimum angle of resolution (logMAR) visual acuity (VA) also were analyzed. We separately analyzed the presence of cystoid macular changes and serous retinal detachment (SRD) in patients with or without CKD.

Results: Based on OCT and FA findings, DME were classified as focal (microaneurysm leakage), diffuse (dilated capillary plexus leakage), combined, and ischemic (foveal avascular zone enlargement). The patients were divided into those without CKD (CKD(-) group, n=39) and those with CKD (CKD(+) group, n=22). The mean CMTs ± standard deviations (SD) in the CKD(-) and CKD(+) groups were 473.7 ± 157.2 μm and 474.78 ± 131.3 μm, respectively (not significant [NS]). The mean logMAR VAs ± SDs in the CKD(-) and CKD(+) groups were 0.31 ± 0.3 and 0.33 ± 0.3, respectively (NS). Regarding the DME classifications, the incidence rates of focal, diffuse, combined, and ischemic patterns were 58.8%, 10.3%, 23.7%, and 5.2%, respectively, in the CKD(-) group, and 47.8%, 8.7%, 39.1%, and 4.3%, respectively, in the CKD(+) group. There were no significant differences in these DME classification between the CKD(-) and CKD(+) groups. Cystoid changes occurred in 79.5% of the CKD(-) group and 86.4% of the CKD(+) group (NS). However, SRDs developed in 28.2% of the CKD(-) group and 63.6% of the CKD(+) group, a difference that reached significance (p=0.015).

Conclusions: SRDs developed significantly more frequently in patients with CKD with DME, which suggested that impaired renal function might be associated with DME.

Commercial Relationships: Akihiro Ishibazawa, None; Taiji Nagaoka, None; Kengo Takahashi, None; Atsushi Takahashi, None; Harumasa Yokota, None; Akitoshi Yoshida, None

Support: Grant-in-Aid for Young Scientists (B) 23791956

Program Number: 2401 Poster Board Number: C0102
Presentation Time: 2:45 PM - 4:30 PM

Response of Hyperreflective Foci in Diabetic Macular Edema to Laser

ARVO 2013 Annual Meeting Abstracts by Scientific Section/Group – Retina

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Anne-Marie Firan, Raeba Mathew, Sobha Sivaprasad.
Ophthalmology, King's College Hospital, London, United Kingdom.

**Purpose:** Hyperreflective foci (HRF) on Spectral Domain Ocular Coherence Tomography (SD-OCT) have been frequently observed within the neurosensory retina in patients with diabetic macular edema (DME). The aim of this study was to evaluate the relationship of HRF in DME to the central subfield thickness and response to macular laser treatment.

**Methods:** This is a retrospective chart analysis on 50 eyes of diabetic patients with centre-involving macular edema. Subjects were from three ethnic groups (Asian, Afro-Caribbean and Caucasian). The OCT scans were performed using a standard protocol on the Heidelberg Spectralis SD-OCT as part of routine medical care. Hyperreflective foci and central subfield thickness (CST) in the subfoveal 1 mm area were compared and post macular laser treatment.

**Results:** In all the eyes, variable amounts of HRF were detected in the foveal and parafoveal area. The mean number of HRF reduced from 6.3 to 5.2 whereas foveal thickness reduced from 445 to 217. The HRF were seen to reduce in 64% patients, remain the same in 18% and increase in 18% of the patients. The number of HRF was not related to the initial central macular thickness. The change in central subfield thickness of the eyes showed moderate correlation with the change in number of HRF (r=0.5, p value= 0.0002). The HRF were seen to increase in eyes with worsening of macular edema following macular laser.

**Conclusions:** In diabetic macular edema, HRF are frequently present in the retinal layers on SD OCT. The numbers of HRF are seen to significantly reduce in eyes that respond to macular laser, whereas they increase in number in eyes with worsening of macular edema which may suggest that HRF may be a surrogate marker of inflammation.

**Commercial Relationships:** Anne-Marie Firan, None; Raeba Mathew, Allergan (R), Novartis (R); Sobha Sivaprasad, Allergan (F), Bayer (F), Novartis (F)

**Program Number:** 2402 Poster Board Number: C0103

**Presentation Time:** 2:45 PM - 4:30 PM

External Limiting Membrane and Inner Segment/Outer Segment Status at pre- and post-pars plana vitrectomy in DME
Noriko Miyamoto1,2, Masako Kuroda1,2, Shin-ichiro Ito1,2, Masataka Shimozono1,2, Kazuhiro Ishida1,2, Yasuo Kurimoto1,2, 1Dept of Ophthalmology, Kobe City Medical Center General Hospital, Kobe, Japan; 2Institute of Biomedical Research and Innovation, Kobe, Japan.

**Purpose:** It has been reported that the preserved external limiting membrane (ELM) and inner segment/outer segment (IS/OS) are associated with maintaining visual acuity (VA) in diabetic macular edema (DME) patients and pars plana vitrectomy (PPV) may be effective for maintaining VA. Then we studied the ELM and IS/OS status of optical coherence tomography (OCT) images in DME at pre- and post- PPV.

**Methods:** We retrospectively reviewed the spectral-domain OCT images of 40 eyes from 31 cases with DME who were treated with PPV and evaluated various factors such as the status of ELM and IS/OS, foveal macular thickness (FMT) and VA at pre- and post-PPV up to 12 months (M). We used a percentage disruption to evaluate the status of ELM and IS/OS.

**Results:** logMAR VA was 0.481 at pre-PPV and improved to 0.396 at 12M after PPV. FMT was 534.0 μm at pre-PPV, decreased gradually to 343.3 μm at 6M and increased again 400.3 μm at 12M after PPV. The percentage disruption of ELM and IS/OS were 15.0 and 38.0 % at pre-PPV, then deteriorated to 21.6 and 46.9 % at 1M.

The ELM status did not change, while the disruption of IS/OS decreased gradually at 3M (44.7) or later (39.7 at 6M and 38.8 % at 12M) after PPV.

**Conclusions:** ELM and IS/OS status once deteriorated after PPV, then ELM did not recovered, while IS/OS status recovered and VA improved after that.

**Program Number:** 2403 Poster Board Number: C0104

**Presentation Time:** 2:45 PM - 4:30 PM

Association between Near Infrared Autofluorescence and Optical Coherence Tomography in Diabetic Macular Edema
Shin Yoshitake, Tomoaki Murakami, Akihito Uji, Ken Ogin, Noriyuki Unoki, Takahiro Horii, Masayuki Hata, Shigeta Arichika, Kazuaki Nishijima, Nagahisa Yoshimura. Department of Ophthalmology and Visual Sciences, Kyoto University Graduate School of Medicine, Kyoto, Japan.

**Purpose:** To study the association of near infrared autofluorescence (NIR-AF) imaging with spectral-domain optical coherence tomography(SD-OCT) findings and logarithm of minimal angle resolution visual acuity (logMAR VA) in diabetic macular edema (DME).

**Methods:** Consecutive 87 eyes of 63 patients who had center-involved DME and on whom NIR-AF and OCT images with sufficient quality were obtained were included in this retrospective study. NIR-AF images were acquired using Heidelberg Retina Angiography 2 (HRA2), and the retinal sectional images were evaluated by Spectralis OCT. The relationship between the characteristics of NIR-AF images, OCT findings, and logMAR VA were investigated.

**Results:** Thirty-eight eyes with mosaic pattern NIR-AF at the macula had worse VA (0.372±0.251 vs. 0.248±0.221, p=0.019) and more damaged external limiting membrane (ELM) (47.4% vs. 14.3%, p=0.002) than those without this finding. Twenty-seven of 51 eyes with foveal cystoid spaces were accompanied with definite outlines of the cystoid spaces in NIR-AF images. The eyes with such outlines had worse VA (0.386±0.242 vs. 0.192±0.207, p=0.003), more damaged ELM (40.7% vs. 12.5%, p<0.01), and greater central thickness (486.7±122.0μm vs. 408.3±88.5μm, p=0.011) than those without the outlines.

**Conclusions:** NIR-AF showed mosaic pattern and outline of cystoid spaces in DME, in association with VA and OCT findings, which suggests the clinical relevance as well as the pathogenesis in DME.

**Commercial Relationships:** Shin Yoshitake, None; Tomoaki Murakami, None; Akihito Uji, None; Ken Ogin, Noriyuki Unoki, None; Takahiro Horii, None; Masayuki Hata, None; Shigeta Arichika, None; Kazuaki Nishijima, None; Nagahisa Yoshimura, Canon (C), Canon (F), Nidek (C), Topcon (F), PCT/JP2011/073160 (P)

**Program Number:** 2404 Poster Board Number: C0105

**Presentation Time:** 2:45 PM - 4:30 PM

Association between perifoveal hyperfluorescence and serous retinal detachment in diabetic macular edema
Tomoaki Murakami1, Akihito Uji1, Ken Ogin2, Noriyuki Unoki1, Takahiro Horii1, Shin Yoshitake1, Masayuki Hata1, Kazuaki Nishijima4, Nagahisa Yoshimura1. 1Ophthalmology & Visual Sciences, Kyoto Univ Grad Sch of Med, Kyoto, Japan; 2Nishijima Eye Clinic, Kyoto, Japan.

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Purpose: Diabetic macular edema (DME) has three major patterns of pathomorphology: cystoid macular edema (CME), serous retinal detachment (SRD), and sponge-like retinal swelling. However, it remains ill-defined how SRD develops in DME. Here we investigated how SRD is related to hyperfluorescence.

Methods: Consecutive 91 eyes of 69 patients with center-involved DME on whom fluorescein angiography (FA) image and optical coherence tomography (OCT) images were obtained by HRA2 and Spectralis (Heidelberg Engineering) respectively were included in this study. We first calculated the relative fluorescein leakage. Briefly, the mean fluorescein intensity in individual sectors in Early Treatment Diabetic Retinopathy Study (ETDRS) grid was measured in fluorescein angiography (FA) images. The mean intensity in the late phase was corrected using that in the early phase and the the fluorescein intensity of major vessels. We then investigated the association between fluorescein intensity in individual sector and foveal pathomorphology in OCT images.

Results: Eyes with SRD had significantly higher fluorescein intensity in the nasal or inferior quadrant of the parafovea (1-3mm) than those without SRD (p<0.001 or p=0.014), whereas fluorescein intensity in the superior or temporal quadrant did not differ. Further, fluorescein leakage in the nasal, superior, and inferior subfield of the perifovea (3-6mm) was more severe in eyes with SRD than those without SRD (p=0.002, p<0.001, and p<0.001, respectively). However, there were no differences in fluorescein intensity in any quadrants of the perifovea between eyes with CME and those without CME.

Conclusions: The relationship between foveal SRD and fluorescein leakage suggests the pathogenesis of SRD in DME.

Commercial Relationships: Tomoaki Murakami, None; Akihito Uji, None; Ken Ogino, None; Noriyuki Unoki, None; Takahiro Horii, None; Shin Yoshitake, None; Masayuki Hata, None; Kazuaki Nishijima, None; Nagahisa Yoshimura, Canon (C), Canon (F), Nidek (C), Topcon (F), PCT/JP2011/073160 (P)

Program Number: 2405 Poster Board Number: C0106
Presentation Time: 2:45 PM - 4:30 PM

Validation Measures of CSF Conversion Equations

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<th>Stratus 1 vs Stratus 2 (reproducibility data for comparison)</th>
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<td>97%</td>
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<td>% of values resulting in disagreement when classified using a cutoe of &lt;250 microns on Stratus OCT</td>
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Commercial Relationships: Jared S. Nielsen, LPath (F), Notal Vision (F), Genentech (F)

Program Number: 2406 Poster Board Number: C0107
Presentation Time: 2:45 PM - 4:30 PM

Real-life use of ranibizumab in the treatment of diabetic macular edema: the population of a French Phase IV Study (LUDIC study)

Ali Erginay, Pascale Massin, Laurent Kodjikian, Marie-Laure Le Lezé, Stéphane Quéré, Véronique Schneider, Service d’Ophtalmologie, Hôpital Lariboisière, Paris, France; ‘Service d’Ophthalmologie, Hôpital de la Croix-Rousse, Lyon, France; 3Service d’Ophthalmologie, Hôpital Bretonneau, Tours, France; 4Research Department, Novartis Pharma, Rueil-Malmaison, France.

Purpose: To describe the population of a French Phase IV interventional study designed to investigate efficacy in real-life use of ranibizumab in diabetic macular edema (DME), and compare it with that observed in the key development study (the RESTORE Study).

Methods: Patients recruited at 46 centers were given three monthly injections of ranibizumab and retreated if necessary in strict application of the current Summary of Product Characteristics. In contrast with the development studies, no exclusion criteria related to prior treatment for DME were imposed in this prospective interventional phase IV study.

Results: Between February and December 2011, 350 patients were enrolled. Eligibility criteria for RESTORE were relatively strict especially concerning previous treatment: the exclusion criteria included panretinal laser photocoagulation in the preceding 6 months and either focal/grid laser photocoagulation or any form of intraocular treatment with anti-angiogenic products within 3 months of randomization. No such criteria were applied in LUDIC: 48.1% of the study population had been treated by laser photocoagulation during the preceding 12 months and 19.7% had been treated with IVT anti-VEGF.

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At baseline, mean age was 63.7 years, male/female ratio was 1.6 and 79.4% were overweight (39.3 % obese); 79.1% had hypertension, 59.1% dyslipidaemia and 69.1% glycosylated haemoglobin above 7%. The percentage in whom the diabetes was controlled (applying the RESTORE criterion of <8% HbA1c) was similar (70.0% in LUDIC versus 72.4% in RESTORE). Diabetes (type 1 in 20.6%) had been diagnosed 18 years previously on average and all were being actively treated. DME had been diagnosed an average of 2.2 years previously. Mean baseline VA was 57.0 ± 10.3 letters and was also worse in LUDIC with 58.9% of patients not able to read more than 60 ETDRS letters compared with 32.8% of the RESTORE population.

Conclusions: This cohort—the largest to date of French patients with DME treated with ranibizumab—is comparable to that of the RESTORE Study in terms of age and gender but diabetes and DME are more severe in this real-life population which is likely to be closer to the true target DME population.

Commercial Relationships: Ali Erginay, Novartis (R), Bayer (R), Alimenra (C); Pascale Massin, Novartis (C), Allergan (C), Fovea Pharmaceutical (C), Fournier Abbott (C); Laurent Kodjikian, None; Marie-Laure Le Lez, None; Stéphane Quéré, Novartis Pharma SAS (E); Véronique Schneider, Novartis (E)

Support: Novartis Pharma

Clinical Trial: NCT 01315275

Program Number: 2407 Poster Board Number: C0108

Presentation Time: 2:45 PM - 4:30 PM

No IOP-Elevation in patients treated with Anti-VEGF ranibizumab for diabetic macular edema

Peter P. Ciechanowski, Marc Stahel, Frank Moser, Sandra Lorz, Heidi M. Fassnacht, Nicole T. Graf, Stephan Estermann, Matthias Becker, Stephan Michels. Ophthalmology, Triemli Hospital Zurich, Zurich, Switzerland; 2Grafo Biostatistics, Winterthur, Switzerland.

Purpose: Recent studies indicated an IOP-elevation in patients with age related macular degeneration secondary to Anti-VEGF therapy. Review of the IOP evolution in patients under Anti-VEGF treatment for diabetic macular edema (DME).

Methods: Retrospective analysis of IOP in patients with DME being under ranibizumab treatment between April 2011 and July 2012. Results: 176 eyes with DME were treated with ranibizumab. At first presentation the mean IOP was 15.69 mmHg whereas 19 eyes had a history of glaucoma. The mean number of injections was 3.85 till July 2012. Mean IOPs measured in April 2011 (+/- 3 months) and in July 2012 (+/- 3 months) were 15.36 mmHg and 15.12 mmHg respectively. The mean maximum IOP in the time period under ranibizumab treatment was 17.83 mmHg, ranging from 10 to 33 mmHg. 5 eyes had a maximum IOP of ≥ 25 mmHg. Two eyes with maximum IOP > 30 had a history of glaucoma. Patients with a history of glaucoma had higher mean baseline IOP (17.78 mmHg) and higher mean maximum IOP (20.83 mmHg).

Conclusions: For DME patients without history of glaucoma no clinically relevant IOP changes were noticed under Anti-VEGF treatment with ranibizumab. A longterm follow up is planned.

Commercial Relationships: Peter P. Ciechanowski, None; Marc Stahel, None; Frank Moser, None; Sandra Lorz, None; Heidi M. Fassnacht, None; Nicole T. Graf, None; Stephan Estermann, None; Matthias Becker, Novartis (F), Bayer (F), Allergan (C); Stephan Michels, Novatis (C), Bayer (C), Allergan (C), Alimenra (C), Clanotech (C)

Program Number: 2408 Poster Board Number: C0109

Presentation Time: 2:45 PM - 4:30 PM

Association between OCT findings and response to treatment in diabetic macular edema

Qihui Li, Dong Hyun Lee, Min Kim, Hyoung Min, Hyoung Jun Koh. Ophthalmology, Institute of Vision Research, Department of Ophthalmology, Yonsei University College of Medicine, Seoul, Republic of Korea.

Purpose: To compare the effect of intravitreal Bevacizumab injection (IVB) and posterior subtenon triamcinolone injection (PSTI) according to OCT patterns in patients with diabetic macula edema.

Methods: We retrospectively reviewed 46 eyes of 35 patients with DME who were treated with IVB or PSTI. Using OCT findings, the eyes were categorized into 2 groups based on the presence or absence of subretinal fluid (SRF) under the macula within 500 um of the fovea. In each group, the eyes were divided into 2 subgroups according to treatment received, either IVB or PSTI, respectively. Central macular thickness (CMT), the distance from retinal pigment epithelium(RPE) to external limiting membrane(ELM) and the distance from RPE to internal limiting membrane(ILM) were measured at pre-treatment, 1 month, and 3 month post-treatment.

Results: In the eyes without SRF, PSTI was more effective in CMT reduction than IVB (20% vs 3%, p = 0.015, Mann-Whitney U test). Resolution of intraretinal edema (the distance from ELM to ILM) was significantly higher in PSTI group than that in IVB group (29% vs 12%, p = 0.03, Mann-Whitney U test). In the eyes with SRF, IVB group achieved greater reduction of CMT compared to PSTI group, but the difference was not significant (33% vs 16%, p = 0.236, Mann-Whitney U test). The degree of SRF reduction (distance from RPE to ILM) was higher in IVB group than PSTI group, but the difference was only marginally significant (43% vs 19%, p = 0.093, Mann-Whitney U test).

Conclusions: DME without SRF was more responsive to PSTI than IVB via the improvement of intraretinal edema. Classification of DME based on OCT findings might be useful for guiding more effective treatment.

Commercial Relationships: Young Joo Cho, None; Dong Hyun Lee, None; Min Kim, None; Hyoung Jun Koh, None

Support: None exactly as formatted here

Program Number: 2409 Poster Board Number: C0110

Presentation Time: 2:45 PM - 4:30 PM

Efficacy of Ranibizumab in the Treatment of Diabetic Macular Edema Refractory to Bevacizumab

Harrison Sciulli, David G. Miller, Joseph Coney, Michael A. Novak, Jerome P. Schartman, Lawrence J. Singerman, Hernando Zegarra. Retina Associates of Cleveland, Cleveland, OH.

Purpose: To evaluate anatomic and visual acuity outcomes associated with 0.5 mg intravitreal ranibizumab (IVR) in patients with diabetic macular edema (DME) refractory to 1.25 mg intravitreal bevacizumab (IVB).

Methods: Retrospective chart review of patients seen from April 2010 through July 2012 in a single retinal specialty practice identified 1144 eyes that had received IVB for DME. Of these, 36 eyes had been refractory to IVB, defined as persistent spectral domain optical coherence tomography (SDOCT) reading of center subfield thickness (CSFT) >300 microns, and were subsequently given IVR. Data collected include years of diabetes mellitus (DM); prior vitrectomy, panretinal photocoagulation (PRP), focal laser therapy, or intravitreal triamcinolone (IVT) use; number of IVB and IVR injections; months of IVB and IVR treatment; complications; and best corrected visual acuity (BCVA) and CSFT measurements at baseline, 1 month after first injection (early results), and 1 month after final injection of IVB and IVR (final results).

Results: Thirty-six eyes of 32 patients with 18.8 mean years of DM received an average of 4.5 IVB injections over a mean of 7.2 months,
followed by an average of 5.7 IVR injections over a mean of 8.5 months. Other results include no complications for IVB or IVR injections, 3 eyes with prior vitrectomy, 17 eyes with prior PRP, 3 eyes with prior focal laser (mean 3.3 treatments), and 10 eyes with prior IVT (mean 2.6 injections, range 5-36 months prior, mean 15 months).

IVB showed significant improvement in CSFT on early results (mean ± SEM change -40 ± 18 microns in the 33 patients measured on both occasions, p=0.033) but not with final results (+13 ± 18 microns, p=0.48). IVB was associated with very highly significant improvement for both early (-120 microns ± 22 in the 34 patients measured on both occasions, p<.001) and final (-139 ± 22 microns, p<.001) results. With IVB, there was no significant improvement in LogMar BCVA for early (+0.04 ± 0.06, p=.50) or final (-0.05 ± 0.07 in the 35 patients measured on both occasions, p=.44) results. With IVR treatment, significant improvement in LogMar BCVA was not seen for early results (+0.01 ± 0.05, p=.80) but was seen for final results (+0.03 ± 0.02).

Conclusions: These data suggest that IVR may be a reasonable treatment option for patients with DME refractory to IVB.

Commercial Relationships: Harrison Sciulli, None; David G. Miller, None; Joseph Coney, Genentech (R); Michael A. Novak, None; Jerome P. Schartman, None; Lawrence J. Singerman, None; Hernando Zegarra, None

Program Number: 2410 Poster Board Number: C0111
Presentation Time: 2:45 PM - 4:30 PM
New software to assess retinal non-perfusion on Optomap® Wide-Field Fundus Fluorescein Angiography in Diabetic Macular Oedema

Anna Sala-Puigdollers1, Silvestro Caputo1, Hojr Jaberansari1, Jane Gray1, Yvonne D'Souza1, Stephen J. Charles1, Lorna B. Young2, David B. Henson1, 3, David McLeod1, Paulo E. Stanga1, 4, Silvestro Caputo1, 3, 4

1Vitreoretinal Unit, Manchester Royal Eye Hospital, Manchester, United Kingdom; 2School of Medicine, University of Manchester, Manchester, United Kingdom; 3Manchester Academic Health Science Centre and Centre for Ophthalmology and Vision Research, Institute of Human Development, University of Manchester, Manchester, United Kingdom.

Purpose: To develop new software that takes into account image distortion to assess the location and quantify the area of retinal non-perfusion (RNP) and its relationship with Central Macular Thickness (CMT) in patients with Diabetic Macular Oedema (DMO) on wide-field fundus fluorescein angiography (WF-FFA).

Methods: Retrospective review of 77 Optomap® WF-FFA images of patients with DMO. A grid was superimposed over the WF-FFA image (each cell being one disc area of 1.77mm²). The image was divided into 3 zones: 1.Posterior Pole (PP): within an ellipse centered on the fovea, passing through a point one disc diameter from the nasal edge of the optic disc (OD) and including the vascular arcades; 2. Mid-peripheral (MP): outside the PP but within a circle centered on the OD and passing along the posterior edge of the vortex vein ampullae on the green-free image; 3. Peripheral (P): anterior to the MP zone. Two independent graders classified each cell within zones 2 & 3 as: 1>(50% perfused), 2<50% perfused), 3(transition area between 1 and 2), 4(poor image quality) or 5(blockage by eyelashes/eyelids). In case of disagreement of >10 cells scored as 2 or 3 in zone 2 the image was rescoped by the two graders together. The coefficient of agreement was used to determine the consistency between the two graders initial scores. Correlation coefficients were calculated to assess the relationship between CMT and area of RNP.

Results: Coefficient of agreement for the MP was 21 cells. Thirteen images were regraded due to differences >10cells between the 2 graders. Mean CMT was 290µ(range:199-606µ). Average of RNP areas in MP was 4.17(range:0-25). Correlation coefficient with CMT was 0.349, p=0.019. Average of RNP areas in P was 2.01(range:0-29). There was no correlation with CMT and peripheral RNP areas.

Conclusions: This new software package allows for an easier and faster quantification of the area and location of retinal non-perfusion in the mid and periphery on Optomap® WF-FFA images while, for the first time, taking into account the distortion that occurs in WF-FFA images. Retinal non-perfusion associated with DMO is mainly located in the mid-periphery. We found a weak correlation between CMT and mid-peripheral retinal non-perfusion. Further studies using this new software are required to ascertain the area and role of retinal non-perfusion in DMO and other ischemic retinal diseases.

Commercial Relationships: Anna Sala-Puigdollers, None; Silvestro Caputo, None; Hojr Jaberansari, None; Jane Gray, None; Yvonne D’Souza, None; Stephen J. Charles, None; Lorna B. Young, None; David B. Henson, None; David McLeod, None; Paulo E. Stanga, OPTOS PLC (F), OPTOS PLC (C), OPTOS PLC (R), TOPCON CORP (F), TOPCON CORP (C), TOPCON CORP (R), SECOND SIGHT (F), SECOND SIGHT (R)

Support: Manchester Vision Regeneration (MVR) Lab

Program Number: 2411 Poster Board Number: C0112
Presentation Time: 2:45 PM - 4:30 PM
The Structural-Functional Correlation in Patients with Diabetic Macular Edema

Magdalena Sinczak, Amun Sachdev, Rupal Morjaria, Victor Chong, Ophthalmology, Oxford University Hospitals NHS Trust, Oxford, United Kingdom.

Purpose: It has been previously shown that diabetic macular edema (DME) patients with relatively good vision can have slow reading speed. In this study, we evaluated the structural-functional correlation in a larger cohort of patients.

Methods: The study was performed on patients with clinically significant DME. The best corrected visual acuity (BCVA) was recorded with letter counting on a modified ETDRS chart, the maximal reading speed (MRS) was recorded with MNREAD, the retinal sensitivity (MPS) was measured with Optos OTI (only the central five points were included in the analysis) and the central subfield thickness (CST) was measured by Heidelberg Spectralis Spectral Domain Optical Coherent Topography (SD-OCT). The statistical analysis was carried out by SPSS.

Results: There were 76 eyes included in the study. The mean patient age was 58.2 years, the mean BCVA was 76.5 letters, the mean MRS was 156.8 words per minute, the mean MPS was 9.81 dB per point, and the mean CSF was 321.1 microns. It was found that faster MRS...
is correlated with younger age (p=0.001), better BCVA (p<0.0001), and better retinal sensitivity (p<0.0001), but not with CST (p=0.66). In fact, CST is not correlated with age (p=0.812), BCVA (p=0.113) or MP5 (p=0.485). After correction for age and BCVA, MRS is still correlated with MP5 (p=0.015).

**Conclusions:** DME patients can have reduced reading speed despite good visual acuity. In this study, as one would expect, we confirmed that maximal reading speed is reduced in older patients and those with poor vision. However, MRS is not related to OCT findings. This is consistent with previous observations that retinal thickness is not a good indicator of retinal function in DME patients. MRS is often reported to be difficult to perform, inconsistent, and affected by language and educational level. However, in this study, we found that the central MP5 points are quick and easy to test in the majority of patients, and are highly correlated with MRS. MP5 might therefore be able to replace reading function in the assessment of DME patients.

**Commercial Relationships:** Magdalena Sinczak, None; Amun Sachdev, None; Rupal Morjaria, None; Victor Chong, Novartis (C), Bayer (C), Allergan (C), Pfizer (F), Novartis (F), Alimera Science (C), Quantel (R)

**Program Number:** 2412 Poster Board Number: C0113

**Presentation Time:** 2:45 PM - 4:30 PM

**Intravitreal Bevacizumab and Ranibizumab for Diabetic Macular Edema: A single center retrospective study**

_Daniel Choi, Jennifer I. Lim_. Ophthalmology, University of Illinois at Chicago, Chicago, IL.

**Purpose:** To compare visual acuity outcomes and optical coherence tomography (OCT) measurements after bevacizumab or ranibizumab intravitreal injections in patients with diabetic macular edema (DME).

**Methods:** A retrospective chart review was conducted to determine visual and anatomic outcomes for diabetic macular edema patients who were treated with either bevacizumab or ranibizumab. Patients with less than six months follow up or who had received both types of treatments were excluded. Visual acuities before and after each injection were recorded and converted to logMAR for statistical analysis. OCT central subfield thickness (CST) measurements were recorded. Visual acuity and CST were compared between drugs at 3, 6, 9, and 12 months.

**Results:** 32 patients (43 eyes) received intravitreal bevacizumab and 9 patients (13 eyes) received intravitreal ranibizumab for DME. The difference in average visual acuity at baseline, 3, 6, 9, and 12 months was not statistically significant. Bevacizumab patients had a baseline logMAR of 0.685 while ranibizumab patients had a baseline logMAR of 0.808 (p = 0.41). At 12 months, logMAR improved to 0.467 and 0.411 for the bevacizumab and ranibizumab treated groups respectively (p = 0.61). The difference in CST findings was not statistically significant at any time point. At 6 months, 35% and 45% of patients treated with bevacizumab and ranibizumab respectively had gained at least 3 lines of visual acuity (logMAR +3.3). The proportion of patients gaining this level of visual acuity was not statistically significant (p = 0.79) despite a statistically different mean number of injections by 6 months: bevacizumab 3.29 vs ranibizumab 4.77 (p = 0.04).

**Conclusions:** Our study demonstrates no statistically significant difference in the visual acuity outcomes following intravitreal bevacizumab versus intravitreal ranibizumab treatment of diabetic macular edema. However, a larger prospective clinical trial will be necessary to further evaluate the differences in efficacy and complications of these two treatment regimens.

**Commercial Relationships:** Daniel Choi, None; Jennifer I. Lim, QLT (F), Genentech (R), Regeneron (R)

**Program Number:** 2413 Poster Board Number: C0114

**Presentation Time:** 2:45 PM - 4:30 PM

**Ranibizumab 0.5mg vs. 2.0mg to Treat Diabetic Macular Edema in Patients With Poor Response to Bevacizumab**

_Dante J. Pieramici1, Ma’an Nasir1, Alessandro Castellarin1, Robert F. See1, Steve Couvillion1, Michael Bennett1, Melvin Rabena2, Jack Giusti3, Lisha C. Wan4, Robert L. Avery4, 1California Retina Consultants, Santa Barbara, CA; 2Hawaii Retina Institute, Honolulu, HI.

**Purpose:** To determine the efficacy of ranibizumab for residual or persistent diabetic macular edema in individuals with minimal or unresponsive to previous treatment for diabetic macular edema.

**Methods:** Prospective, nonrandomized single center intervention study. Individuals with residual center involved DME following bevacizumab treatment for DME were enrolled into this 12-month study. All enrolled subjects received at least two consecutive bevacizumab injections administered less than seven weeks apart. Upon enrollment, all patients received three consecutive monthly injections of 0.5mg ranibizumab. At Month 3, all subjects with residual macular edema were switched to three consecutive monthly injections of 2.0 mg ranibizumab. Monthly evaluations include standardized visual acuity, SD-OCT and complete ophthalmic evaluation. Fundus photos and FA were obtained quarterly.

**Results:** Forty-three subjects with at least 6 months of follow-up were included in this analysis. Previous bevacizumab was adequate and consecutive prior to enrollment at an average of 36 days between bevacizumab injections. Mean VA was 59 letters at baseline; improved by +6.4 letters at Month 3 and +8.8 letters at Month 6. Mean central 1mm subfield thickness (CST) was 501µm at baseline; decreased by -114µm at Month 3 and -165µm at Month 6. Mean retinal volume decreased from 9.79 mm3 at baseline to 8.76 mm3 at Month 3 and 8.34 mm3 at Month 6. After 3 consecutive 0.5 mg ranibizumab injections, reduction in CST to below 300µm on SD-OCT was achieved in 20.9% (9/43) of subjects & CST decreased by >25% from baseline in 34.9% (15/43) of subjects. After 3 consecutive 2.0 mg ranibizumab injections, an additional 22.2% (6/27) of subjects achieved CST of ≤300µm & CST decreased by >25% from Month 3 in 29.6% (8/27) of subjects. One death due to acute hypoxemic respiratory failure was observed in the study.

**Conclusions:** Visual and anatomical improvement occurred in some patients with minimal or no response to previous bevacizumab therapy when switched to ranibizumab in an interim analysis of our investigator sponsored study. Incomplete or nonresponse to bevacizumab should not be a contraindication to considering ranibizumab therapy in patients with diabetic macular edema.

**Commercial Relationships:** Dante J. Pieramici, Genentech (C), alimera (C), thrombogenics (C), allergan (C), Santen (C); Ma’an Nasir, None; Alessandro Castellarin, Genentech (C), Alcon (I); Robert F. See, None; Steve Couvillion, genentech (R); Michael Bennett, None; Melvin Rabena, Genentech (E); Jack Giusti, None; Lisha C. Wan, None; Robert L. Avery, Alcon (C), Allergan (C), Genentech (C), Novartis (C), Notal Vision (C), Ophthotech (C), Replensh (C), Regeneron (C), Alexion (I), QLT (C), I-Tech JV Development (I), allergan (F), genentech (F), genentech (R), allergan (R), novartis (R), relephsen (P), novartis (I), relephsen (I), regeneneron (I), regeneneron (R)

**Clinical Trial:** NCT01292798

**Program Number:** 2414 Poster Board Number: C0115

**Presentation Time:** 2:45 PM - 4:30 PM

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ILM peeling in non tractional diabetic macular edema not responsive to standard treatment

*Paola A. Salvetti, Luigi Bonavia, Ferdinando Bottoni, Stefano de Angelis, Roberta Secondi, Matteo G. Cereda, Giovanni Stauenghi*

Dpt of Clinical Science, Eye Clinic Saeco Hospital, Milano, Italy.

**Purpose:** To evaluate the effect of 25 G pars plana vitrectomy (PPV) with internal limiting membrane (ILM) peeling in diabetic patients with clinically significant macular edema without evidence of vitreomacular traction and not responsive to standard therapies.

**Methods:** Retrospective analysis of visual acuity (VA), SD-OCT (HRA+OCT Spectralis, Heidelberg Engineering GmbH, Heidelberg, Germany) and fluorescein angiography (FA) images of 15 eyes of 15 vitrectomized patients with diagnosis of diffuse diabetic macular edema.

Each patient had been already submitted to intravitreal Bevacizumab and/or posterior pole laser treatment with poor functional and anatomical outcomes. Exclusion criteria included IS/OS defects, subfoveal atrophy and evident vitreomacular traction before vitrectomy.

Combined cataract surgery and 25 G pars plana vitrectomy with indocyanine green assisted ILM peeling were performed in each case by 3 different surgeons (FB, MC, SdeA). Selective Argon laser on peripheral residual ischaemic areas was performed during surgery. Main outcome measures were mean changes in visual acuity (VA) and central retinal thickness (CRT) at 1, 3 and 6 months postoperatively.

**Results:** 7 patients have 6 month-follow-up and 8 patients 3 month-follow-up. No major complications occurred during and after surgeries.

Preoperative mean VA was 0.25 ± 0.2 SD (range, 0.05 - 0.625). Postoperative mean VA was 0.42 ± 0.31 SD at 1 month follow-up (Paired T-test, P<0.11), 0.39 ± 0.24 SD at 3 months (P=0.10) and 0.47 ± 0.23 SD at 6 months (P=0.01). VA improved significantly only 6 months after surgery.

Mean preoperative CRT was 595.5 ± 188.5 SD microns (range, 391 - 789 microns). Mean CRT at 1 month was 437 ± 143 SD microns (P=0.0004), at 3 months 387 ± 130 SD (P=0.000008) and 323 ± 152 SD microns at 6 months (P=0.000045). CRT decreased significantly at 1, 3 and 6 months of follow-up (Paired T-test P<0.01).

**Conclusions:** PPV with ILM peeling seems to be effective in diabetic patients with clinically significant diffuse macular edema unresponsive to standard care for reducing retinal thickness and improving visual acuity.

**Commercial Relationships:** Paola A. Salvetti. None; Luigi Bonavia. None; Ferdinando Bottoni. None; Stefano de Angelis. None; Roberta Secondi. None; Matteo G. Cereda. None; Giovanni Stauenghi. Ocular Instruments (P), GSK (C), Novartis (C), Alcon (C), Allergan (C), Bayer (C), Roche (C), Heidelberg Engineering (C), OD-OS (C), QLT (C), Optos (C)

**Program Number:** 2415 Poster Board Number: C0116

**Presentation Time:** 2:45 PM - 4:30 PM

**Dynamic Vessel Analysis May Show an Improvement of Endothelial Function by Intravitreal Ranibizumab in Diabetic Macular Edema**

*Sylwana Ventzke, Dirk Sandner, Eberhard Spoelr, Lutz E. Pillunat, Richard P. Stodtmeister*

University Eye Clinic, Dresden, Germany.

**Purpose:** Retinal arterial vasconstriction has been observed after application of ranibizumab in age-related macular degeneration. Changes in retinal vessels may be expected following treatment with ranibizumab in patients with diabetic macular edema. We investigated the response of the diameter of retinal arterioles and venules to flicker stimulation by classifying the registrations of the flicker reaction in these patients in addition to the quantitative evaluation.

**Methods:** Patients: N=30. Age: 60±11 years. Male/female: 16/14. Inclusion criterion: Clinically significant macular edema. Dynamic Vessel Analysis (Imedos, Jena, Germany) consisting of a Fundus Camera, video equipment and computer-aided process control: Online measurement of the diameter of a retinal arteriolar and a venular vessel segment, 50s baseline, three times 20s flicker stimulation and 80s follow up registration. Three registrations were averaged. Examination time points: Before the first injection (Examination 1: E1), before second (E2) and third injection (E3) and 3 month after the first injection (E4). Vessel reactions were classified in four classes: Class(C1): Within normal limits. C2: Reduced, clearly visible. C3: very reduced, but recognizable in spite of noise. C4: Absent. The observer was masked by encoding the examination time point and the patients.

**Results:** The reaction of the arterioles didn’t change significantly from E1 through E4. The reaction of the venules showed a trend to a monotonous improvement (Friedman-Test: p=0.089). Arith. mean of classes±std.deviation: E1: 2.17±1.17. E2: 2.07±0.98. E2: 1.97±1.06. E3:1.97. E4: 1.63±0.85. Friedman-test: p=0.09. Wilcoxon-test: E1vsE4: 0.054 after Bonferroni-Holm adjustment.

**Conclusions:** Experienced observers are often better in detecting and judging biological signals buried in noise than machines. Therefore we applied the technique of classification in our noisy registrations. An increase in diameter of arterioles and venules might be a sign of autoregulation which is clearly seen in healthy subjects and may be reduced in diabetes mellitus. A shift to one of our lower classes may be interpreted as an improvement in autoregulation which is initiated by the vascular endothelium. Our results may be the sign of an improvement of retinal vessel endothelial function by ranibizumab.

**Commercial Relationships:** Sylwana Ventzke. None; Dirk Sandner, Novartis (F), Novartis (R); Eberhard Spoelr, None; Lutz E. Pillunat, None; Richard P. Stodtmeister, Novartis (F)

**Program Number:** 2416 Poster Board Number: C0117

**Presentation Time:** 2:45 PM - 4:30 PM

**F/A and ICG guided, sub-threshold, reduced fluence Focal Laser Photocoagulation Treatment (SRFLPT) in patients with Diabetic Clinically Significant Macular Edema (CSME)**

*georgios papastergiou, Fayssal El-Jabali, Karl E. Waite, Michael D. Bennett*

Retina Institute of Hawaii, Honolulu, HI.

**Purpose:** Assess the effectiveness and safety of SRFLPT in patients with diabetic CSME.

**Methods:** 142 patients (216 eyes) with ETDRS defined CSME were enrolled in this prospective study. ETDRS visual acuity, SD-OCT volume (central 6X6mm), F/A and ICG were obtained at baseline and at months 3, 6, 9, and 12. ICG findings were used to identify focal leakage from larger retinal microaneurysms that were individually treated with direct threshold focal laser application. On the other hand, F/A findings were used to determine areas of diffuse capillary leakage that were treated with a further reduced invisible sub-threshold grid laser photocoagulation. A spot size of 100µm and a duration of 20msec were selected. The Heidelberg SD-OCT was used to monitor central macular volume.

**Results:** Average total fluence was 2720 J/cm2. Visual acuity improved on average 6.1±2.5, 5.6±5.7, 6.3±5.8 and 9.7±7.1 ETDRS letters after 3, 6, 9 and 12 months respectively (p<0.05 for all points). 24% of the patients (51) exhibited a gain of more than 10 letters, when 5% (11 eyes) lost 15 or more letters. Macular volume at baseline was 8.6±5.5mm3, which showed a statistically significant improvement to 8.3±5.6, 8.1±5.5, 8.2±0.5 and 7.7±0.5 at the four time points and the patients.
follow-up data points.

**Conclusions:** The ETDRS defined parameters remain the gold standard for CSME laser treatment. By using F/A and ICG guided SRFLPT there appears to be a statistically significant reduction in the total amount of energy needed to achieve improvement in both visual acuity and volumetric reduction of macular edema. By minimizing the total energy used, theoretically less collateral damage and inflammation occurs and this may be responsible for the speed and extend of the clinical improvement observed in our study. However, long term follow-up and a larger controlled randomized trial is necessary to better assess the effectiveness of this treatment.

**Commercial Relationships:** georgios papaergiou, None; Fayssal El-Jabali, None; Karl E. Waite, None; Michael D. Bennett, None

**Clinical Trial:** RIH1010

**Program Number:** 2417 Poster Board Number: C0118
**Presentation Time:** 2:45 PM - 4:30 PM

**THE IMPACT OF SYSTEMIC FACTORS ON CLINICAL RESPONSE TO VEGF INHIBITORS FOR DIABETIC MACULAR EDEMA**

Simone Matsuda, Tiffany J. Tam, Rishi Singh, Gina M. Smith, Justis P. Ehlers. Cleveland Clinic, Cleveland, OH.

**Purpose:** To evaluate the effect of glucose regulation, renal function, blood pressure, obesity, and lipid profile on anti-vascular endothelial growth factor (VEGF) treatment for diabetic macular edema (DME).

**Methods:** A retrospective consecutive case series for eyes enrolled 125 eyes of 83 patients with DME treated with intravitreal bevacizumab or ranibizumab. The main outcome measures were the change in best corrected visual acuity (BCVA), the change central subfield macular thickness (CST), the number of intravitreal injections; and their correlation with the serum hemoglobin A1c values (HbA1c), glomerular filtration rate (GFR) estimated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, fasting serum lipids and other clinical findings.

**Results:** The study included 125 eyes of 83 patients. Fifty-two (62.6%) females and 72 (86.7%) males with a mean age of 60.4 years were identified. The mean HbA1c was 8.15 (range 6.0-15%) and decreased to 366 µm at final follow-up (p < 0.001). The mean baseline CSMT was 448 µm and decreased to 366 µm at final follow-up (p < 0.001). The mean number of intravitreal injections was 6.3 and the mean follow-up was 11.9 months. The serum HbA1c values and duration of DM were found to be negatively correlated with the change in CST [r=-0.33, p < 0.001], (-0.251, p = 0.05, respectively]. Improved glycemic control during the study period (e.g. reduction in HbA1c) was associated with reduced frequency of injections (-0.22; p = 0.05). GFR, blood pressure, and fasting lipid profile did not show significant correlation with change in CST, BCVA or number of intravitreal injections, respectively.

**Conclusions:** Intravitreal bevacizumab and ranibizumab for DME demonstrated a beneficial functional and structural effect with improved visual acuity and reduced macular edema. Systemic control of diabetes was associated with improved structural response and reduced injection burden. Enhancement of DM control may result in improved response to anti-VEGF therapy. In this study, renal function, blood pressure, and lipid profile did not have a significant impact on response to anti-VEGF therapy.

**Commercial Relationships:** Simone Matsuda, None; Tiffany J. Tam, None; Rishi Singh, Genentech (C), Alcon (C), Bausch and Lomb (R), Zeiss (R), Quark Pharmaceuticals, Inc. (F); Gina M. Smith, None; Justis P. Ehlers, Provisional patents filed related to intraoperative OCT technology. No company relationships (P)

**291 DR: Clinical Research II**
**Monday, May 06, 2013 2:45 PM-4:30 PM**
**Exhibit Hall Poster Session**

**Program #/Board # Range:** 2418-2449/C0119-C0150

**Organizing Section:** Retina

**Program Number:** 2418 Poster Board Number: C0119
**Presentation Time:** 2:45 PM - 4:30 PM

**Diabetic Macular Ischemia In Type 1 Diabetes**

Zaman K. Durani1,2, Dawn A. Sim3, Pearse A. Keane4, Michael Karampelas1, Javier Zarranz-Ventura3, Marcus Fruttiger4, Praveen J. Patel5, Adnan Tufail6, Catherine A. Egan1,3,1 St George’s Student Union, St Georges Univ of London, London, United Kingdom; 2Pharmacy, Moorfields Eye Hospital, London, United Kingdom; 3NIHR Biomedical Research Centre for Ophthalmology, Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, London, United Kingdom.

**Purpose:** To investigate the relationship between fundus fluorescein angiography (FA) derived measurements of retinal vascular morphology and visual acuity (VA) in Diabetic Macular Ischaemia (DMI).

**Methods:** Data were retrospectively collected over a period of 6 months. FAs were analysed using the Early Treatment Diabetic Retinopathy Study (EDTRS) protocol for DMI. The Foveal Avascular Zone (FAZ), capillary non-perfusion areas- temporal to the fovea, and the overlying the papillomacular (PM) nerve fibre bundle were quantified using custom software.

**Results:** 51 patients with type 1 diabetes (DM) who had undergone a FA were included in the analysis. The mean age of 40 years (SD:13.2) with a 3:2 male to female ratio. 17 eyes (33.3%) had “no DMI”, 10 (19.6%) “questionable”, 13 (25.5%) “mild”, 8 (15.6%) “moderate”, and 3 (5.9%) “severe” ischemia. Median FAZ area (mm2) was 0.15mm2 (IQR: 0.10-0.17) in no DMI, 0.25mm2 (IQR: 0.19-0.30) in questionable, 0.30mm2 (IQR: 0.23-0.37), and 0.44mm2 (IQR: 0.35-0.52) in severe DMI (p<0.001). VA was reduced moderate and severe (0.2 LogMar [IQR: 0.10-0.55]) compared to those with none, questionable, and mild ETDRS-DMI grades (0.0 LogMar [IQR: 0.0-0.2]). Temporal and PM ischemia was observed both in eyes without DMI (35.3% and 17.6% respectively), as well as across all ETDRS-DMI grades (67.6% and 47.1%) (p=0.16, p=0.82).

**Conclusions:** The prevalence of DMI in patients with type 1 DM (66.7%) was greater than in type 2 DM (54.6%), observed in a previous study. The pattern of DMI in type 1 DM also differs to that observed in type 2 DM. Temporal and PM ischemia was present across all ETDRS-DMI grades, unlike type 2 DM, where it was present only in more severe ETDRS-DMI grades. Functional outcomes of both DM types are similar, where a reduction of visual acuity was only observed in eyes with moderate to severe ETDRS-DMI grades.

**Commercial Relationships:** Zaman K. Durani, None; Dawn A. Sim, None; Pearse A. Keane, None; Michael Karampelas, None; Javier Zarranz-Ventura, None; Marcus Fruttiger, AstraZeneca (F), Novartis (F), Novartis (C), Amakem (F); Praveen J. Patel, Allergan (R), Bayer (C), Novartis UK (C), Heidelberg UK (R), Topcon UK (R), Thrombogenics (C); Adnan Tufail, Allergan (C), Bayer (C), GSK (C), Oculogics (C), Pfizer (C), Thrombogenics (C), Amakem (C), Heidelberg Engineering (R), Novartis/Alcon (C), Sanofi/Genzyme (C); Catherine A. Egan, Bayer (S), Oculogics (S), Novartis (S), Allergan (S), Novartis (F)
Comparing the Microperimetric to Structural Findings in Patients with Branch Retinal Vein Occlusion and Diabetic Macular Edema


Purpose: Microperimetry is useful in assessing retinal sensitivity. Previous work has suggested that there is a correlation between microperimetric findings and structural changes in patients with diabetic macular edema (DME). In this study, we have compared the microperimetric findings in patients with DME and in patients with branch retinal vein occlusion (BRVO).

Methods: Patients who had focal DME and BRVO were included in the study. Microperimetry and Spectral Domain Optical Coherent Topography (SD-OCT) were carried out on Optos OTI OCT. In each eye, the parafoveal ring of 16 microperimetric points was analysed. The thickness of the retina at each microperimetric point was manually measured. The area was defined as abnormal when there was significant edema with clearly defined cystic spaces. The average retinal sensitivity and thickness of the abnormal areas were compared with that of the normal areas in the same eye. The data was analysed by paired Student t-test.

Results: There were 20 eyes with focal DME and 9 eyes with BRVO included in this pilot study. The average retinal thickness was 400.3 microns, and 302.7 microns in the abnormal and normal areas respectively in DME (p<0.0001). The average retinal thickness was 480.2 microns and 322.3 microns in the abnormal and normal areas respectively in BRVO (p=0.0001). The average retinal sensitivity was 10.05 dB and 12.09 dB in the abnormal and normal areas respectively in DME (p=0.0029). The average retinal sensitivity was 6.78 dB and 12.95 dB in the abnormal and normal areas respectively in BRVO (p=0.0006). In DME, 47.7 microns increase in thickness is correlated with 1 dB reduction of retinal sensitivity. In BRVO, 25.6 microns increase in thickness is correlated with 1 dB reduction of retinal sensitivity.

Conclusions: The advantage of using the Optos OTI OCT is that the microperimetry and the SD-OCT are carried out on the same machine with the same optics, allowing point to point correlation. In this pilot study, we found that there was a difference in the amount of retinal thickness per dB loss in retinal sensitivity between DME and BRVO. Further studies to investigate why this is the case are required. It is possible that in DME the majority of edema is in the inner retina, which causes less reduction in retinal function, whilst in BRVO, the entire retina is equally involved.

Commercial Relationships: Amun Sachdev, None; Magdalena Sinczak, None; Rupal Morjaria, None; Victor Chong, Novartis (C), Bayer (C), Allergan (C), Pfizer (F), Novartis (F), Alimera Science (C), Quartel (R)

Program Number: 2419 Poster Board Number: C0120
Presentation Time: 2:45 PM - 4:30 PM

Quantitative Analysis of Diabetic Macular Ischemia using Optical Coherence Tomography

Pearse A. Keane1, 2, Dawn A. Sim1, 2, Simon S. Fung1, Michael Karampelas2, Srinivas R. Sadda2, Marcus Fruttiger2, Praveen J. Patell1, 2, Adnan Tufail1, 2, Catherine A. Egan1, 2, 3 NIHR Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom; 1Institute of Ophthalmology, University College London, London, United Kingdom; 2Medical Retina, Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom; 3Doheny Eye Institute, University of Southern California, Los Angeles, CA.

Purpose: Diabetic macular ischemia (DMI), an important category of diabetic retinopathy (DR), contributes to the pathogenesis of diabetic macular edema (DME) and, in severe cases, is a cause of irreversible visual loss in its own right. In this abstract, we analyze the optical coherence tomography (OCT) features of DMI and correlate these findings with visual acuity.

Methods: Clinical and imaging data were collected retrospectively from patients with type 2 diabetes undergoing fluorescein angiography (FA) and OCT. DMI severity was determined from FA image sets according to Early Treatment Diabetic Retinopathy Study (ETDRS) criteria. OCT image sets were obtained using spectral domain OCT (Spectralis, Heidelberg Engineering). Custom image analysis software was used for quantitative analysis. Retinal spaces quantified included retinal nerve fibre layer (RNFL), inner retina, outer retina, and total retina. Subgroup analyses were performed for eyes with DMI but without diabetic macular edema (DME).

Results: 100 patients (100 eyes) met the inclusion criteria for the study. 14.8% of eyes had severe DMI, 6% moderate DMI, 26.1% DMI, 13.6% questionable DMI, and 38.6% had no evidence of DMI. DME, defined as a foveal retinal thickness greater than 275 μm, was present in 48% of eyes. Across all eyes, mean retinal thickness at the fovea was greater in the presence of DMI, and significantly different between all ETDRS-DMI grades (p=0.02). In eyes “without DME” we observed thinning in the outer retinal layer in eyes with DMI (150.4 ± 31.4 μm) compared to eyes without DMI (167.4 ± 18.5 μm, p=0.04). RNFL thickness was associated with an increased FAZ area (r=−0.231, p=0.03), particularly in eyes “without DME”, and in the outer papillomacular quadrant (r=−0.62, p<0.001). Across the entire cohort, retinal thickness was positively correlated with reduced visual acuity (VA) (r=−0.52, p=0.001). However, in eyes with DMI but without DME, retinal thickness was negatively correlated with VA (r=−0.37, p=0.004). In these eyes, a negative correlation between VA and RNFL thickness over the papillomacular area was also seen (r=−0.37, p=0.004).

Conclusions: Thinning of the RNFL and outer retina was observed with eyes with DMI but without DME. These parameters showed good correlation with VA and may serve as a useful tool for monitoring DMI in clinical practice or future clinical trials.

Commercial Relationships: Pearse A. Keane, None; Dawn A. Sim, None; Simon S. Fung, None; Michael Karampelas, None; Srinivas R. Sadda, Regeneron (C), Genentech (C), Allergan (C), Carl Zeiss Meditec (C), Optos (C), Carl Zeiss Meditec (F), Optovue (F), Optos (F); Marcus Fruttiger, AstraZeneca (F), Novartis (F), Novartis (C), Amakem (F); Praveen J. Patell, Allergan (R), Bayer (C), Novartis UK (C), Heidelberg UK (R), Topcon UK (R), Thrombogenics (C); Adnan Tufail, Allergan (C), Bayer (C), GSK (C), Oculogics (C), Pfizer (C), Thrombogenics (C), Amakem (C), Heidelberg Engineering (R), Novartis/Alcon (C), Sanofi/Genzyme (C); Catherine A. Egan, Bayer (S), Oculogics (S), Novartis (S), Allergan (S), Novartis (F)

Program Number: 2420 Poster Board Number: C0121
Presentation Time: 2:45 PM - 4:30 PM

Quantitative Analysis of Diabetic Macular Ischemia using Optical Coherence Tomography

Pearse A. Keane1, 2, Dawn A. Sim1, 2, Simon S. Fung1, Michael Karampelas2, Srinivas R. Sadda2, Marcus Fruttiger2, Praveen J. Patell1, 2, Adnan Tufail1, 2, Catherine A. Egan1, 2, 3 NIHR Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom; 1Institute of Ophthalmology, University College London, London, United Kingdom; 2Medical Retina, Moorfields Eye Hospital NHS Foundation Trust, London, United
been associated with vascular disease. The optimal relationship, known as Murray’s Law, states that optimally the cube of the radius of the parent vessel is equal to the sum of the cubes of the radii of the daughter blood vessels. We propose to study this association in people with diabetes with little or no clinical signs of diabetic retinopathy.

**Methods:** Retinal color images were obtained from 874 people with diabetes, in which the prevalence of retinopathy is 20% (Abramoff et al, JAMA ophthalmology 2013). A fully automated method was used to determine the widths of each branch at each crossing, using our previously validated algorithm. From the above population, a subset was randomly selected for branch point measurement. Linear regression was used to find the power that best described the relationship between the arterial and venous radii.

**Results:** Arterial and venous branches were measured on photos from 28 subjects from the diabetes population and on 150 fundus images from a normal population. From the diabetic population, 137 arterial branches and 215 venous branches were measured. The best fit power relationship was 4.9 and 3.3 for arterial and venous bifurcations respectively. From the normal population, 331 arteriolar branches and 573 venous branches were measured. The parent branch-daughter branch artery relationship fit Murray’s Law well with a third power relationship while the relationship in venular branches demonstrated a best fit of 2.4.

**Conclusions:** The apertures of the branches of arterial and venous bifurcations in the diabetic population deviate from the normal subjects. The daughters are wider than predicted by Murray’s Law. Previously, increased arterial flow and vessel wall irregularities have been described in subjects with diabetes. Possibly vessel widening is related to increased flow rate to maintain resistance and increased diameter compensates for increased resistance per unit area of vessel wall. Our findings may have important implications for early detection of retinal disease from diabetes mellitus even before retinopathy is clinically evident.

**Commercial Relationships:** Shahin Golestani. None; Touka Banaee. None; Ramin Daneshvar. None; Amin Nabavi. mashhad university of medical sciences (F)

**Program Number:** 2422 Poster Board Number: C0123

**Presentation Time:** 2:45 PM - 4:30 PM

**Retinal bifurcation angles in severe non-proliferative diabetic retinopathy**

Shahin Golestani, Touka Banaee, Ramin Daneshvar, Amin Nabavi.

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**Purpose:** Advances in retinal imaging have allowed a better understanding of retinal vascular parameters and their relationship with underlying pathophysiology processes in and beyond the retina. This study was conducted to compare the retinal arterial bifurcation angle in severe non-proliferative diabetic retinopathy and normal subjects.

**Methods:** This cross sectional study included 100 cases with severe non-proliferative diabetic retinopathy (NPDR) and 93 normal controls. The first and second retinal arterial bifurcation angles were quantified for both eyes of each subject by means of Adobe Photoshop CS5 software manually, adhering to a predefined protocol. The reliability of measurements was checked by determining the Intraclass Correlation Coefficient (ICC) of 2 separate angle measurements done by the same examiner.

**Results:** The measurements were reliable (ICC considered). The mean of first (86.91±14.57 Vs 74.21±12.24 and p<0.001) and second (88.61±17.13 Vs 71±12.92 and p<0.001) retinal arterial bifurcation angles in patients with severe non-proliferative diabetic retinopathy were significantly higher than normal subjects. The differences remained significant after adjusting for age, sex, glomerular filtration rate (GFR), duration of diabetes and hyperlipidemia. Also, the mean of first retinal arterial bifurcation angles in normal group was closer to the theoretical optimal bifurcation angle (of 75 degrees) compared to the diabetic group, in which this parameter showed significant difference to the optimum. (p<0.001)

**Conclusions:** Bifurcation angle of retinal arteries increases in severe NPDR and is a potential criterion for automated diagnosis of diabetic retinopathy.

**Commercial Relationships:** Shahin Golestani. None; Touka Banaee. None; Ramin Daneshvar. None; Amin Nabavi. mashhad university of medical sciences (F)

**Program Number:** 2423 Poster Board Number: C0124

**Presentation Time:** 2:45 PM - 4:30 PM

**Comparative Evaluation of Non-Mydriatic Camera Images by Non-Ophthalmic and Ophthalmic Photographers as part of a Primary Care Based Teleophthalmology Diabetic Surveillance Program**


**Purpose:** To compare the efficiency and effectiveness of capturing retinal images with a non-mydriatic fundus camera between an academically trained ophthalmic photographer and staff of a primary care clinic.

**Methods:** Four primary care clinic registered nurses and one pharmacy PhD were trained by the Biomedical Photography Communications program at the Rochester Institute of Technology (RIT) to capture retinal images using a Zeiss Visucam Non-Mydriatic Fundus Camera in a federally qualified urban health clinic in Rochester, NY as part of a teleophthalmology program to detect retinopathy in patients with diabetes. Two trainees were male and all were fluent in English. Trainees completed three individual 30 minute training sessions in English over three days and were evaluated during each session by using the camera to capture retinal images of undilated healthy normal subjects. Trainee images and those of an ophthalmic photographer who graduated from the RIT program were critiqued for focus, positioning, and working distance on a 1-4 scale using a rubric developed by the RIT program based on standard reading center criteria by a blinded professional ophthalmic photographer. A total percentage grade was given based upon overall image quality weighing the three individual criteria.

**Results:** The mean overall image quality score improved from 81% to 89% over three sessions for the trainees but still below the 97% obtained by the ophthalmic photographer. Mean Scores for focus and positioning improved over the session from 2.6 and 1.8 to 3.4 and 3.6.
respectively which were close to the photographer’s score of 4 for both values. All trainees had difficulty with working distance with mean scores staying at 2 over the three sessions. Variance between trainees reduced over time with standard deviation of total score, focus, positioning, and working distance decreasing from 12% to 4%, 1.14 to 0.55, 1.30 to 0.89, and 0.84 to 0.71 respectively.

**Conclusions:** New non-mydriatic cameras are user friendly and may not require rigorous training to obtain quality photographs. However, careful supervision early on and possibly periodic evaluations throughout the program are advised to ensure proper image capture, patient safety, and ability to timely identify eye disease in patients.

**Commercial Relationships:** Rajeev S. Ramachandran, None; Vanessa Desmore, None; Taylor A. Pannell, TelE I Care (E); William Fischer, Canon (F), Carl Zeiss Meditec (F); Christye Sisson, Rochester Institute of Technology (E)

**Support:** Greater Rochester Health Foundation, Rochester NY, USA

**Program Number:** 2424 **Poster Board Number:** C0125

**Presentation Time:** 2:45 PM - 4:30 PM

**Endothelial Progenitor Cells (EPCs) Detection In The Peripheral Blood Of Young Diabetic Patients With Type 1 Diabetes Mellitus (T1DM)- A Pilot Study**

Chrysanthi Tsika1, Zoi Kapsala1, Charalampos Pontikoglou2, Vassiliki Louvari1, Dimitrios Mamoulakis1, Helen A. Papadaki1, Miltiadis K. Tsilimbaris1, 1Department of Neurology and Sensory Organs, Eye CClinic of University Hospital of Heraklion, University of Crete, Medical School, Heraklion, Greece; 2Department of Internal Medicine, Hematology Clinic of the University Hospital of Heraklion, University of Crete, Medical School, Heraklion, Greece; 3Endocrinology & Diabetes, Department of Pediatrics, University of Crete, Medical School, Heraklion, Greece.

**Purpose:** To evaluate the presence of EPCs in the peripheral blood of young patients with DM type 1- a pilot study.

**Methods:** Blood samples were collected and analyzed from 9 patients with DM type 1 and 9 controls. The median age was 17(range:8-30) years old and 19(range 10-30) years old in the control group. The median of DM duration was 12 years (range: 5-30). The presence of Diabetic Retinopathy (DR) was documented with indirect ophthalmoscopy and Fluorescence Angiography, according to the Early Treatment of Diabetic Retinopathy Study (ETDRS) criteria. The EPCs were detected with flow cytometry using the following primary antibodies: anti-CD34, anti-CD133, anti-CD45 and anti-VEGFR2.

**Results:** Four out of nine patients had evidence of Diabetic Retinopathy (DR), three mild Non Proliferative DR(NPDR) and one Proliferative DR (PDR). EPCs, defined as CD45-/CD34+/CD133+/VEGFR2+ cells, were detected in 3/9 patients, among whom one was unaffected; one had NPDR and one PDR. The respective percentages of EPCs were: 0.0039%, 0.0035%, and 0.0118%. Finally, circulating EPCs were identified in 1/9 individuals of the control group (0.0098%).

**Conclusions:** CD45-/CD34+/CD133+/VEGFR2+ EPCs populations were detected in the peripheral blood of this group of young diabetic patients. Not all of them had retinal microangiopathy, while our EPC population was also detected in the control group. The clarification of the presence of EPCs in the peripheral blood early in the disease course could potentially offer significant information regarding the progress of diabetic angiopathy.

**Commercial Relationships:** Chrysanthi Tsika, None; Zoi Kapsala, None; Charalampos Pontikoglou, None; Vassiliki Louvari, None; Dimitrios Mamoulakis, None; Helen A. Papadaki, None; Miltiadis K. Tsilimbaris, None

**Program Number:** 2425 **Poster Board Number:** C0126

**Presentation Time:** 2:45 PM - 4:30 PM

**Differences in Aqueous Concentrations of Various Cytokines in Macular Edema Due to Non-proliferative and Proliferative Diabetic Retinopathy**

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**Purpose:** The purpose of this study was to investigate the differential aqueous concentrations of interleukin 6, 8, 1β (IL-6, IL-8, IL-1β), serum amyloid A (SAA), transforming growth factor (TGF-β), basic fibroblast growth factor (bFGF), and vascular endothelial growth factor (VEGF) in eyes with macular edema due to non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR).

**Methods:** Eighteen eyes of 18 patients with NPDR, 8 eyes of 8 patients with PDR, and 10 eyes of 10 patients with non-diabetic ocular disease were included in the study sample. Aqueous humor samples were collected just before intravitreal injection, and were assessed for 7 cytokines using multiplex bead assay.

**Results:** Significantly increased concentrations of IL-6, IL-8, IL-1β, SAA, TGF-β, bFGF, and VEGF were found in the aqueous humor of NPDR and PDR patients compared with control samples. Higher concentrations of IL-1β were measured in the aqueous humor of patients with PDR compared with NPDR (P=.007). A significant correlation was observed between concentration of VEGF and both the full and outer central macular thickness of NPDR patients (r=.513 & .515; P=.030 & .029, respectively). In the PDR group, the level of IL-8 was significantly associated with inner central macular thickness (r=.763, P=.028). Following the injection of intravitreal bevacizumab at 4 weeks, the full and outer central macular thickness was significantly reduced in NPDR patients compared with PDR patients.

**Conclusions:** Intraocular concentration of VEGF was significantly associated with both full and outer central macular thickness in NPDR patients whose macular edema responded well to anti-VEGF therapy. IL-1β and IL-8 promoting fibrosis was associated with macular edema in PDR patients, which may explain why intravitreal bevacizumab single injection did not markedly improve macular edema in PDR patients.

![Fig 1. Aqueous humor levels of cytokines (Log concentration pg/ml) in eyes with NPDR and PDR.](image-url)
Factors Affecting Successful Completion of Panretinal Photocoagulation

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Purpose: To determine if the method of anesthesia (topical versus retrobulbar) and the type of laser (Pascal versus conventional green laser) affect the completion rate of panretinal photocoagulation (PRP).

Methods: This was a retrospective chart review study from a single institution. All patients undergoing PRP in previously untreated eyes for the diagnosis of diabetic retinopathy or central retinal vein occlusion during the past four years were identified. Eyes were included in the study if the type of laser and anesthetic used, the number and size of laser spots, and the presence or absence of vitreous hemorrhage were obtainable from the medical records for the first PRP session and all subsequent visits within 90 days. Eyes were excluded if they underwent vitrectomy or developed new vitreous hemorrhage within 90 days of the first laser treatment. Completed treatment was defined as 1200 or more laser burns with retinal spot size of 500 microns or 1800 burns with spot size of 400 microns within 90 days of the first PRP treatment. Completion rate was defined as the percentage of treated eyes receiving complete PRP.

Results: 132 eyes (109 patients) were treated with conventional green laser using topical anesthesia (CGT), 26 eyes (23 patients) with conventional green laser using retrobulbar anesthesia (CGRB), 48 eyes (43 patients) with Pascal laser using topical anesthesia (PT), and 1 eye with Pascal laser using retrobulbar anesthesia (PRB). The completion rates were as follows: CGT 46 of 132 (34.8%), CGRB 25 of 26 (96.2%), PT 21 of 48 (43.8%), and PRB 1 of 1 (100%). The relative risks of incomplete treatment were: CGT vs. CGRB 16.9 (CI, 2.5 to 116.3, P=0.004), CGT vs. PT: 1.5 (CI, 1.055 to 2.1, P=0.023), and PT vs. CGRB: 11.4 (CI, 1.6 to 79.8, P=0.0145).

Conclusions: Conventional green laser with retrobulbar anesthesia and Pascal laser with topical anesthesia both have higher completion rates than conventional laser using topical anesthesia. The magnitude of this difference suggests that the use of retrobulbar anesthesia or Pascal laser should be strongly considered when performing PRP.

Commercial Relationships: Jan A. Kylstra, provisional 61/653,171 (P); Hugh E. Wright, None; Rupal Trivedi, None

Program Number: 2427 Poster Board Number: C0128
Presentation Time: 2:45 PM - 4:30 PM

Auto Anti-retinal Antibodies in Diabetic Retinopathy


Purpose: To identify the retinal proteins targeted by serum antibodies from diabetic retinopathy patients.

Methods: Western blots were performed on diabetic retinopathy patients’ serum using eye bank normal retinal proteins. Protein A magnetic beads captured the antibody/antigens immune complexes. We then ran the eluted complexes on SDS gels stained with Sypro Ruby stain and excised the bands and sent them for mass spectrometry for protein identification. The immunoglobulins in the serum were bound to the protein A magnetic beads and then incubated with normal retinal extracts. The immune complexes were eluted and ran on SDS gels. The gels were stained with Sypro Ruby stain and the distinct bands were excised from the gels and sent for mass spec analysis. Gel slices were processed for mass spec including an overnight digestion with trypsin, the peptides were extracted and the samples were run on Thermo Q exactive mass spectrometer. Data analysis was performed with Proteome Discoverer 1.3 and retinal protein sequences were blasted against the SwissProt_2012_09 database for identification. Scaffold, proteome software, was used for secondary analysis.

Results: Over 280 proteins were identified from the runs. The initial mass spec results identified several retinal proteins from the immunocomplexes with diabetic patients’ sera. These proteins include: type I and II cytoskeletal keratin, fibronectin, Complement C4-B and C3, myosin 9, cytoplasmic I actin, microtubule-associated protein 1, non-erythrocytic spectrin alpha and beta chains and filamin-A. These proteins were differentially pulled down by the diabetic patients’ sera compared to control sera.

Conclusions: This is a new approach to study the role of serum antibodies from diabetic patients. Immune complexes were generated first using protein A magnetic beads. This is a simpler method than the time consuming 2D gels. Various proteins were identified as work is in progress to generate more data. These proteins need to be verified regarding their role in diabetic retinopathy. Further work is planned to investigate the retinal targets of the antibodies by indirect immunohistochemistry.

Commercial Relationships: John R. Heckenlively, None; A. J. Karoukis, None; Mohammad I. Othman, None; Thomas W. Gardner, Kelvista (C), Aerpio (C), Akebia (C), Penn State University (P)
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Program Number: 2428 Poster Board Number: C0129
Presentation Time: 2:45 PM - 4:30 PM

Subretinal layer thickness ratio changes for early detection of diabetes

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Purpose: To determine if the subretinal layer thickness ratio changes for early detection of diabetes.

Methods: The subretinal layer thickness ratio (SLTR) was measured using an optical coherence tomography (OCT) system with adjustable capture range to compensate for varying macular thickness. The OCT system was designed to image the subretinal layer with a resolution of 3 μm. The SLTR was calculated as the ratio of the subretinal layer thickness at the fovea to the subfoveal choroidal thickness. The SLTR was measured in 100 diabetic patients with and without diabetic retinopathy and compared to the SLTR in 100 healthy control subjects. The SLTR was analyzed using a one-way ANOVA with post-hoc comparisons using the Tukey test.

Results: The SLTR was significantly lower in diabetic patients with diabetic retinopathy compared to healthy control subjects (P<0.05). The SLTR was also lower in diabetic patients without diabetic retinopathy compared to healthy control subjects (P<0.05). The SLTR was significantly lower in diabetic patients with diabetic retinopathy compared to diabetic patients without diabetic retinopathy (P<0.05).

Conclusions: The subretinal layer thickness ratio changes for early detection of diabetes.
The Eye Center/The Retina Center, Champaign, IL; 3University of Illinois at Urbana-Champaign, Urbana, IL.

**Purpose:** To investigate the use of ratiometric analysis of retinal layer thicknesses as an early indicator of diabetes.

**Methods:** Eight patients were chosen for this study. Four of the patients were clinically diagnosed to have diabetes (DM+) and four were used as control subjects (DM-). All patients’ retinas were imaged using optical coherence tomography (RTVue, Optovue, Inc.) and showed no morphological abnormalities. Retinal images were then manually segmented at selected layers (see fig. 1) and ratios between various layer thicknesses were compared between DM- and DM+ cases. After analysis, these ratios were correlated to the presence or absence of diabetes.

**Results:** It was found that a ratiometric analysis of retinal layer thicknesses in the foveal region highlighted many ratios in which the mean of the DM+ group differed from the mean of the DM- group by at least one standard deviation. Figure 2 shows 12 ratios taken from the foveal region in which both means lie outside of their respective standard deviations, indicating a statistically significant difference. While there is some interdependence between these ratios, they include contributions from every segmented layer. A physiologically significant correlation is the fact that all of these ratios involve the inner segment and almost half of them involve the retinal pigment epithelium, two layers that would be directly affected by vascular changes associated with diabetic retinopathy.

**Conclusions:** A ratiometric analysis on layer thicknesses in the retina of diabetic and control patients reveals a statistically different set of thickness ratio values for diabetic patients. These results are encouraging for future efforts to diagnose or screen for diabetes at an early stage, before symptoms or gross retinal abnormalities occur. Previous studies have investigated layer thicknesses in the retina to draw conclusions about the presence of diabetes; however, an analysis of the ratios of these layer thicknesses is a more robust measure. Variations in overall retinal thickness between patients will not affect the accuracy of ratio measurements.

Figure 1: Representative OCT image of the retina of a DM+ patient with manual layer segmentation.

Figure 2: Statistical analysis of 12 retinal layer thickness ratios. Red squares: control subjects, blue circles: diabetic subjects.

**Commercial Relationships:** Ryan Shelton, None; Jessica N. Taibl, None; Nathan D. Shemonski, None; Samir I. Sayegh, None; Stephen A. Boppart, Diagnostic Photonics, Inc. (F), Welch Allyn, Inc. (C), Texas Instruments, Inc. (R)

**Support:** NIH Grants EB013723 and EB012479

**Program Number:** 2429 **Poster Board Number:** C0130 **Presentation Time:** 2:45 PM - 4:30 PM

**Purpose:** The purpose of this study was to report the technical efficacy and convenience of panretinal photococoagulation for proliferative diabetic retinopathy using a slit lamp based monospot laser (532nm, Iridex Oculight) versus navigated laser (532nm, Navilas).

**Methods:** Case series of eyes with proliferative diabetic retinopathy were included. Each eye underwent panretinal photococoagulation: half inferior retina with slit lamp laser and the other half inferior retina field with navigated laser during the same day. Grade 3 burns with a 300microns spot size were placed with both modalities. Laser parameters and laser burn spread were evaluated.

**Results:** Using pulse duration of 30ms in both lasers, slit lamp laser required an average power intensity of 745mW compared to an average of 400mW when using navigated laser. Average time required per sitting was 15minutes and 5 minutes for slit lamp and navigated laser respectively. Pain level was considerably less when using navigated laser. Images taken at 3 months after laser session showed similar spot spread in both laser modalities.

**Conclusions:** When using same short pulse duration, Navigated laser is convenient, less time consuming and less painful for the patient compared with slit lamp monospot laser modality.

**Commercial Relationships:** Stephanie Y. Lu, None; Ken Y. Lin, None

**Program Number:** 2430 **Poster Board Number:** C0131 **Presentation Time:** 2:45 PM - 4:30 PM
Diabetic self-management and its association with diabetic retinopathy in patients with type 2 diabetes

Ningpu Liu, Na Li, Xiufen Yang, Yu Deng, Hong Gu, Xuetao Ren, Jun Xu, Kai Ma. Beijing Tongren Eye Center, Beijing Tongren Hospital, Beijing, China.

Purpose: To investigate the association of diabetic self-management with the risk of diabetic retinopathy (DR) in patients with type 2 diabetes mellitus.

Methods: A total of 1100 patients with type 2 diabetes mellitus were recruited in the Desheng community of urban Beijing. All patients were surveyed using a standardized questionnaire and underwent detailed ophthalmic examination. Patients were classified into DR group or no diabetic retinopathy (NDR) group according to the ETDRS standard grading protocol. The overall levels of diabetes self-management were assessed and compare for the differences between DR and NDR groups.

Results: In the study population, the prevalence of DR was 32.1%. Sixty-three percent (63.0%) of the patients had the glycated hemoglobin (HbA1C) level less than <7.0%. Majority of patients (85.4%) conducted a diet control, 77.3% had exercise, 56.0% monitored blood glucose regularly, 41.5% detected blood glucose more than three times a month, 40.8% detected HbA1C more than one time every six months, 71.7% had ophthalmologic examination after the diagnosis of diabetes mellitus, and 68.5% had mydriatic check-up. Increased risk of DR was associated with higher HbA1C levels of ≥7.0% (OR=3.23, 95%CI: 2.44-4.28), insulin therapy (OR=7.48, 95%CI: 4.48-12.76), lower obedience to diet control (OR=1.72, 95%CI: 1.22-2.43), no exercise (OR=1.42, 95%CI: 1.04-1.94), change of therapeutic protocol during the last five years (OR=1.78, 95%CI: 1.32-2.41), lower level of education (OR=1.9, 95%CI: 1.39-2.62), male gender (OR=1.41, 95%CI: 1.08-1.84), lower monthly income (OR=1.46, 95%CI: 1.12-1.91), and family history of diabetes (OR=1.62, 95%CI: 1.1-2.37). In the multifactor logistic regression model, male gender (OR=2.21, 95%CI:1.57-3.11), lower level of education (OR=1.98, 95%CI:1.33-2.94), lower monthly income (OR=1.66, 95%CI:1.15-2.39), duration of diabetes more than 10 years (OR=2.46, 95%CI:1.77-3.41), HbA1C ≥7.0% (OR=2.24, 95%CI: 1.64-3.07) and insulin therapy (OR=3.38, 95%CI: 2.38-4.8) were associated with higher risk of DR.

Conclusions: The prevalence of DR in the study population was 32.1%. Longer duration of diabetes, insulin therapy, higher HbA1C level, male gender, and lower level education are associated with higher risk of DR, suggesting that lower level of diabetic self-management increased the risk of DR.

Commercial Relationships: Ningpu Liu. None; Na Li. None; Xiufen Yang. None; Yu Deng. None; Hong Gu. None; Xuetao Ren, None; Jun Xu. None; Kai Ma. None

Program Number: 2431 Poster Board Number: C0132
Presentation Time: 2:45 PM - 4:30 PM

Association between Diabetic Foot Ulcer and Diabetic Retinopathy

Duck Jin Hwang1,2, Kyung Min Lee1,3, Moon Seok Park1,3, Sung Hee Choi4, Ji In Park1,2, Kyu Hyung Park1,2, Se Joon Woo1,2.

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Purpose: The aim of this study was to investigate the prevalence of diabetic retinopathy (DR) in patients with diabetic foot ulcer (DFU) and to elucidate the association between severity of DR and DFU.

Methods: A retrospective review was conducted for consecutive patients who were diagnosed with DFU from October 2004 to October 2011 and received ophthalmic examination within 6 months after diagnosis of DFU. The prevalence and severities of DR in patients with DFU was assessed. In addition, the association between severity of DR and DFU was evaluated. Patients with DFU were divided into two groups according to the severity of DR, and demographic, clinical, and biochemical characteristics were compared between two groups.

Results: A total of 100 patients (mean age, 66.7 ± 10.6 years) were analyzed and 74 patients (74%) were male. Mean diabetes duration was 18.5 ± 10.6 years and HbA1c (%) was 8.0 ± 1.8. Ninety patients (90%) had DR and 55 patients (55%) had proliferative DR (PDR). There was no significant association between the severity of DR and DFU (r=0.034, p=0.734). In the subgroup comparison, the PDR group had a longer duration of diabetic mellitus, higher BUN and creatinine levels than the non-PDR group had.

Conclusions: Most patients with DFU had DR and more than a half of patients had PDR. Therefore, patients with DFU, especially with the presence of high BUN/Cr, long diabetes duration, should have a cautious retinal examination for diagnosis and management of DR.

Commercial Relationships: Duck Jin Hwang. None; Kyung Min Lee. None; Moon Seok Park. None; Sung Hee Choi. None; Ji In Park. None; Kyu Hyung Park. None; Se Joon Woo. None

Program Number: 2432 Poster Board Number: C0133
Presentation Time: 2:45 PM - 4:30 PM

Retinal morphometry changes observed in vivo measured with SD-OCT after pan-retinal photocoagulation in patients with proliferative diabetic retinopathy

Christoph Mitsch, Matthias Bolz, Berthold Pemp, Andreas Reitner, Christoph D. Scholda, Ursula Schmidt-Erfurth. Ophthalmology and Optometrics, Medical University of Vienna, Vienna, Austria.

Purpose: To analyze the morphometric changes of distinct retinal layers measured around the optic disc by SD-OCT after pan-retinal photocoagulation.

Methods: Patients were examined monthly with Fluorescence Angiography (FA) following a specific examination protocol for diabetic retinopathy and a peri-papillary ring-scan with Spectral-Domain Optical Coherence Tomography before and after undergoing a single-session pan-retinal photocoagulation during 6 months. Thickness measurements of distinct retinal layers were then performed and analyzed.

Results: One month after pan-retinal photocoagulation a significant increase of average peripapillary outer nuclear layer (p = 0.007) and whole retinal thickness (p = 0.006) was found. This was followed by a slow decline to baseline values over the following five months. The mean combined thickness of the retinal pigment epithelium and the photoreceptor cell layer was significantly reduced one month after laser treatment (p < 0.001). This decrease was followed by a slow increase until month 6, but did not reach original thickness values.

Conclusions: Pan-retinal photocoagulation leads to diffuse, but reversible morphometric changes of retinal layers measurable by peripapillary OCT. The found short-term increase of retinal thickness can be mainly attributed to an increase of outer nuclear layer thickness and was accompanied by a permanent attenuation of retinal pigment epithelium and photoreceptor cell layer. The reversible changes of peripapillary retinal structure observed in-vivo could be interpreted as signs of diffuse retinal inflammation following laser treatment.

Commercial Relationships: Christoph Mitsch. None; Matthias Bolz. None; Berthold Pemp. None; Andreas Reitner. None; Christoph D. Scholda. None; Ursula Schmidt-Erfurth. Alcon (C), Bayer Healthcare (C), Novartis (C)
Program Number: 2433 Poster Board Number: C0134
Presentation Time: 2:45 PM - 4:30 PM
Proliferative diabetic retinopathy, maculopathy and choroidal neovascularization: concurrent pathology
Neda Minakaran1, Gillian Vafidis2, Evelyn Mensah2.
1Ophthalmology, Whipps Cross University Hospital, London, United Kingdom; 2Ophthalmology, Central Middlesex Hospital, London, United Kingdom.
Purpose: Large epidemiological studies suggest that the co-existence of choroidal neovascularization in patients with diabetic retinopathy is uncommon. We describe a case series of patients in whom the two pathologies co-exist and propose a hypothesis for the underlying pathophysiology.
Methods: Retrospective case note, fundal photography, ocular coherence tomography (OCT) and fluorescein angiography review.
Results: Three eyes of 3 patients under the care of the hospital eye service with chronic diabetic macular oedema and proliferative retinopathy developed choroidal neovascularization, confirmed on OCT and fluorescein angiography. All patients were male of Asian ethnicity, with mean age 66 years (range 54-77 years). All eyes were treated for diabetic macular oedema over mean 5 years (range 6 months-10 years) with mean 5 sessions of macular laser (range 1-12). One eye had quiescent treated proliferative and 2 active new proliferative diabetic retinopathy at the time of diagnosis with choroidal neovascular membrane. Visual acuity pre-treatment with intravitreal ranibizumab was LogMAR 1.02. At 1 year follow up, mean number of injections was 6 (range 3-10) and visual acuity was LogMAR 1.30.
Conclusions: Elevated levels of vascular endothelial growth factor in eyes with chronic diabetic macular oedema and ischaemia are likely to be implicated in choroidal neovascular membrane formation. Asian ethnicity and male sex may be risk factors, and prognosis despite treatment with anti-VEGF agents appears to be poor. It is important to consider choroidal neovascularization as a co-existent diagnosis in patients with treated diabetic macular oedema or proliferative diabetic retinopathy who have a drop in visual acuity. This will enable prompt treatment that may improve final visual outcome.

Commercial Relationships: Neda Minakaran, None; Gillian Vafidis, None; Evelyn Mensah, None

Program Number: 2434 Poster Board Number: C0135
Presentation Time: 2:45 PM - 4:30 PM
Metamizole as analgesic during panretinal photocoagulation in proliferative diabetic retinopathy
Rafael B. Araújo1, Leandro C. Zacharias1, Walter Y. Takahashi1, Maiara M. Leitão1, Vinicius P. Nascimento2, Gabriela S. Melo2.
1Ophthalmology, Universidade de São Paulo, São Paulo, Brazil; 2Universidade Federal do Rio Grande do Norte, Natal, Brazil.
Purpose: To evaluate the effectiveness of oral metamizole in reducing pain during panretinal photocoagulation (PRP) in patients with proliferative diabetic retinopathy (PDR).
Methods: Twenty patients from a single center (Department of Ophthalmology of Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo) with PDR and indication of bilateral PRP were recruited for a double-masked, controlled, prospective study. The exclusion criteria were: previous photocoagulation treatment, media opacity such as cataracts, corneal diseases or vitreous haemorrhage, unilateral PDR, chronic use of analgesics or history of any side-effects reported after metamizole use. The treated eyes were randomly assigned eyes in two groups, and each patient had one eye assigned per group. Group A received 1000 mg of metamizole and group B received a placebo pill forty minutes before initiating the treatment. Each patient scored the pain sensation immediately after PRP using Scott’s visual analogue scale (VAS). Statistics were calculated with SPSS version 20.0. The paired Student t test was used to measure the significance between the two groups VAS scores, with significance level adopted of p<0.05.
Results: The patients referred a significant lower level of pain during PRP when they were submitted to PRP after oral metamizole treatment when compared to baseline placebo (p=0.002) and this difference was significant, with a p value of 0.002. The data was expressed in mean, maximum, minimum scores and standard deviation. The mean pain scores for groups A and B were 4.72 ± 1.708 and 5.89 ± 1.967, respectively. The minimum/maximum scores within groups A and B were 2/8 and 3/8, respectively (Table 1). The patients referred a lower level of pain during PRP when they were submitted oral metamizole treatment than placebo and this difference was significant, with a p value of 0.002. There was no significant difference between gender, age or chronic disease profile.
Conclusions: The use of 1000 mg of metamizole 40 minutes before PRP significantly reduced the pain associated with the procedure in patients with proliferative diabetic retinopathy. Thus, metamizole is effective in reducing pain during PRP and can be applied before the procedure, specially in patients with no history of drug allergy.

<table>
<thead>
<tr>
<th></th>
<th>Data</th>
<th>Metamizole (Minimum-maximum)</th>
<th>Placebo (Minimum-maximum)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS (Acu. Analogue)</td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td></td>
</tr>
<tr>
<td>(5-8)</td>
<td>4.72</td>
<td>4.706</td>
<td>5.89</td>
<td>1.967</td>
</tr>
</tbody>
</table>

Table 1: Mean, maximum and minimum VAS scores for groups A and B

Commercial Relationships: Rafael B. Araújo, None; Leandro C. Zacharias, None; Walter Y. Takahashi, Novartis (C), Bayer (C), Bayer (R); Maiara M. Leitão, None; Vinicius P. Nascimento, None; Gabriela S. Melo, None

Clinical Trial: 0766/11

Program Number: 2435 Poster Board Number: C0136
Presentation Time: 2:45 PM - 4:30 PM
The Relationship of Retinal Vessel Caliber to Diabetic Macular Ischemia
Gerald Liew1,2, Dawn A. Sim1,1, Pearse A. Keane1,1, Ava G. Tan2, Paul Mitchell2, Jie Wang3, Tien Y. Wong3, Marcus Frattiger4, Adnan Tufail5, Catherine A. Egan1,1, 1Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom; 2University of Sydney, Sydney, NSW, Australia; 3UCL Institute of Ophthalmology, London, United Kingdom; 4National University of Singapore, Singapore, Singapore.
Purpose: Diabetic macular ischemia (DMI) is an important cause of visual loss. However the relationship of DMI to retinal vessel diameter has not been examined. We examined if retinal vessel caliber is related to the presence and severity of DMI to determine if retinal vessel diameter may be a marker of DMI.
Methods: Clinic based cross-sectional study of patients with type 2 diabetes presenting to a tertiary hospital over 6 months. Presence and severity of DMI was assessed using Early Treatment Diabetic Retinopathy Study (ETDRS) protocols from fundus fluorescein images and classified as none/mild, moderate or severe according to foveal avascular zone (FAZ) size, capillary loss or dilatation, and perifoveal vascular abnormalities. Custom software was used to quantify the greatest linear dimension and area of the FAZ. Retinal vessel caliber was measured using a validated semi-automated software on fundus fluorescein images.
Results: Of 53 patients examined, 18 (34%), 18 (34%) and 17 (32%)...
had none/mild, moderate and severe DMI respectively. Persons with moderate or severe DMI had narrower mean retinal arteriolar caliber than persons with no DMI (140.6 µm 95% Confidence Interval (CI) 134.7, 146.4 vs 150.7 µm, 95% CI 142.5, 158, p=0.04). Table The association remained after multivariate adjustment for age, gender, previous panretinal photocoagulation and neovascularisation at the disc and elsewhere (adjusted mean retinal arteriolar caliber of 140.7 µm 95% CI 135.5, 146.0 vs 150.4 µm, 95% CI 142.9, 157.8, p=0.04)

Increasing severity of DMI was also associated with narrower arterioles, with multivariate adjusted mean retinal arteriolar calibers of 150.6, 142.1 and 139.1 µm in participants with none/mild, moderate and severe DMI respectively. Increased FAZ (greatest dimension and area of ischemia) were also associated with narrower arterioles, with multivariate adjusted mean retinal arteriolar calibers of 150.6, 142.1 and 139.1 µm in participants with none/mild, moderate and severe DMI respectively. Increased FAZ (greatest dimension and area of ischemia) were also associated with narrower arterioles, with multivariate adjusted mean retinal arteriolar calibers of 150.6, 142.1 and 139.1 µm in participants with none/mild, moderate and severe DMI respectively. Increased FAZ (greatest dimension and area of ischemia) were also associated with narrower arterioles, with multivariate adjusted mean retinal arteriolar calibers of 150.6, 142.1 and 139.1 µm in participants with none/mild, moderate and severe DMI respectively.

Conclusions: Retinal arteriolar narrowing is associated with macular ischemia in eyes with diabetic retinopathy, suggesting it may be a marker for DMI.

### Table. Retinal vessel calibers by severity of diabetic macular ischemia.

<table>
<thead>
<tr>
<th>Severity of DMI</th>
<th>Mean arteriolar diameter (µm)</th>
<th>Mean venular diameter (µm)</th>
<th>Mean arteriolar-to-venule ratio (AVR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None/mild</td>
<td>150.6</td>
<td>142.1</td>
<td>139.1</td>
</tr>
<tr>
<td>Moderate</td>
<td>142.1</td>
<td>134.7</td>
<td>133.2</td>
</tr>
<tr>
<td>Severe</td>
<td>134.7</td>
<td>128.5</td>
<td>127.8</td>
</tr>
</tbody>
</table>

Figure 1) Retinal venular caliber and arteriole to venule ratio (AVR) and 0.19 mm² (95% CI 0.04, 0.33) increase in diameter were associated with 0.21 mm (95% CI 0.05, 0.38) increase in arteriolar caliber; each standard deviation decrease in arteriolar caliber was associated with 0.21 mm (95% CI 0.05, 0.38) increase in diameter and 0.19 mm² (95% CI 0.04, 0.33) increase in area.(p=0.01 for both, ε=0.05)

 Increasing severity of DMI was also associated with narrower arterioles, with multivariate adjusted mean retinal arteriolar calibers of 150.6, 142.1 and 139.1 µm in participants with none/mild, moderate or severe DMI respectively. Increased FAZ (greatest dimension and area of ischemia) were also associated with narrower arterioles, with multivariate adjusted mean retinal arteriolar calibers of 150.6, 142.1 and 139.1 µm in participants with none/mild, moderate or severe DMI respectively. Increased FAZ (greatest dimension and area of ischemia) were also associated with narrower arterioles, with multivariate adjusted mean retinal arteriolar calibers of 150.6, 142.1 and 139.1 µm in participants with none/mild, moderate or severe DMI respectively. Increased FAZ (greatest dimension and area of ischemia) were also associated with narrower arterioles, with multivariate adjusted mean retinal arteriolar calibers of 150.6, 142.1 and 139.1 µm in participants with none/mild, moderate or severe DMI respectively. Increased FAZ (greatest dimension and area of ischemia) were also associated with narrower arterioles, with multivariate adjusted mean retinal arteriolar calibers of 150.6, 142.1 and 139.1 µm in participants with none/mild, moderate or severe DMI respectively. Increased FAZ (greatest dimension and area of ischemia) were also associated with narrower arterioles, with multivariate adjusted mean retinal arteriolar calibers of 150.6, 142.1 and 139.1 µm in participants with none/mild, moderate or severe DMI respectively.
Purpose: Diabetes is a common condition disproportionately impacting African-Americans (AA). One in two AAs is projected to develop diabetes during their lifetime, increasing the risk of developing diabetic eye complications. Our study aim was to evaluate the efficacy of a behavioral intervention to increase rates of dilated fundus exams (DFEs) and to characterize perceived risks of ophthalmic disease in older AAs non-adherent to follow-up.

Methods: A prospective clinical trial of AA patients aged ≥65, with type 2 diabetes, and no DFE within the past year was performed. We collected the baseline data including: education level, diabetes risk perceptions and self-care behaviors, vision function (NEI-VFQ), and A1C level. Analysis of relationships between perceived risk of future vision problems and self-care behaviors, A1C, and visual function was performed.

Results: Data are reported on 169 subjects. Subjects were grouped according to perceived vision risk (low (42%), moderate (33.7%), and high (24%) risk). Vision risk perception was not related to A1C, self-care behaviors, or education. However, it was related to the following NEI-VFQ scales: near activities (p<0.01), distance activities (p<0.01), mental health (p<0.01), role difficulties (p=0.01), and driving (p=0.03). Compared to the other 2 groups, those in the high risk group had worse near and distance scores, general health, mental health, role function, and driving scores.

Conclusions: African Americans with diabetes who perceive themselves as being at a high risk for future vision problems are more likely to report impairments in vision-related functioning. Despite subject’s increased perceived risk to eye care problems and functional impairment, there was not an increased adherence to recommended ophthalmic care in the high risk perception population. Additional research is needed to better understand health promoting behaviors in AA with diabetes.

Commercial Relationships: Bianca Collymore, None; Ann P. Murchison, None; Lisa A. Hark, None; Bianca Collymore, None; Robin J. Casten, None; David M. Weiss, None; Betina M. Johnson, None; Barry Rovner, None; Jeffrey D. Henderer, None; Julia A. Haller, Allergan (F), Advanced Cell Technology (C), Regeneron (C), Merck (C), Second Sight (C), KalVista (C), ThromboGenics (C), OptimaMed (I)

Support: Pennsylvania Department of Health

Clinical Trial: NCT01179555

Program Number: 2438 Poster Board Number: C0139
Presentation Time: 2:45 PM - 4:30 PM

David M. Weiss1, Ann P. Murchison1,2, Lisa A. Hark1,2, Bianca Collymore1, Robin J. Casten1,2,3, Rickie Brawer3, James D. Plumb3, Barry Rovner1,2, Jeffrey D. Henderer1, Julia A. Haller1,2,1 Wills Eye Institute, Philadelphia, PA; 2Thomas Jefferson University, Philadelphia, PA; 3Ophthalmology, Temple University Hospital, Philadelphia, PA.

Purpose: Research recruitment, particularly among African Americans (AAs), can be difficult. Given the different requirements of IRBs, both opt-in and opt-out recruitment methods were used for a single ophthalmic study involving AAs with diabetes. The success of the two methods as well as their characteristics are compared.

Methods: A prospective, multi-site clinical trial was designed to test the efficacy of a culturally-relevant, home-based behavioral intervention to improve the rates of annual dilated fundus examinations in older AAs with diabetes. Patients were recruited from clinical practices at two academic medical centers. Depending on the medical center affiliation, patients were sent either opt-out or opt-in recruitment letters. Opt-out letters instructed patients to decline study participation via mail or telephone. Patients who did not opt out were called by study personnel. Opt-in directed patients to contact study personnel if they were interested in being screened for enrollment. Baseline measures included various cognitive assessments, the Diabetes Self-Care Inventory, Risk Perception Survey - Diabetes Mellitus, Cultural Relevancy Scale, and Visual Functioning Questionnaire-25. The number of recruitment letters mailed, recruitment calls made, enrollment, and all baseline measures were tracked and compared between the two sites.

Results: A total of 2730 opt-in letters and 879 opt-out letters were mailed and 107 subjects enrolled in the trial. Enrollment rates were higher with opt-out recruitment (7.0% vs. 4.0%, p=0.01) but required more staff time (1271 telephone calls vs. 283 telephone calls). Participants recruited with an opt-out letter had better cognitive function (p=0.01), were less likely to be dependent on others due to their vision (p=0.04), and were more likely to have higher perceived personal control over their health (p=0.03). There were no significant differences between the groups in age, gender, education, hemoglobin A1C, diabetes self-care behaviors, or ratings of cultural characteristics.

Conclusions: In the current study, opt-out recruitment resulted in improved enrollment but required more staff time. Rising rates of diabetes and diabetic retinopathy will increase the need for ophthalmology research. To optimize recruitment of older and minority patients, researchers should be aware of optimal methods in their population.

Commercial Relationships: David M. Weiss, None; Ann P. Murchison, None; Lisa A. Hark, None; Bianca Collymore, None; Robin J. Casten, None; Rickie Brawer, None; James D. Plumb, None; Barry Rovner, None; Jeffrey D. Henderer, None; Julia A. Haller, Allergan (F), Advanced Cell Technology (C), Regeneron (C), Merck (C), Second Sight (C), KalVista (C), ThromboGenics (C), OptimaMed (I)

Support: Pennsylvania Department of Health

Clinical Trial: NCT01179555

Program Number: 2439 Poster Board Number: C0140
Presentation Time: 2:45 PM - 4:30 PM
Combination of Intravitreal Injection of Pegaptanib plus Progressive PRP versus Full PRP alone in Patients with High Risk Proliferative Diabetic Retinopathy

Sérgio Leal1,2, João Figueira1,2, Luís Ribeiro1,2, Maria Luz Cachulo1,2, Rufino Silva1,2, Sandra Nunes1,2, Ana M. Pedroso1, Miguel Costa1,2, Jose G. Cunha-Vaz1,2, AIBLI - Association for Innovation and Biomedical Research on Light and Image, Coimbra, Portugal; 2CRIOP / CHUC - Centro de Responsabilidade Integrado de Oftalmologia, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal.

Purpose: To evaluate safety and efficacy of intravitreal (ITV) injection of pegaptanib combined with progressive panretinal photocoagulation (PRP) versus full PRP alone in the regression of retinal neovascularization in eyes with high-risk proliferative diabetic retinopathy (HR-PDR).

Methods: Twenty-two patients were included in a prospective, randomized, open label exploratory, phase II study to assess safety and efficacy of pegaptanib (0.3 mg ITV injections)+progressive PRP and full PRP alone in the treatment of patients with HR-PDR without previous laser treatment. Patients were randomized in a 1:1 ratio to one treatment arm: standard photocoagulation (PRP according the Diabetic Retinopathy Study; DRS), or combination treatment of pegaptanib ITV injections+progressive PRP (2 weeks±1 week after the first injection, starting with DRS third ring, extending from the ora serrata to the mid-periphery with coalescing spots followed, if needed, by the DRS second and first ring). One eye was selected and treated as the study eye. Patients underwent at baseline, months 3, 6
Results: After screening of the corresponding abstracts and full text papers, four trials totalling 1786 patients with DME were included. In all the four RCTs, patients with recent systemic vascular events were not included. In two RCTs ranibizumab was administered monthly for two years, and in the other two RCTs as needed for one year. In patients treated with 0.3 mg/0.5 mg ranibizumab, the risk ratios (RR) and 95% confidence interval (CI) for CVA, MI and total death compared to the control groups were 0.640 (0.313-1.310, P=0.222), 0.785 (0.371-1.659, P=0.526), and 1.461 (0.696-3.065, P=0.316).

Conclusions: Intravitreal injections of VEGF inhibitors for DME were not associated with the increased risk of CVA, MI or mortality, although data on systemic safety for high risk patients has been remained unknown.

Commercial Relationships: Yasuko Yanagida, None; Takahiro Yamaguchi, None; Takashi Ueta, None

Program Number: 2442 Poster Board Number: C0143
Presentation Time: 2:45 PM - 4:30 PM
Change of retinochoroidal thickness after pars plana vitrectomy with endophotocoagulation for proliferative diabetic retinopathy
Kentaro Yamamoto, Takeshi Iwase, Hiroaki Ushida, Hiroko Terasaki. Ophthalmology, Nagoya University Hospital, Nagoya, Japan.
**Purpose:** Choroidal thickness may change after vitrectomy for proliferative diabetic retinopathy (PDR), because the surgery includes various procedures. One of the factors affecting choroidal thickness may be the application of endophotocoagulation. On the other hand, swelling the retina after photocoagulation was reported. The purpose of this study was to determine whether there was a thickening of the peripheral and posterior retina-choroid after PPV with photocoagulation.

**Methods:** The medical charts of 24 eyes of 22 patients that had undergone 23 or 25-gauge PPV with endophotocoagulation for proliferative diabetic retinopathy were reviewed. For control, 26 eyes of 26 consecutive patients that had undergone PPV without photocoagulation for an epiretinal membrane were studied. All surgeries were performed at the Nagoya University Hospital from June to November 2012. The peripheral retina-choroid thickness (RCT) was measured at 5 mm from the limbus in the four quadrants with a swept source optical coherence tomography (SSOCT) before and 3 days, and 1, and 2 week(s) after surgery. The posterior RCT was measured by enhanced depth imaging OCT (EDI-OCT) at the same time points.

**Results:** In the diabetic group with photocoagulation, the mean peripheral RCT before surgery, 3 days, 1, and 2 week(s) after surgery were 225 µm, 780 µm, 351 µm, and 247 µm, respectively. The peripheral RCT at 3 days and 1 week after surgery was significant thicker than that before the surgery (P<0.001, P=0.003). In the control group, the mean peripheral RCT before surgery, 3 days, 1, and 2 weeks after surgery was 167 µm, 248 µm, 212 µm, and 191 µm, respectively. The increase in the peripheral RCT at 3 days after surgery in the diabetes group was significantly greater than in the control group (P<0.001). There was a significant correlation between the number of photocoagulation burns (mean, 1653 ±1057) and the peripheral RCT at 3 days after surgery (r=0.528; P=0.024). There was no significant difference in the peripheral RCT between pre- and any postoperative period in both groups (P>0.05).

**Conclusions:** The peripheral RCT after PPV with endophotocoagulation in the diabetic group became thicker in the earlier postoperative period and the increase in the thickness was significantly correlated with the number of photocoagulation burns.

**Commercial Relationships:** Kentaro Yamamoto, None; Takeshi Iwase, None; Hiroaki Ushida, None; Hiroko Terasaki, None

**Program Number:** C0144

**Presentation Number:** C0144

**Competition of Outcomes in the Use of Intravitreal Bevacizumab Vs. Triamcinolone for Patients with Diabetic Macular Edema at the Time of Cataract Surgery (The DiMECAT Trial) Sukhpal S. Sandhu1,2, Marios Constantinou1,2, Julie L. Morrison1,2, Carly J. D’Sylva1,2, Ryo Kawasaki1,3, Sanjeeva Wickramsinghe1,2, Salmaan Al-Qureshi1,2, Lyndell Lim1,2, 1Centre for Eye Research Australia, Melbourne, VIC, Australia; 2University of Melbourne, Melbourne, VIC, Australia; 3Yamagata University Faculty of Medicine, Yamagata, Japan.

**Purpose:** Cataract surgery in diabetic patients often results in poor visual outcomes due to the progression of diabetic retinopathy and accelerated development of Diabetic Macular Edema (DME). This study reports on the comparison of the use of intravitreal bevacizumab (BVB, Avastin®) vs triamcinolone (TA, TriensenceTM) administered at the time of cataract surgery on the final visual and anatomical outcome.

**Methods:** Prospective randomized trial of intravitreal injection of either 1.25mg of BVB or 2mg of TA at the time of cataract surgery, and at subsequent review if required, in diabetics with visually significant cataract and one of the following:i) refractory DMY at the time of surgery, ii) treated DME within the 12 months prior to surgery, or iii) microaneurysms within the foveal avascular zone not amenable to focal macular laser. End points include best-corrected visual acuity (BCVA, LogMAR letters), change in central macular thickness (CMT) on SD-OCT from baseline, number of injections and ocular complications at months 1 and 6 post-operatively.

**Results:** To date, 24 patients have been recruited at the Royal Victorian Eye and Ear Hospital, Melbourne, Australia, 10 of whom have had surgery (5 in each treatment group). The BVB group were all males, with a mean age of 69±6 years, the TA group had 1 female and a mean age of 67±4 years.

At baseline, the BVB group with 59±13 LogMAR letters and CMT of 390±61µm, was similar to the TA group with 55±11 LogMAR letters and CMT of 395±103µm.

Five TA and 3 BVB subjects have currently reached the 1-month post-operative time point. Although, in comparison to baseline, the CMT had an improved but not significant trend in the TA group (380±105µm vs. 394±69µm BVB group, p=0.42), the BCVA was found to be significantly better in the BVB group (75±6 letters vs. 59±11 letters TA group, p=0.03). One subject in the BVB group was retreated at this time point. There were no incidences of raised intraocular pressure (≥22mmHg) or any other adverse event recorded in either group.

**Conclusions:** When administered at the time of cataract surgery in patients with DME, interim results suggest that at 1 month BVB is associated with an improvement in BCVA and TA a reduction in CMT from baseline. Further data regarding longer term outcomes and the need for ongoing retreatment is still pending.

**Commercial Relationships:** Sukhpal S. Sandhu, None; Marios Constantinou, None; Julie L. Morrison, None; Carly J. D’Sylva, None; Ryo Kawasaki, None; Sanjeeva Wickramsinghe, Novartis (R); Salmaan Al-Qureshi, None; Lyndell Lim, None

**Clinical Trial:** ACTRN1261100888965

**Program Number:** 2444 Poster Board Number:** C0145

**Presentation Time:** 2:45 PM - 4:30 PM

**Identifying progression of retinal disease in eyes with NPDR in diabetes type 2 using non-invasive procedures Jose G. Cunha-Vaz, 1AIBILLI - Association for Innovation and Biomedical Research on Light and Image, Coimbra, Portugal; 2EVICR.net - European Vision Institute Clinical Research Network, Coimbra, Portugal.

**Purpose:** To identify eyes that show worsening and diabetic retinopathy (DR) progression using non-invasive techniques.

**Methods:** Three hundred seventy five (375) type-2 diabetic patients with mild NPDR (ETDRS levels 20 or above) were included in a 1-year observational and prospective study to identify phenotypes of retinopathy progression. Patients were included in 19 clinical sites from the European Vision Institute Clinical Research Network (EVICR.net). The study started in September 2010 and conclusion is expected by May 2013. Four visits are scheduled at months 0, 3, 6 and 12 with the following examinations: color fundus photography (CFFP), spectral domain optical coherence tomography (SD-OCT) and blood tests. ETDRS severity level in the first and last visits, and microaneurysm (MA) turnover (formation plus disappearance rates), using the RetmarkerDR®, are assessed by the Coimbra Ophthalmology Reading Centre (CORC). SD-OCT Cirrus and/or Spectralis are used to measure retinal thickness (RT), nerve fiber and ganglion cell layers. One eye per patient is selected by the Reading Centre as the Study Eye.

**Results:** 375 patients were included (65.4% males and 34.6% females) with ages ranging from 35 to 82 years. Mean BCVA was 84.8±6.6 ETDRS letters. Mean HbA1C was 7.8±4.2% and the
systolic and diastolic blood pressure was respectively of 137.7±16.6 and 77.4±10.1 mmHg. Eyes/patients showed at baseline a mean number of MA of 3.6±5.2. The mean RT in the central subfield was 265.0±21.8 μm for Cirrus OCT and 278.4±26.6 μm for Spectralis OCT. Males showed a higher RT than females (p<0.05). A wide range of abnormal RT values is observed, from higher to lower RT values. Comparing the mean RT in the central subfield with normal RT values (mean±2SD), 8.6% of the eyes/patients showed a decreased RT, and 8.3% of the eyes/patients showed an increased RT. Conclusions: MA and RT at baseline showed a wide range of values indicating involvement of different components of the disease process, vascular and neuronal, in different patients.

Commercial Relationships: Jose G. Cunha-Vaz. Allergan (C), Pfizer (C), Novartis (C), Alimera Sciences (C), Roche (C), Fovea Pharmaceuticals (C), Gene Signal (C)

Clinical Trial: NCT01145599

Program Number: 2445 Poster Board Number: C0146
Presentation Time: 2:45 PM - 4:30 PM

Retinal Oximetry Differences in Vessel Oxygen Saturation by Severity of Diabetic Retinopathy
Alexa M. Waters, Justin Miller, Jean-Claude Mwanza, Seema Garg. Ophthalmology, University of North Carolina, Chapel Hill, NC.

Purpose: To measure retinal vessel oxygen saturation (SO₂) using retinal oximetry in healthy subjects and in diabetic patients with one of three clinical stages: no diabetic retinopathy (DR), mild non-proliferative DR (NPDR) and moderate NPDR. In order to evaluate SO₂ in the context of diabetic status and retinal vascular perfusion, HbA1c, urine microalbumin and fluorescein angiography (FA) were obtained.

Methods: Retinal vessel SO₂ was measured in 16 diabetics with no DR, 16 diabetics with early DR (5 with mild NPDR and 11 with moderate NPDR) and 27 age-matched healthy subjects using a retinal oximeter (Oxymap ehf., Reykjavik, Iceland). Arterial saturation (SaO₂), venous saturation (SvO₂) and arteriovenous (A-V) difference for each subject were calculated within a ring-shaped measurement area concentric to the optic disc. For diabetic patients, HbA1c, urine microalbumin and FA (% ischemia in ring) were also analyzed for correlation.

Results: Patients with moderate NPDR showed a significant increase in SvO₂ compared to healthy subjects and diabetics with no DR (p=0.018, 0.047; respectively) and a nearly significant increase compared to diabetics with mild NPDR (p=0.057). Moderate NPDR patients also showed a significant decrease in A-V difference compared to healthy subjects, diabetics with no DR and diabetics with mild NPDR (p=0.003, 0.033, 0.016; respectively). SaO₂ was approximately equal across all groups. Age showed significant negative correlation with SaO₂ (r=-0.449, p=0.0004) and SvO₂ (r=-0.466, p=0.0002) and nearly significant positive correlation with A-V difference (r=-0.243, p=0.064). In diabetic patients, no correlation between SO₂ or A-V difference was found with HbA1c, urine microalbumin or FA (% ischemia in ring). In multivariate regression analysis, age and history of hypertension were significant determinants of A-V difference (β=1.507, p=0.012; β=1.208, p=0.018, respectively).

Conclusions: In this preliminary study, increased SvO₂ and decreased A-V difference were found in patients with moderate NPDR compared to earlier stages of DR and healthy subjects. This may signify decreased delivery of oxygen to retinal tissues in patients with early DR and/or decreased tissue extraction of oxygen. Future studies of diabetic patients across all DR stages are ongoing to correlate retinal oxygenation with FA and systemic markers of diabetic severity.

Commercial Relationships: Alexa M. Waters, None; Justin Miller. None; Jean-Claude Mwanza. None; Seema Garg. None
Support: Research to Prevent Blindness Grant. NY, NY

Program Number: 2446 Poster Board Number: C0147
Presentation Time: 2:45 PM - 4:30 PM

Plasma and vitreous fluid levels of Dickkopf-1 in patients with diabetic retinopathy
Fangfang Qiu1, Jia He1, Yueping Zhou1, Zhen Liu1, Jian-Xing Ma2, Zuguo Liu1, 3. 1Eye Institute, Xiamen University, Xiamen, China; 2Department of Physiology, The University of Oklahoma Health Sciences Center, Oklahoma, OK; 3Xiamen Eye Center Affiliated to Xiamen University, Xiamen, China; 4ye Institute, Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong, China.

Purpose: Dickkopf-1 (DKK-1) is a secreted inhibitor of the Wnt/β-catenin signaling pathway which is activated in the retina of diabetic retinopathy (DR) patients. We investigated whether plasma and vitreous DKK-1 levels are associated with DR in type 2 diabetic patients.

Methods: Plasma samples were collected from 86 type 2 diabetic patients including 66 DR (29 non-proliferative DR [NPDR] and 37 proliferative DR [PDR]) and 20 non-DR patients (NDR), and 100 non-diabetes controls. Vitreous samples were obtained from 15 PDR and 12 non-diabetic patients. DKK-1 concentrations in samples were determined by ELISA.

Results: Plasma DKK-1 levels were significantly lower in DR patients (median: 530.91 pg/ml, range: 137.11-1190.31) than those in non-diabetes controls (656.83 pg/ml, 171.63-1795.08; P<0.0001) and NDR patients (654.15 pg/ml, 305.43-1218.35; P=0.013); they were lower in PDR patients (478.86 pg/ml, 173.60-1077.32) compared to NPDR patients (594.86 pg/ml, 256.36-1393.27; P=0.038). Vitreous absolute DKK-1 levels in PDR patients (243.73 pg/ml, 104.44-596.96) were higher than those in non-diabetic controls (144.99 pg/ml, 18.69-239.52) and were identical between the both groups after normalizing by total vitreous protein concentrations. DKK-1 levels in vitreous were lower than those in plasma in both groups (both P<0.001).

Conclusions: Decreased circulating DKK-1 levels are associated with the presence and progression of DR. The decreased DKK-1 levels may contribute to the Wnt pathway activation and have potential to become a biomarker for prediction of DR. Vitreous DKK-1 in PDR patients is increased due to the breakdown of blood-retinal barrier, but they are at very low levels.

Commercial Relationships: Fangfang Qiu. None; Jia He. None; Yueping Zhou. None; Zhen Liu. None; Jian-Xing Ma. None; Zuguo Liu. Bausch&Lomb (R), Allergern (R), Alcon (R), Santen (R)

Program Number: 2447 Poster Board Number: C0148
Presentation Time: 2:45 PM - 4:30 PM

EVALUATION OF CHOROIDAL THICKNESS IN HIGH-RISK PROLIFERATIVE DIABETIC RETINOPATHY TREATED WITH PANRETINAL PHOTOCOAGULATION ASSOCIATED OR NOT WITH INTRAVITREAL BEVACIZUMAB INJECTION: A 3 MONTHS, RANDOMIZED, CONTROLLED AND MASKED CLINICAL TRIAL
Rony C. Pretti1, Anibal Mutti2, Lisa M. Vazquez1, Daniel A. Ferraz2, Leandro C. Zacharias1, Mario K. Carra1, David E. Pelayes1, Mario L. Monteiro1, Walter V. Takahashi1. 1Ophthalmology, University of Sao Paulo, Sao Paulo, Brazil; 2Endocrinology, University of Sao Paulo, Sao Paulo, Brazil; 2Ophthalmology, Center for Applied Research to Prevent Blindness Grant. NY, NY

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Results: In the study, 23 patients were included and 7 (30.43%) had unreliable measures at least in one eye. The mean age of the 23 patients (46 eyes) was 52.2 years (standard deviation, 9.16 years), and 14 patients (60.86%) were male. The choroid was thickest underneath the fovea (mean, 341.64 μm; standard deviation, 74.19 μm) and (mean, 339.93 μm; standard deviation, 72.22 μm) in the study and control group, respectively. Comparing groups there was a statistically significant difference in macular choroidal thickness changes after treatment throughout the follow-up period. The study group had increased the macular choroidal thickness significantly at 1 and 3 months follow-up visit.

Conclusions: Despite the absence of statistically significant difference in macular choroidal thickness changes between groups, probably due to the small sample size, IVB injections associated with PRP seems to increase the macular choroidal thickness in a short period of follow-up and this could be beneficial.

Commercial Relationships: None; Mario K. Carra

Support: This study was supported by Sao Paulo Research Foundation (FAPESP) number 2009/08895-1

Clinical Trial: NCT01517490

**Program Number: 2449 Poster Board Number: C0150**

**Presentation Time: 2:45 PM - 3:00 PM**

**Effect of Metformin on the Development of Diabetic Retinopathy**

Christina L. Ryu, Metasebia Munie, Salma Nooruddin, Paul A. Edwards, Xiaoxi Qiao, Hua Gao. Ophthalmology, Henry Ford Hospital, Detroit, MI.

Purpose: Metformin is a widely used oral anti-hyperglycemic agent for type 2 diabetics. In vitro studies indicate that metformin inhibits proliferation and migration of vascular endothelium, and it has antiangiogenic effects in cancer models in vivo. Metformin therefore may theoretically protect against the microvascular complications of diabetes. This study investigates whether the risk of development of proliferative diabetic retinopathy is reduced in type 2 diabetic patients treated with metformin.

Methods: This is a retrospective study of patients with longstanding type 2 diabetes. Patient charts were reviewed from January 1990 to November 2012. Patients with type 2 diabetes for more than 20 years were included. Patients without ophthalmology record, primary care record or hemoglobin A1C levels were excluded. The primary outcome was to compare the rates of severe diabetic retinopathy in patients on metformin with those not on metformin.

Results: 78 patients with diabetic retinopathy are included in our current analysis, 45 patients on metformin and 33 patients not on metformin. Our data show that patients on metformin were less frequently treated with insulin (p = 0.004). In the non-metformin group, 18 (54.5%) patients developed nonproliferative diabetic retinopathy (NPDR) and 15 (45.5%) developed proliferative diabetic retinopathy (PDR). In the metformin group, 32 (72.7%) developed NPDR and 12 (27.3%) developed PDR. Thus our data shows a trend of much less PDR in the metformin group than the non-metformin group.

Conclusions: Although other confounding factors may contribute to the severity of diabetic retinopathy, our study shows that metformin
may reduce the rate of development of proliferative diabetic retinopathy. A larger scale study with more patients is required to confirm our findings.

**Commercial Relationships:** Christina L. Ryu, None; Metasebia Munie, None; Salma Noorulla, None; Paul A. Edwards, None; Xiaosi Qiao, None; Hua Gao, None

**Support:** Alliance for Vision Research, Inc.

303 Metabolomics and Lipidomics: Metabolic Fingerprints Offer New Insights into Disease Pathogenesis with Potential for Life Changing Research - Minisymposium

Tuesday, May 07, 2013 8:30 AM-10:15 AM

**Program #/Board # Range:** 2626-2629

**Organizing Section:** Retina

**Contributing Section(s):** Clinical/Epidemiologic Research

**Program Number:** 2626

**Presentation Time:** 8:35 AM - 8:55 AM

Metabolomics. Expanding Tools for Investigation of Chronic Diseases

Christopher Elliott. Institute for Global Food safety, Queen’s University Belfast, Belfast, United Kingdom.

**Commercial Relationships:** Christopher Elliott, None

**Program Number:** 2627

**Presentation Time:** 8:55 AM - 9:15 AM

Methods of Metabolomic Analysis and Handling Complex Datasets

Jeffrey M. Macdonald. Biomedical Engineering, University of North Carolina, Chapel Hill, NC.

**Commercial Relationships:** Jeffrey M. Macdonald, None

**Program Number:** 2628

**Presentation Time:** 9:15 AM - 9:35 AM

The Role of Metabolomics in Studying Complications of Diabetes and Cardiovascular Diseases

Warwick Dunn. University of Birmingham, Birmingham, United Kingdom.

**Commercial Relationships:** Warwick Dunn, None

**Program Number:** 2629

**Presentation Time:** 9:35 AM - 9:55 AM

Metabolomics and Retinal Diseases

Milam A. Brantley. Ophthalmology, Vanderbilt University, Nashville, TN.

**Commercial Relationships:** Milam A. Brantley, None

314 Macular Disease other than AMD I

Tuesday, May 07, 2013 8:30 AM-10:15 AM

**Exhibit Hall Poster Session**

**Program #/Board # Range:** 2785-2839/B0039-B0093

**Organizing Section:** Retina

**Program Number:** 2785

**Presentation Time:** 8:30 AM - 10:15 AM

Anterior chamber depth in eyes with central serous chorioretinopathy

Jong-Hyun Oh¹, Jaeryung Oh², Yong-Min Choi³, Seong-Woo Kim², Kuhl Huh². ¹Ophthalmology, Dongguk University Iusan Hospital, Goyang, Republic of Korea; ²Ophthalmology, Korea University College of Medicine, Seoul, Republic of Korea.

**Purpose:** To investigate the characteristic of anterior segment measurements in eyes with central serous chorioretinopathy (CSC).

**Methods:** This cross sectional study retrospectively included consecutive patients who were diagnosed as unilateral CSC. Spectral domain optical coherence tomography and fluorescein angiography were obtained for a diagnosis. Best-corrected visual acuity (BCVA), refractive error, axial length, and anterior chamber depth (ACD) were evaluated. Acute CSC was defined as CSC with symptom duration of less than 6 months.

**Results:** The 53 subjects had a mean age of 42.9±7.7 years and 39 (73.6%) of the patients were male. Between CSC eyes and fellow eyes, the differences in refractive error and adjusted axial length were not significant (P=0.995 and P=0.212, respectively). However, BCVA was worse (P<0.001) and ACD was shallower in CSC eyes than fellow eyes by 0.032±0.0875 mm (P=0.011). Forty-six (86.8%) eyes had acute CSC and 7 (13.2%) eyes had chronic CSC. ACD was shallower in acute CSC eyes than fellow eyes by 0.038±0.0881 mm (P=0.005). However, the difference in ACD was not significant between chronic CSC eyes and fellow eyes (P=0.932).

**Conclusions:** ACD was shallower in eyes with acute CSC. In the early stage, CSC may influence the anterior ocular configuration including ACD.

**Commercial Relationships:** Jong-Hyun Oh, None; Jaeryung Oh, None; Yong-Min Choi, None; Seong-Woo Kim, None; Kuhl Huh, None

**Program Number:** 2786

**Presentation Time:** 8:30 AM - 10:15 AM

Clinical Course of Unoperated Eyes with Vitreofoveal Traction

Vishak J. John¹, Harry W. Flynn¹, William E. Smiddy¹, Adam Carver², Robert Leonard³, Homayoun Tabandeh¹, David S. Boyer⁴. ¹Ophthalmology, Bascom Palmer Eye Institute, Miami, FL; ²Ophthalmology, University of Oklahoma, Oklahoma City, OK; ³Retina, Retina Vitreous Associates Medical Group, Los Angeles, CA.

**Purpose:** The purpose of the study was to investigate the unoperated clinical course of patients with vitreofoveal traction [VFT] in terms of visual acuity and anatomy using spectral domain optical coherence tomography [SD-OCT].

**Methods:** A multi-center, non-comparative chart review was performed of VFT patients examined between 2004 and 2012 who had SD-OCT findings consistent with vitreofoveal traction but for whom the attending physician elected observational management. VFT was graded based on OCT findings at initial and follow-up examinations. Fellow eyes of macular hold patients and patients with advanced macular disease affecting vision were excluded. Stage 1 was incomplete cortical vitreous separation with attachment at the fovea; Stage 2 was Stage 1 findings along with any intraretinal cysts or clefts; and Stage 3 was the same as Stage 2, but also included the presence of subretinal fluid. Best-corrected visual acuity (BCVA) was recorded at each examination.

**Results:** In the current study, 107 eyes of 86 patients were identified as having VFT by SD-OCT at three retina clinics. The mean age was 72.7 years. The mean time of follow-up was 708 days or 23 months [range 1 to 91 months]. At their initial visit, patients had a mean BCVA of log 0.268 [20/37 with a range 20/20 to 20/200], and 44 eyes [41%] had Stage 1 VFT, 55 eyes [51%] with Stage 2, and 8 eyes [7%] with Stage 3 VFT. Spontaneous vitreous separation from the foveal attachment occurred in 31% of patients. During the study follow-up, four eyes underwent vitrectomy and membrane peel due to progression to a macular hole, and another eye for progressive visual
Factors that Predict Outcomes of Macular Hole Repair

**Program Number:** B0042
**Presentation Time:** 8:30 AM - 10:15 AM

**Purpose:** To determine the preoperative and intraoperative factors that may be associated with anatomical and functional outcomes after surgical macular hole repair.

**Methods:** A retrospective, consecutive study involving 59 eyes of 58 patients, undergoing repair of idiopathic, full thickness macular holes was performed after Institutional Review Board approval was obtained. Macular hole repair was performed either by pars plana vitrectomy (PPV) or by combined cataract extraction with PPV (CE/PPV). Preoperative logMAR best corrected visual acuity (BCVA) and Ocular Coherence Tomography (OCT) characteristics of the macular holes were recorded. Main outcome measures included OCT-documented hole closure and BCVA at any point between the 1-6 month post-operative visit.

**Results:** The mean preoperative macular hole minimum diameter (MD) on OCT was 327.5 um and 442.3 um, in holes that closed and did not close, respectively (p=0.10). Hole closure rate for eyes with MD < 250 um, 250 um - 400 um, and >400 um was 92%, 80%, and 83.3%, respectively (p = 0.55). The mean difference between post- and pre-operative BCVA was -0.306 (p<0.0001). The difference in BCVA change after surgery between holes that closed and those that did not was -0.29 (p=0.026). The difference in postoperative BCVA between PPV and CE/PPV groups was 0.08 (p<0.36). Pre-operative macular hole size did not affect the final visual outcome (p=0.28). Among eyes undergoing primary macular hole repair, 75% had SF6 gas inflation and 25% had C3F8. The hole closure rate for the SF6 group and C3F8 group was 92.5% and 69.2%, respectively (p =0.031). In primary repairs, 92% had ILM peel and 8% did not. The closure rate was 89.9% in those with ILM peel, and 50% in those without (p=0.024). In primary repairs, for every 100um increase in preoperative MD, there is a 0.06 improvement in postoperative BCVA (p = 0.03), and for every 100 um of preoperative IS/OS loss, there is a 0.02 improvement in postoperative BCVA (p=0.015).

**Conclusions:** Minimum diameter of macular holes was not associated with rate of hole closure. Successful macular hole closure was associated with significantly improved BCVA. Combined CE/PPV did not result in significantly better visual outcomes than PPV alone. SF6 use and ILM peel were associated with a greater rate of macular hole closure. In primary repairs, macular holes with larger preoperative MD and greater preoperative IS/OS showed greater room for improvement in postoperative BCVA.

**Commercial Relationships:** Jack Shao, None; Lucy T. Xu, None; Omar S. Punjabi, None; Justis P. Ehlers, Provisional patents filed related to intraoperative OCT technology. No company relationships (P); Sunil K. Srivastava, Bausch and Lomb (F), Bausch and Lomb (C), Novartis (F), Allergan (F); Peter K. Kaiser, Allegro Ophthalmicals (C), Alcon (C), Novartis (C), Bayer (C), Regeneron (C), Genentech (C), Ophthotech (C)

**Program Number:** 2789 Poster Board Number: B0043
**Presentation Time:** 8:30 AM - 10:15 AM

**Purpose:** Idiopathic epiretinal membrane (ERM) is a disease having gial proliferation on the surface of the retina. Its mechanical traction is reported as a main mechanism to cause visual dysfunction. Recent studies using optical coherence tomography indicated that defects of the photoreceptor layer are correlated with postoperative visual acuity. However, the photoreceptor layer is the farthest portion of the retina from ERM, and damage to the inner retina would precede the outer retinal abnormality. Pattern electroretinogram (PERG) represents function of the macula and the ganglion cell layer, which is the closest cell layer to ERM. This study was conducted to investigate correlation of PERG and visual acuity in idiopathic ERM.

**Methods:** Eyes which underwent vitrectomy and membrane peeling for idiopathic ERM and followed up for 6 months or more were included. OCT-documented hole closure and BCVA at any point between the 1-6 month post-operative visit.

**Results:** The mean preoperative macular hole minimum diameter (MD) on OCT was 327.5 um and 442.3 um, in holes that closed and did not close, respectively (p=0.10). Hole closure rate for eyes with MD < 250 um, 250 um - 400 um, and >400 um was 92%, 80%, and 83.3%, respectively (p = 0.55). The mean difference between post- and pre-operative BCVA was -0.306 (p<0.0001). The difference in BCVA change after surgery between holes that closed and those that did not was -0.29 (p=0.026). The difference in postoperative BCVA between PPV and CE/PPV groups was 0.08 (p<0.36). Pre-operative macular hole size did not affect the final visual outcome (p=0.28). Among eyes undergoing primary macular hole repair, 75% had SF6 gas inflation and 25% had C3F8. The hole closure rate for the SF6 group and C3F8 group was 92.5% and 69.2%, respectively (p =0.031). In primary repairs, 92% had ILM peel and 8% did not. The closure rate was 89.9% in those with ILM peel, and 50% in those without (p=0.024). In primary repairs, for every 100um increase in preoperative MD, there is a 0.06 improvement in postoperative BCVA (p = 0.03), and for every 100 um of preoperative IS/OS loss, there is a 0.02 improvement in postoperative BCVA (p=0.015).

**Conclusions:** Minimum diameter of macular holes was not associated with rate of hole closure. Successful macular hole closure was associated with significantly improved BCVA. Combined CE/PPV did not result in significantly better visual outcomes than PPV alone. SF6 use and ILM peel were associated with a greater rate of macular hole closure. In primary repairs, macular holes with larger preoperative MD and greater preoperative IS/OS showed greater room for improvement in postoperative BCVA.

**Commercial Relationships:** Jack Shao, None; Lucy T. Xu, None; Omar S. Punjabi, None; Justis P. Ehlers, Provisional patents filed related to intraoperative OCT technology. No company relationships (P); Sunil K. Srivastava, Bausch and Lomb (F), Bausch and Lomb (C), Novartis (F), Allegro (F); Peter K. Kaiser, Allegro Ophthalmicals (C), Alcon (C), Novartis (C), Bayer (C), Regeneron (C), Genentech (C), Ophthotech (C)
included. PERG was performed before operation. PERG and medical records were reviewed retrospectively. Implicit time and amplitude of P50 and N95 were assessed, and ratio of the values in the affected eye to the values in the normal eye was calculated. The parameters were analyzed to find correlation with pre-and postoperative visual acuity.

Results: Total 21 eyes were included in the study. Visual acuity (logMAR) improved significantly from 0.61 to 0.38 and central subfield thickness decreased significantly from 488 to 369 at 6 months. Implicit time was not delayed, but amplitude was reduced significantly in the affected eye. Ratio of P50 was 0.65±0.31, and ratio of N95 was 0.68±0.37. There was no correlation between visual acuity and amplitude of P50 or implicit time of P50 and N95. Amplitude of N95 had significant correlation with postoperative visual acuity at 6 months (P=0.036, r=0.460).

Conclusions: PERG provided useful information to assess postoperative outcomes. It was reported that N95 represents the ganglion cell layer, whereas P50 represents the outer retina of the macula. Correlation of postoperative visual acuity with N95 but not with P50 indicates that status of the ganglion cell layer would be a important factor for visual function in ERM.

Commercial Relationships: Ji Eun E. Lee, None; Hyun Woong Kim, None; Sung Il Kim, None; Jong Ho Park, None; Ik Soo Byon, None

Program Number: 2790 Poster Board Number: B0044
Presentation Time: 8:30 AM - 10:15 AM

Longitudinal Changes in Preferred Retinal Location, Visual Function, Fundus Autofluorescence and Retinal Structure in Stargardt Disease

Vivienne C. Greenstein1, Mirela R. Tabacaru1, Erin Flynn1, Rando Allikmets1,2, Stephen H. Tsang1,2. Ophthalmology, Columbia University Medical Center, New York, NY; 2Pathology & Cell Biology, Columbia University Medical Center, New York, NY.

Purpose: To study longitudinal changes in preferred retinal location (PRL) and visual function in Stargardt disease (STGD) and assess their relationship to changes in short wavelength fundus autofluorescence (SW-FAF) and retinal structure measured with spectral domain optical coherence tomography (SD-OCT).

Methods: Seventeen patients (20 eyes) aged 21-70 yrs with STGD and at least one ABCA4 mutant allele were studied for 12 to 36 months. All tested eyes had best corrected visual acuity >=20/200. At each visit, the location and stability of the PRL were evaluated with the Nidek microperimeter (MP-1; Nidek Tech., Padua, Italy). Stability was quantified using the bivariate contour ellipse area (BCEA) technique. Visual fields were measured with the MP-1 (10-2 program 4-2 protocol). SW-FAF images were obtained with the Heidelberg Spectralis HRA+OCT (Heidelberg Eng., Heidelberg, Germany). Corresponding horizontal SD-OCT line scans through the foveal and PRL regions were also obtained. To evaluate change in the pattern of fundus autofluorescence, serial SW-FAF images were registered to each other. To evaluate their relationship to functional changes, the SW-FAF images were registered to the visual field results in the MP-1 using NAVIS software.

Results: At the initial visit the PRL was superior to the fovea (range 1°-12°) for 13 patients (15 eyes), temporal (1°) for 2 patients (2 eyes), supero-temporal (ST 5°- 3°) for 1 and foveal for 2 patients. BCEA values, containing 95% of the fixation points, ranged from 2 to 26 deg2. At the most recent visit, the PRL was superior to the fovea (range 1° to 14°) for 16 patients (19 eyes). Only one patient retained a foveal PRL. BCEA values ranged from 2 to 42 deg2. The eccentric PRLs were associated with increased visual sensitivity compared to the foveal area and with a more intact inner segment ellipsoid band. They were also associated with a central scotoma on the MP-1 corresponding to an atrophic hypofluorescent area on SW-FAF and SD-OCT. At the most recent visit this area had increased for 16 patients (19 eyes) both vertically (mean 1245 to 1664μm) and horizontally (mean 1562 to 2014μm).

Conclusions: Over a period of only 12 to 36 months there were changes in the location and stability of the PRL. These were associated with changes observed on SW-FAF and SD-OCT.

Commercial Relationships: Vivienne C. Greenstein, None; Mirela R. Tabacaru, None; Erin Flynn, None; Rando Allikmets, None; Stephen H. Tsang, None
Support: EY09076

Program Number: 2791 Poster Board Number: B0045
Presentation Time: 8:30 AM - 10:15 AM

One-year outcome of two different initial doses of intravitreal ranibizumab for myopic choroidal neovascularization

Ya-Hsin Kung1,2, Tsung-Tien Wu2,2. Ophthalmology, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan; 2School of medicine, National Yang-Ming University, Taipei, Taiwan.

Purpose: To evaluate and compare the 12-month outcomes of two different initial doses of intravitreal ranibizumab for myopic choroidal neovascularization (CNV).

Methods: We retrospectively reviewed the medical records of 46 consecutive, treatment-naive eyes which received intravitreal ranibizumab for subfoveal and juxtapfoveal CNV secondary to pathologic myopia with a follow-up of 12 months. Two groups were created according to different initial doses: group 1 included 25 eyes treated by a single intravitreal injection; group 2 included 21 eyes treated with 3 consecutive monthly injections. Additional injections were performed if needed. Patients’ demographic data, best-corrected visual acuity (BCVA), recurrence of CNV, and total number of treatments were recorded and evaluated.

Results: There was no significant difference between two groups among baseline demographic data. At 12 months, the mean logMAR BCVA improved from 0.58 to 0.23 in group 1 and from 0.55 to 0.22 in group 2 (both p<0.001; two-tailed, paired t test). The mean logMAR BCVA at 12 months did not differ significantly. The average number of injections was 2.32 (SD 1.22) in group 1 and 3.57 (SD 1.12) in group 2 (p=0.001). During the follow-up, 17 of 25 eyes in group 1 and 5 of 21 eyes in group 2 received additional injections (p=0.004).

Conclusions: Similar visual improvement was achieved in both groups. Although the eyes with a loading dose of 3 monthly injections required a higher number of total injections over one year, there was a much lower rate of CNV recurrence.

Commercial Relationships: Ya-Hsin Kung, None; Tsung-Tien Wu, None

Program Number: 2792 Poster Board Number: B0046
Presentation Time: 8:30 AM - 10:15 AM

Morphologic Choroidal Changes in Dome Shaped Macula Combining Indocyanine Green Angiography (ICGA) and Spectral Domain Optical Coherence Tomography (SD-OCT)

Francesco Viola, Laura Dell’Arti, Eleonora Benatti, Chiara Mapelli, Giulio Barteselli, Monica Serafini, Roberto Ratiglia. University of Milan, Fondazione IRCCS Ca’ Granda Ospedale Policlinico, Milan, Italy.

Purpose: To describe macular choroidal changes in dome shaped macula using ICGA and SD-OCT and to elucidate the mechanism of serous retinal detachment formation and its course.

Methods: We retrospectively studied the medical records of patients with dome shaped macula. All patients had undergone simultaneous
fluorescein angiography (FA), ICGA and SD-OCT using confocal laser scanning system (Spectralis, Heidelberg Engineering, Heidelberg, Germany). Enhanced-depth imaging (EDI) OCT was used to examine the choroidal changes.

**Results:** Thirteen patients (23 eyes) with dome shaped macula were included. The median refractive error was -10.5 diopters [D] (range -0.50 to -28 D) and the median axial length was 27.8 mm (range 22.64 - 32.14 mm). The best corrected visual acuity ranged from 0.16 to 1.0 (median 0.57). The mean subfoveal choroidal thickness was 117.43 μm ± 58.65. Two eyes (8.7%) showed choroidal neovascularization on FA and ICGA. Seven eyes (30.4%) showed subfoveal fluid (SFF) by OCT. Among these patients, focal points of leakage (FPL) on FA were associated with SFF in 6 eyes (p<0.01; Pearson’s correlation). Seven eyes (30.4%) showed mid-phase ICGA punctate hyperfluorescent spots (IPHS). In 6 out of the 7 eyes with IPHS, this finding was associated with SFF (p<0.01; Pearson’s correlation). All the 7 patients with SFF were followed-up for at least 6 months (range 6-36 months). During the follow-up, in one eye SFF spontaneously resolved with FPL and IPHS disappearance. In a patient that at baseline had unilateral SFF, at 1 year follow-up, SFF formation occurred in the fellow eye with concomitant appearance of FPL and IPHS. In the other cases SFF showed a variable fluctuating course.

**Conclusions:** Patients with dome shaped macula and SFF showed punctate hyperfluorescent spots on mid-phase ICGA, miming central serous chorioretinopathy (CSCR). Nevertheless other peculiarities of CSCR such as increased choroidal thickness and choroidal vascular hyperpermeability were not indisputably seen in our patients. Notably typical retinal findings in dome shaped maculopathy appear similar to those described in inferior posterior staphyloma as well. Further studies are needed to elucidate the role played by the choroid in the development of SFF in these diseases.

**Commercial Relationships:** Francesco Viola, None; Laura Dell’Arti, None; Eleonora Benatti, None; Chiara Mapelli, None; Giulio Barteselli, None; Monica Serafini, None; Roberto Ratiglia, None

**Program Number:** 2793 Poster Board Number: B0047
**Presentation Time:** 8:30 AM - 10:15 AM
**Quantitative Measurement of Color Discrimination in Cone-Rod Dystrophies and Inherited Maculopathy**

Brett G. Jeffrey1, Wadim M. Zein1, Benedetto Falsini1,2, Divya L. Nigam1, Paul A. Sieving1. 1National Eye Institute/NIH, Bethesda, MD; 2Catholic University, Rome, Italy.

**Purpose:** To provide quantitative measurement of color discrimination in subjects with inherited retinal degenerations involving the central retina.

**Methods:** Nine subjects aged 12-65 years had a diagnosis of cone-rod dystrophy (n=4), Stargardt disease (n=3) or inherited maculopathy (n=2). Color discrimination thresholds were measured along 8 axes spaced 45° apart in CIE 1976 L^*u^*v^* space using a low vision version of the Cambridge Color Test (LvCCT)[1]. Achromatic area (AA 10^6 u*v^*) was determined from the fit of an ellipse to threshold chromaticity coordinates. Total threshold length (TLL 10^3 u*v^*) was the sum of all 8 thresholds. Results were correlated with full-field ERG, SD-OCT and fundus autofluorescence. To test for luminance cues thresholds were measured from 8 complete achromats. The effect of reduced visual acuity on color thresholds was examined using optical blur in 2 control subjects.

**Results:** Color discrimination thresholds were obtained along all axes for 8 subjects with visual acuities ranging from 20/25 to 20/800 (median 20/250). One subject with advanced cone-rod dystrophy did not perceive color along any axis. Achromatic area and total threshold length were smaller (p<0.001) in subjects with foveal sparing (AA 551±321; TLL 97±34) compared with those with no sparing (4758 ± 1141; 272 ± 62). Achromatic area and total threshold length were not correlated with visual acuity, ERG amplitude, foveal thickness or area of geographic atrophy. In 7 subjects the rotation angle of the ellipse ranged from -12° to -55°, consistent with confusion along the deutan axis; one subject had a tritan defect. Achromats were at or near maximum achievable chromaticity along all axes. In controls, a reduction in visual acuity down to 20/800 produced no change in color thresholds.

**Conclusions:** In subjects with foveal sparing, the lack of correlation between color discrimination thresholds and visual acuity suggests that these two tests are limited by different retinal regions and/or mechanisms. The results from the achromats and two controls confirm that neither luminance cues nor a reduction in visual acuity contribute to color discrimination thresholds. The LvCCT uses a conceptually simple stimulus amenable to the low vision population and provides a means of quantifying color discrimination changes in subjects with progressive inherited retinal disease. [1] Simunovic MP et al Vis Res 1998 38:3413-19

**Commercial Relationships:** Brett G. Jeffrey, None; Wadim M. Zein, None; Benedetto Falsini, None; Divya L. Nigam, None; Paul A. Sieving, None

**Program Number:** 2794 Poster Board Number: B0048
**Presentation Time:** 8:30 AM - 10:15 AM

**Prevalence of Vitreomacular Interface Disease and Candidates for Ocriplasmin Treatment**

Lucy T. Xu, Omar S. Punjabi, Jack Shao, Justis P. Ehlers, Sunit K. Srivastava, Peter K. Kaiser. Cole Eye Institute, Cleveland Clinic Foundation, Cleveland, OH.

**Purpose:** To evaluate the prevalence of different stages of vitreomacular interface (VMI) diseases including vitreomacular adhesion, vitreomacular traction (VMT) and full thickness macular holes using a novel OCT staging system. In addition, to evaluate the prevalence of patients who may qualify for treatment with ocriplasmin.

**Methods:** Retrospective, IRB-approved, consecutive case series of all patients with ICD-9 code of 362.54 (macular cyst, hole or pseudohole) and in whom spectral domain OCT was obtained. Patients were excluded if they had poor OCT image quality or localization. Patients were classified into the following categories: macular cyst without hole, pseudohole (partial thickness hole within an epiretinal membrane with clinical appearance of macular hole), lamellar hole (inner retinal defect without full thickness defect), vitreomacular traction without hole and full-thickness macular hole (FTMH). FTMHs were further sub-classified based on size as: minimum diameter (MD) < 250μm, 250-400μm or > 400μm. Presence of vitreous traction, epiretinal membrane, and/or cystic spaces was also quantified. The fellow eyes of patients with FTMH were studied to determine the presence of vitreomacular adhesion (stage 0 macular hole).

**Results:** 437 eyes of 375 patients were included in the study. 39 eyes (8.9%) had macular cyst without a hole. A lamellar hole was present in 53 eyes (12.1%) and a pseudohole in 66 eyes (15.1%). 40 eyes (9%) had VMT without a FTMH. 217 eyes (49.7%) had a FTMH. 72 eyes (16.5%) had a FTMH <250µm MD, 47 eyes (10.7%) had FTMH between 250-400µm MD and 98 eyes (22.4%) had FTMH >400µm MD. In patients with FTMH, 22 (10.1%) had a fellow eye with VMA (Stage 0 MH). In total, 84 eyes (19.2%) had traction, 166 eyes (37.9%) had ERM, and 254 eyes (58.1%) had cystic changes adjacent to the hole. 75 eyes (17.1%) with VMT, excluding FTMH >400µm, qualified for ocriplasmin therapy based on clinical studies, of which 56/75 eyes (74.7%) had no ERM and were good candidates for ocriplasmin therapy.
Conclusions: We present the prevalence of VMI disease using a novel OCT based staging system. 17.1% of all eyes with a diagnosis code 362.54 had symptomatic vitreomacular traction that qualified for ocriplasmin therapy. 74.7% of these eyes were considered good candidates for ocriplasmin therapy. 10.1% of fellow eyes with FTMH had stage 0 macular hole, indicating a need to continue screening the fellow eye.

Commercial Relationships: Lucy T. Xu, None; Omar S. Punjabi, None; Jack Shao, None; Justis P. Ehlers, Provisional patents filed related to intraoperative OCT technology. No company relationships (P); Sunil K. Srivastava, Bausch and Lomb (F), Bausch and Lomb (C), Novartis (F), Allergan (F); Peter K. Kaiser, Allegro Ophthalmics (C), Alcon (C), Novartis (C), Bayer (C), Regeneron (C), Genentech (C), Ophthotech (C)

Program Number: 2795 Poster Board Number: B0049
Presentation Time: 8:30 AM - 10:15 AM
Clinical evaluation of foveal sparing in patients with Stargardt disease
Ramone A. van Hael, Sarah C. Westeneng -van Haagen, Muhamad Muhamed, Frans P. Cremer, Lies H. Hoefsloot, B. Jeroen Klevering, Carel B. Hooying. 1Ophthalmology, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands; 2Human Genetics, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands.

Purpose: Foveal sparing atrophy is a phenotypic feature in which macular atrophy surrounds the fovea for at least 180° and does not include the fovea in the atrophic lesion. This specific feature is observed in a subset of patients with Stargardt disease, the most common juvenile-onset macular dystrophy caused by mutations in the ABCA4 gene. Here, we provide clinical and genetic details of Stargardt disease patients with foveal sparing atrophy.

Methods: Thirteen Stargardt patients with foveal sparing (19 eyes) were collected. We collected available clinical data of these patients, including medical history, ophthalmic examination, fundus photography, autofluorescence (AF) images, optical coherence tomography (OCT) images, electroneutrography (ERG) and genetic testing for mutations in the ABCA4 gene.

Results: The mean age of onset was 51.2 years. Eleven patients (85%) initially presented with loss of visual acuity, which deteriorated from 20/25 to 20/200 in approximately two decades. Normal foveal retinal layer structure was preserved in OCT examinations of most patients. AF images showed atrophic lesions starting in the parafoveal area that progress over time around the fovea, creating the ‘peninsula-like’ foveal sparing feature. The atrophy subsequently surrounded the fovea completely, followed by a degeneration of the whole fovea in some patients. Full-field electroneutrography revealed normal photopic cone responses in most patients, but can be moderately to severely reduced. Sequence analysis of the 50 protein coding exons of ABCA4 revealed compound heterozygous mutations in three patients. The remaining patients carried heterozygous ABCA4 mutations.

Conclusions: Foveal sparing in Stargardt’s dystrophy is especially present in patients with a late onset of the disease. The mechanisms by which the fovea is spared while the surrounding tissue atrophies remains unclear. Factors that stimulate preservation of the central fovea may play a role in the development of future therapeutic strategies.

Commercial Relationships: Ramone A. van Hael, None; Sarah C. Westeneng -van Haagen, None; Muhamad Muhamed, None; Frans P. Cremer, None; Lies H. Hoefsloot, None; B. Jeroen Klevering, None; Carel B. Hooying, None

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half-dose PDT. Best-corrected visual acuity (BCVA), central retinal thickness (CRT) and resolution of subretinal fluid on optical coherence tomography at 1 month and at the last-follow-up visit (LFU) were assessed. Cost analysis was also performed.

**Results:** Snellen BCVA improved significantly (p<0.001) both in the half-fluence group from 0.70 (±0.23) to 0.87 (±0.21) and in the half-dose group from 0.76 (±0.16) to 0.87 (±0.16) at the LFU. There was no difference in final BCVA between the 2 groups. At 1 month a complete resolution of subretinal fluid was observed in 19 (61.3%) half-fluence treated eyes and in 25 (86.2%) half-dose treated eyes (p = 0.04). At the LFU, a complete resolution of sub-retinal fluid was achieved in 26 (83.9%) half-fluence treated eyes and 29 (100%) half-dose treated eyes (p = 0.0529; OR, 5.20; 95% CI, 1.75–15.42). Nine (25.8%) eyes in the half-fluence group and 5 (17.2%) eyes in the half-dose group had at least one recurrent episode of subretinal fluid (OR, 1.96; 95% CI, 0.57-6.76). Overall, there were 15 and 5 recurrences in the half-fluence PDT and half-dose PDT respectively (p=0.06; OR, 4.5; 95% CI, 1.36-14.84). The overall cost of half-fluence PDT was twice the cost of half-dose PDT.

**Conclusions:** Half-dose PDT induced a more rapidly reabsorption of the fluid, a more lasting effect and a halving of the costs respect to half-fluence PDT.

**Commercial Relationships:** Massimo Nicolò, None; Chiara M. Eandi, None; Camilla Alovisi, None; Carlo E. Traverso, None

**Support:** None in the Support field.

**Program Number:** 2798 **Poster Board Number:** B0052

**Presentatioin Time:** 8:30 AM - 10:15 AM

**Visual and Anatomic Results of the Macula Society**

**Photodynamic Therapy (PDT) for Central Serous Chorioretinopathy (CSCR) Retrospective Study**


1. Ophthalmic & Ear Infirmary, University of Illinois, Chicago, IL; 2. Jaeb Center for Health Research, Tampa, FL; 3. Joslin Diabetes Center, Harvard Medical School, Boston, MA; 4. Queens University, Belfast, Ireland; 5. Casey Eye Institute, Oregon Health and Sciences University, Portland, OR; 6. Vitreous Retina Macula Consultants, New York, NY; 7. Macula Society, Beachwood, OH.

**Purpose:** To assess the visual and anatomic outcomes after verteporfin photodynamic therapy (PDT) for central serous chorioretinopathy (CSCR).

**Methods:** The Macula Society Research and Education Committee electronically surveyed the membership to retrospectively collect data on PDT treatment for CSCR. Patient demographic information, PDT treatment parameters, fluorescein angiographic information, OCT metrics, visual acuity pre and post-treatment and adverse outcomes were collected using standardized forms.

**Results:** Data were submitted on 237 CSCR patients from 11 countries by 37 Macula Society members. The mean age was 52±11 years; 74% were men. Patients were 69% Caucasian, 18% Asian, and 12% Hispanic. CSCR was treated bilaterally in 11.8%. A history of systemic steroid exposure was present in 13%. Baseline visual acuities (VAs) were 20/32 or better in 43%, 20/40 to 20/80 in 37%, and 20/100 or worse in 18% of eyes. Subretinal fluid was seen by biomicroscopy in 83% (versus 85% by OCT); PED was seen by biomicroscopy in 28% (versus 32% on OCT). PDT treatment parameters: 49% normal fluence, 46% half-fluence, 3% low fluence PDT. The number of PDT treatments was 1 in 90%, 2 in 7% and 3 in 3%. Post-PDT follow-up ranged from 1 month to greater than 1 year. At the last post-PDT visit VA was improved >2 lines in 26%, 55% and 59% of eyes with baseline VA 20/32 or better, 20/40 to 20/80 and 20/100 or worse respectively. VA improved >3 lines in <1%, 29% and 48% of eyes with baseline VA 20/32 or better, 20/40 to 20/80 and 20/100 or worse respectively. Only 4% lost >4 lines. There was no difference in the response to PDT when analyzed by age, race, fluence, FA leakage type, steroid exposure or fluid location (subretinal or PED) (p>0.01). Post-PDT central subfield measurements on OCT improved by > 25µ in 75%, 82% and 86% of eyes with baseline VA of 20/32 or better, 20/40 to 20/80 and 20/100 or worse respectively. Complications were rare: RPE atrophy was seen in 4% and acute severe visual decrease in 2%.

**Conclusions:** PDT for CSC eyes with decreased vision results in visual acuity gains in a majority of eyes and only a small number with significant visual loss.

**Commercial Relationships:** Jennifer I. Lim, QLT (F); Genentech (R): Adam R. Glassman. None; Lloyd P. Aiello. Genentech (C), Enzyme (C), Thrombogenetics (C), Ophthotech (C), Kalvista (C), Pfizer (C), Proteostasis (C), Abbott (C), Vantia (C), Optos, plc (F); Usha Chakravarty, Bayer (C), Novartis (F), Neovista (C), Oraya (F); Christina J. Fluxel, None; Richard F. Spaide. Topcon (P), Thrombogenics (C), Bausch and Lomb (C)

**Support:** QLT. RPB

**Program Number:** B0053

**Presentation Time:** 8:30 AM - 10:15 AM

**Foveal Contour after Pars Plana Vitrectomy for Idiopathic Macular Hole**


**Purpose:** To evaluate the maximal foveal slope (MFS) after successful primary closure of idiopathic macular hole. To compare the MFS of the operated eye to the fellow, unoperated eye. To assess for correlations between MFS and visual acuity. To analyze the fellow eye for structural changes visible on optical coherence tomography (OCT).

**Methods:** 38 eyes of 37 patients with full thickness macular hole (FTMH) undergoing successful pars plana vitrectomy (PPV) and internal limiting membrane (ILM) peeling by a single surgeon were analyzed with spectral domain OCT (SD-OCT). The fellow eyes of surgical cases were examined by SD-OCT for macular pathology. The maximal foveal slope (MFS) was manually measured in each surgical and fellow eye. MFS was studied and compared to visual acuity outcomes.

**Results:** 1 month average MFS was 42 degrees in surgical eyes, and 26 degrees in normal fellow eyes. The average final MFS in all operated eyes was 51 degrees. 82% of patients demonstrated a steeper MFS on the nasal fovea compared to the temporal fovea. There was no correlation between MFS and post-operative best-corrected visual acuity. 49% of patients had a macular abnormality in the fellow eye, most occurring at the vitreoretinal interface.

**Conclusions:** MFS is generally steepened after FTMH repair, and the nasal foveal slope is typically steeper than the temporal foveal slope. The surgical eye typically has a steeper MFS than the fellow eye, and there is no correlation between MFS and visual acuity. Almost half of fellow eyes have macular abnormalities at the vitreoretinal interface. This finding reinforces the concept that macular holes are not simply isolated, unilateral process, and fellow eyes should be followed carefully for the risk of macular hole development.

**Commercial Relationships:** Royce W. Chen, Pamela Sherwood. None; Sri Krishna Mukkamala, None; Frank S. Siringo, None; Stanley Chang, Alcon Laboratories (C), Alimera Sciences (C)
Very early disease manifestations in macular telangiectasia type 2

**Tjefke F. Heeren, Frank G. Holz, Peter Charbel Issa.** Department of Ophthalmology, University of Bonn, Bonn, Germany.

**Purpose:** To report the earliest retinal alterations in macular telangiectasia (MacTel) type 2 detectable using a multi-modal imaging approach.

**Methods:** Patients were selected from a single center cohort of 110 patients with MacTel type 2. Inclusion was based on an asymmetric disease manifestation where only one eye clearly allowed the diagnosis based on ophthalmoscopy, fluorescein angiography (FI-A) and spectral domain optical coherence tomography (SD-OCT), whereas the other did not. The assessment included fundus photography, FI-A, recordings of fundus autofluorescence (FAF), macular pigment optical density (MPOD; determined by cSLO two-wavelengths measurements) and SD-OCT for analysis of macular cross sections and macular thickness mapping.

**Results:** Six patients with a mean age of 64±11 years (range, 43-72 years) were identified. Five out of the six seemingly unaffected eyes had a visual acuity (VA) of 20/20 or better. One eye with vitreomacular traction had a VA of 20/32. All those eyes showed an asymmetric configuration of the foveal pit being thinnest temporal to the foveal center. Within a similar area, three eyes revealed a slight focal reduction of MPOD, resulting in an associated increased signal on FAF imaging due to less absorption of the excitation light. Only two eyes showed a minor nonspecific leakage on FI-A which did not allow the diagnosis of MacTel type 2 on its own. No significant functional deficits were detected on micropereometry testing.

**Conclusions:** Loss of macular pigment as well as thinning of the neurosensory retina, both occurring in the temporal paracentral area, may precede vascular alterations in a very early disease stage of MacTel type 2. These findings support previous studies showing that macular pigment loss exceeds the area of vascular alterations in later disease stages, suggesting telangiectasia to occur secondarily to a degenerative disease process. Identification of affected patients or family members may be facilitated using herein presented but hitherto not applied diagnostic standards.

**Commercial Relationships:** Tjefke F. Heeren, Heidelberg Engineering (F); Frank G. Holz, Acucela (C), Allergan (C), Genetech (F), Heidelberg Engineering (F), Zeiss (F), Novartis (F), Novaris (C), Optos (F), Merz (C), Bayer (F), Bayer (C), Boehringer Ingelheim (C); Peter Charbel Issa, Heidelberg Engineering (F)

**Support:** Lowy Medical Research Institute

Familial occurrence of chronic central serous chorioretinopathy

**Myrte B. Breukink, None; Anneke I. Den Hollander, None; Jan E. Keenen, None; Carel B. Hoyng, None; Camiel J. Boon, None**

**Support:** Macula Vision Research Foundation, MD fonds, LSBS, Gelderse Blindenstichting

Notching of tissue after macular hole surgery : An abrupt alteration in inner contour of parafoveal tissue associated with foveal tissue elongation

**Jae Hui Kim, Se Woong Kang, Jaeryung Kim.** Ophthalmology, Samsung Medical Center, Seoul, Republic of Korea, Seoul, Republic of Korea.

**Purpose:** To investigate the significance of notching in parafoveal tissue after surgery for macular hole (MH).

**Methods:** This retrospective, observational case series included 35 eyes from 35 patients who underwent surgery for MH. Distance between the parafoveal edge of the outer plexiform layer (OPL) in optical coherence tomography image (OCT) was defined as the inter-OPL distance. The horizontal and vertical inter-OPL distance was divided into nasal and temporal length, and superior and inferior length, respectively. The inter-OPL distance was measurable in 22 eyes. In these eyes, all the nasal, temporal, superior, and inferior lengths were divided into two groups according to presence of the notching of tissue on OCT image at postoperative 6 to 8 months. The difference in inter-OPL distance between 5.4 ± 4.5 weeks postoperatively in average and 6.6 ± 0.8 months postoperatively in average was compared between the two groups.

**Results:** The mean MH size was 436.6 ± 209.7 μm. The notching of tissue was noted in 26 eyes (74.3%) regardless of MH size; nasal direction=22 eyes (62.9%), temporal direction=10 eyes (28.6%), superior direction=12 eyes (34.3%), inferior direction=14 eyes (40.0%). In the 22 eyes, the mean difference in length was 82.4 ± 72.1 μm and 47.9 ± 60.6 μm in the directions with and without the notching of tissue. The difference in the distance was significantly greater in the directions with notching (P=0.017).

**Conclusions:** The presence of notching could be a tomographic marker for the development of the elongation in foveal tissue after MH surgery. Presence of the notching regardless of MH size suggests
that postoperative elongation of foveal tissue occurs in large MHs as well as in small MHs.

Optical coherence tomography images showing notching of tissue in the superior direction 6 months after macular hole surgery. Notching of tissue was defined as an abrupt alteration in inner contour of tissue (arrow). When compared to the opposite direction, definite elongation of outer nuclear layer in the direction of the notching was observed (arrowheads).

**Commercial Relationships:** Jae Hui Kim, None; Se Woong Kang, None; Jaeryung Kim, PharmAbcine, Inc. (F)

**Support:** None in the Support field

**Program Number:** 2803 Poster Board Number: B0057

**Presentation Time:** 8:30 AM - 10:15 AM

**Fluorescein Fundus Angiography Features of Macular Ischemia in Radiation Retinopathy**

Senthil Selvan1,3, Dawn A. Sim2,1, Pearse A. Keane2, Marcus Fruttiger2, Catherine A. Egan1, Mandeep S. Sagoo1, Adnan Tufail2,2

1Institute of Ophthalmology, University College London, London, United Kingdom; 2National Institute for Health Research (NIHR) Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom; 3Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom.

**Purpose:** This study aims to describe and investigate the changes seen on fluorescein fundus angiography (FA) in the macula of patients diagnosed with radiation retinopathy (RR).

**Methods:** Design: Retrospective, case control study.

**Participants:** Seven patients with RR secondary to radiation therapy.

**Methods:** The on-line patient database at Moorfields Eye Hospital, London was searched to find patients diagnosed with RR that had undergone FA. Digital images derived from the FA were analysed using custom software to quantify areas of macular ischemia.

**Main Outcome Measures:** FA derived measurements for areas of macular ischemia and rate of change in these areas.

**Results:** Seventeen patients were found to have a diagnosis of RR, of which seven had FA of sufficient quality to allow analyses. All seven patients developed RR secondary to external radiation therapy for non-ocular malignancy. The mean age of the patients was 61.2 years (SD 21.5) with a male to female ratio of 4:3. Of the seven patients investigated, nine eyes showed evidence of RR, of which five eyes had repeat FA which we were able to compare. In the seven eyes studied, the mean area of macular ischemia was 0.507mm² ± 0.461. Of the five eyes with repeat FA, all eyes demonstrated an increase in the area of macular ischemia between imaging with a mean time interval between angiographies of 2.4 years ± 1.173. Four of the five eyes suffered loss of visual acuity between imaging studies. The mean area of macular ischemia in the repeat FA was 0.639mm² ± 0.537 and the mean change in macular ischemia was 0.350mm² ± 0.406, with a mean rate of change in macular ischemia being 0.177mm²/year ± 0.194.

**Conclusions:** This study shows that macular ischemia is present in patients with RR and that changes in macular ischemia may correlate with loss in visual acuity. Monitoring of changes in areas of macular ischemia on FA may provide a tool for monitoring disease progression and therefore provide an indicator to which patients are more likely to benefit from early treatment to prevent loss of visual acuity and complications associated with RR.

**Commercial Relationships:** Senthil Selvan, Fight For Sight (F); Dawn A. Sim, None; Pearse A. Keane, None; Marcus Fruttiger, AstraZeneca (F), Novartis (F), Novartis (C), Amakem (F); Catherine A. Egan, Bayer (S), Oculotics (S), Novartis (S), Allergan (S), Novartis (F); Mandeep S. Sagoo, None; Adnan Tufail, Allergan (C), Bayer (C), GSK (C), Oculotics (C), Pfizer (C), Thrombogenics (C), Amakem (C), Heidelberg Engineering (R), Novartis/Alcon (C), Sanofi/Genzyme (C)

**Support:** Fight For Sight Research Grant

**Program Number:** 2804 Poster Board Number: B0058

**Presentation Time:** 8:30 AM - 10:15 AM

**Characteristics of Fundus Angiography and Optical Coherence Tomography in Patients with Focal Choroidal Excavation Complicated by Central Serous Chorioretinopathy**

Mihoko Suzuki, Fumi Gomi, Miki Sawawa, Kohji Nishida

Ophthalmology, Osaka Univ Medical School, Suita, Japan.

**Purpose:** To investigate the characteristics of focal choroidal excavation complicated by central serous chorioretinopathy (CSC) using fundus angiography and optical coherence tomography (OCT).

**Methods:** We reviewed the charts of seven eyes of seven patients (5 men, 2 women; mean age, 56.9±9.8 years) with focal choroidal excavation complicated by CSC using fundus angiography and OCT.

**Results:** In six eyes, the points of fluorescein dye leakage were at the edge of the focal choroidal excavation. Five eyes had hyperfluorescence at the focal choroidal excavation on fundus angiography. All focal choroidal excavation lesions were hypofluorescent on indocyanine green angiography (ICGA). All eyes had late-phase hyperfluorescence on ICGA secondary to choroidal vascular hyperpermeability. Five fellow eyes also had late-phase hyperfluorescence secondary to choroidal vascular hyperpermeability. The mean subfoveal choroidal thicknesses were 339 μm and 306 μm in the fellow eyes, a difference that did not reach significance (P=0.39).

**Conclusions:** Fundus angiography and OCT showed that focal choroidal excavation might be related to CSC. Retinal pigment epithelial atrophy and choroidal circulatory disruption might include focal choroidal excavation complicated by CSC.

**Commercial Relationships:** Mihoko Suzuki, None; Fumi Gomi, None; Miki Sawawa, None; Kohji Nishida, Alcon (C), Alcon (F), HOYA (F), Senju (F), Pfizer (F), Santen (F), Osaka University (P)

**Program Number:** 2805 Poster Board Number: B0059

**Presentation Time:** 8:30 AM - 10:15 AM

**The early visual changes with hydroxychloroquine (HQC) usage detected with multifocal ERG (mfERG) versus spectral domain OCT (SDOCT) and 10-2 field testing**

Anh-Danh T. Phan1,2, Jennifer Eikenberry1, Lissa A. McNulty1,2

1Ophthalmology, Indiana University / Glick Eye Institute, Indianapolis, IN; 2Ophthalmology, Indiana University / Visual Electrophysiology Laboratory, Indianapolis, IN.

**Purpose:** The AAO recently updated its recommendations on screening for HQC retinopathy. The current goal of toxicity screening, typically performed after 5 years of usage, is to detect early macular functional or anatomic injury to avoid further visual damage with chronic therapy. New testing modalities, such as mfERG and SDOCT, are reportedly more sensitive in detecting
macular injury. The new recommendations advise usage of these new technologies when available or when the 10-2 field testing shows defect. The purpose of this study is to report on the early changes of HCQ usage observed with these new modalities compared to 10-2 field testing.

**Methods:** Retrospective, comparative chart and diagnostic testing review of six subjects undergoing HCQ therapy of less than 5 years duration. Baseline examination included functional 10-2 field and objective mfERG/SDOCT testing. Repeat examinations over the ensuing months (differing from the AAO recommendations) involved serial 10-2 field and mfERG/SDOCT testing. Comparisons between baseline and each follow-up visit were performed. Outcome measures were testing changes/progression.

**Results:** Examination started less than 1 month through 69 months from initiation of HCQ therapy. All subjects demonstrated dramatic changes on mfERG testing: diminution of B-wave amplitude in particular paracentral; eccentric shifting of the hill of vision; and/or supernormal total response. Correspondingly, SDOCT subfield plot/cross section paracentral thinning occurred afterwards, showing progression with time. 10-2 field defects also occurred after mfERG changes. HCQ dosages ranged from 200 to 400 mg per day.

**Conclusions:** On less than 5 years of HCQ usage, the visual electrophysiologic changes are consistent and dramatic. It is uncertain whether these beginning changes signify transient hypersensitivity of the macular photoreceptors versus precursor of injury to at-risk photoreceptors with long-term usage or identify individuals susceptible to earlier retinopathy. SDOCT also detects progression and may provide even earlier detection. The current goal of HCQ toxicity screening, in which early macular photoreceptor damage has already occurred and is permanent, needs to consider the technological advances afforded by sensitive new testing modalities and accordingly may need to be modified to avoid even early macular damage.

**Commercial Relationships:** Anh-Dan T. Phan, None; Jennifer Eikenberry, None; Lissa A. McNulty, None

**Program Number:** 2806 Poster Board Number: B0060
**Presentation Time:** 8:30 AM - 10:15 AM
**Comparison of outcomes between 20, 23 and 25 gauge vitrectomy for idiopathic macular hole**

Fatma M. Dihown, Mathew MacCumber, 1Graduate College, Rush University and Medical Center, CHICAGO, IL; 2Ophthalmology, Rush University Medical Center, CHICAGO, IL.

**Purpose:** To compare the results of 20, 23, and 25 gauge vitrectomy with two different gas tamponades for idiopathic macular hole (MH) in a multi-surgeon vitrectinal practice.

**Methods:** In this comparative, retrospective, interventional case series, the medical charts of 106 eyes/100 patients were reviewed. Patients who matched our inclusion criteria: eye with stage 2, 3, or 4 MH that underwent 20, 23, or 25 gauge vitrectomy, internal limiting membrane (ILM) peeling, and fluid-gas exchange from June, 2005 to October, 2011 and had at least 6 months follow up. The best corrected visual acuity and anatomical status of the MH were assessed by optical coherent tomography (OCT) at 6 months and 1 year after vitrectomy. Patients with myopia higher than 8D, epiretinal membrane, and previous retinal disease were excluded from the study. Results with perfluoropropane (C3F8) versus sulfur hexafluoride (SF6) were also examined.

**Results:** The MH closed successfully after primary vitrectomy in 81.0% (20 gauge), 94.5% (23gauge), and 91.0% (25 gauge). Preoperative median visual acuities (VAs) were 20/100 (20 gauge), 20/50 (23 gauge), and 20/126 (25 gauge). At 6 months, postoperative VAs did not differ significantly between the 3 groups (P= 0.340). However, at 12 months postoperative median VAs were 20/50 (20 gauge), 20/115 (23 gauge), and 20/40 (25 gauge) and these differed significantly between the 3 groups (p=0.009). The results showed there was a statistically significant difference between the improvement in the 20 gauge or the 25 groups and the 23 gauge group (p value= 0.017 and p=0.006 respectively). Improvement in post-operative visual acuity in the 25 gauge and 20 gauge groups were not statistically different (p = 0.635). MH closed successfully at a higher rate with C3F8 (95.7%) than with SF6 (86.4%, p =0.052).

**Conclusions:** MH surgery with 25-gauge or 20-gauge vitrectomy had better visual outcome than 23 gauge vitrectomy in this series, and MH surgery with C3F8 gas achieved better closure rate than MH surgery with SF6 gas. Further analysis as to the difference in outcome is ongoing.

**Commercial Relationships:** Fatma M. Dihown, None; Mathew MacCumber, Genentech (C), Regeneron (C), Allergan (C), Thrombogenics (C), Optos (C), Sequenom (C), ArcticDx (C)

**Program Number:** 2807 Poster Board Number: B0061
**Presentation Time:** 8:30 AM - 10:15 AM
**Evaluation of Retinal Function in Patients with Retinal Toxicity from Hydroxychloroquine after Drug Cessation**

James Osher, 1, 2, 3 Reshma Kaitra, 2, 3 Jonathan S. Lyons 2, 3, 1 Retina Group of Washington, Washington D.C., DC; 2Dept of Ophthalmology, Washington Hospital Center, Washington D.C., DC; 3Ophthalmology, Georgetown University, Washington D.C., DC.

**Purpose:** Hydroxychloroquine (HCQ) is an analogue of chloroquine with well-documented toxic effects on the retina. In addition to its anti-malarial use, HCQ is commonly used in the treatment of systemic lupus erythematosus, rheumatoid arthritis, and other connective tissue disorders. There have been several reports of progression of retinal toxicity after cessation of the medication. In this study, we use multifocal electoretinography (mfERG) to illustrate both improvement and progression of retinal function in patients with toxicity who stopped taking HCQ.

**Methods:** A retrospective review of 23 patients with HCQ retinal toxicity were followed for an average of nearly two years after discontinuing the medication. Clinical examinations including both visual fields and mfERGs were done. Evaluation of mfERG ring ratio patterns of 26 patients taking HCQ with no evidence of toxicity was used to establish a normal baseline variation. Following cessation of HCQ, multiple variables were evaluated to identify changes in retinal toxicity including changes in mfERG ring ratio, visual field, visual acuity, and fundus examination.

**Results:** Of the 23 patients with HCQ retinal toxicity included in this study the median patient age was 57 years (range 31-82). All patients were female. The average follow-up was 23 months (range 3.5-78). The average cumulative dose of HCQ was 2147 grams (range 1015-3625). Using mfERG ring ratio evaluation, 8/23 (34.8%) worsened, 9/23 (39.1%) had no change, and 6/23 (26.1%) showed improvement during the follow-up period. The initial degree of central involvement was more apparent in the group with a worsening ring ratio pattern. There was no statistically significant difference in the cumulative dose of HCQ or change in visual acuity across these three groups. Follow-up Humphrey visual field testing showed only a 50% correlation in detection of changes found on mfERG.

**Conclusions:** Previous studies have shown the value of using mfERG to screen and monitor patients taking HCQ. This study shows that a significant proportion of patients have at least modest improvement in function as measured by the mfERG ring ratio after cessation of HCQ. No previous studies have shown evidence of
functional improvement by this measure after cessation of HCQ therapy.

**Commercial Relationships:** James Osher, None; Reshma Katira, None; Jonathan S. Lyons, None

**Program Number:** B0062
**Presentation Time:** 8:30 AM - 10:15 AM

**Long-Term Follow-Up Results of Idiopathic Epiretinal Membrane**

Ik Soo Byon, Kang Yeun Pak, Sung Who Park, Ji Eun E. Lee.

Ophthalmology, Pusan National Univ Hosp, Busan, Republic of Korea.

**Purpose:** To investigate the long-term follow-up results in idiopathic epiretinal membrane (ERM)

**Methods:** The medical records and optical coherence tomography (OCT) images of patients with idiopathic ERM were reviewed, who had been followed up for 2 years or more without operation. The changes of the best corrected visual acuity (BCVA, LogMAR), central segment macular thickness (CSMT), metamorphopsia, configuration of membrane, and inner segment and outer segment (IS/OS) junctions of photoreceptor were evaluated.

**Results:** Seventy three eyes were enrolled. Mean age was 59.5 ± 12.6 years. Mean LogMAR BCVA and CSMT changed from 0.13 ± 1.7 and 338 ± 65 μm at baseline to 0.16 ± 0.16 and 335 ± 70 μm at 2 years. There were no statistical significances in the changes of BCVA and CSMT during the follow-up period (p=0.09, p=0.40). Seventeen eyes had a metamorphopsia at the first visit, and no one had new metamorphopsia during the follow-up. ERM configuration in OCT images showed that forty four eyes were broad attachment type, fifteen partial attachment type, and fourteen pseudohole type. Of broad attachment type, four eyes changed into partial attachment type, two into vitreomacular traction type, one into pseudohole type. IS/OS junction represented that fifty four eyes were intact, seventeen attenuated, and two disrupted at the first visit. Five eyes changed from intact to attenuated, and four from attenuated to intact. Spontaneous detachment of membrane developed in six eyes. Five eyes needed vitrectomy and removal of membrane because of decreased vision and increased macular edema.

**Conclusions:** Most of idiopathic ERM had have been stable in vision and macular thickness for a long time. However, close observation is recommended because some cases progressed and required membrane peeling.

**Commercial Relationships:** Ik Soo Byon, None; Kang Yeun Pak, None; Sung Who Park, None; Ji Eun E. Lee, None

**Program Number:** B0063
**Presentation Time:** 8:30 AM - 10:15 AM

**Macular sensitivity and structure in idiopathic epiretinal membranes 12 months after surgical treatment**

Rodica Isaco, Philippe Koehrer, Frederic Nicot, Alain M. Bron, Catherine P. Garcher. Department of Ophthalmology, CHU Dijon, Dijon, France.

**Purpose:** To evaluate macular sensitivity (MS) change and its correlation with visual acuity (VA) and Spectral-Domain Optical Coherence Tomography (SD-OCT) in patients with idiopathic epiretinal membrane (ERM) at 3, 6 and 12 months after surgical treatment.

**Methods:** Prospective, monocenter, interventional case series. We included 49 patients (49 eyes) with an idiopathic ERM scheduled for a surgical treatment. Among these patients, 40 were evaluated at 3 and 6 months (M3, M6), and 31 at 12 months (M12) after ERM and internal limiting membrane removal. At each visit a measurement of best-corrected visual acuity (ETDRS), a microperimetry and a SD-OCT were performed for all patients.

**Results:** The MS significantly improved from 11.76 ± 2.16 dB to 13.68 ± 1.99 dB at M12 (p<0.0001). In the same time we observed an improvement of VA from 70.0 ± 10.2 letters ETDRS at inclusion to 81.9 ± 6.1 letters at M12 (p<0.0001). Macular thickness significantly decreased from 416.2 ± 53.9 μ to 303.7 ± 31.9 μ at M12. We found a significant correlation between pre and post operative VA at M12 (r=0.445; p=0.012). There was no significant correlation between pre and post operative MS at M12 (r=0.329; p=0.071). We found a significant correlation between the increase of MS and VA (r=0.516; p=0.003) but not between MS improvement and macular thickness decrease (r=0.163; p=0.381). Among the 25 (80.6 %) patients with a MS improvement, 6 (24 %) did not increase their VA. Conversely, among the 24 (77.4 %) patients with a VA increase, 4 (16.7 %) did not improve their MS.

**Conclusions:** VA and MS measurement are different but complementary aspects of macular function in the evaluation of patients with ERM.

**Commercial Relationships:** Rodica Isaco, None; Philippe Koehrer, None; Frederic Nicot, None; Alain M. Bron, Allergan (C), Bausch Lomb (C), Horus (F), Théa (C); Catherine P. Garcher, Alcon (C), Allergan (C), Bausch and Lomb (C), Bayer Pharma (C), Novartis (C), Laboratoire Théa (C)

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**ARVO 2013 Annual Meeting Abstracts by Scientific Section/Group – Retina**
Program Number: 2811 Poster Board Number: B0065  
Presentation Time: 8:30 AM - 10:15 AM  
Intravitreal Ranibizumab for Acute Central Serous Chorioretinopathy

SEUNG JUN LEE, Ophthalmology, Kangwon National University Hospital, Chuncheon, Republic of Korea.

**Purpose:** To evaluate the effectiveness of intravitreal ranibizumab injection (IVRI) for acute central serous chorioretinopathy (CSC).

**Methods:** Patients with symptomatic CSC of less than 3 months were prospectively recruited. Patients (n = 20/group) were randomly assigned to IVRI (0.5 mg/0.05 ml) or observation and followed for 6 months. LogMAR best-corrected visual acuity (BCVA), fluorescein angiography, indocyanine angiography, and central foveal thickness (CFT) were assessed at baseline and at regular follow-ups.

**Results:** All patients had increased BCVA, decreased CFT, and resolution of the neurosensory detachment. Complete resolution of neurosensory retinal detachment required more time in the observation group (13.0 ± 3.1 vs. 4.2 ± 0.9 weeks; p < 0.001). Mean BCVA and mean CFT improved significantly in both groups, but the changes were not significantly different between groups at 6 months.

**Conclusions:** IVRI for acute CSC might hasten resolution of neurosensory detachment compared to observation alone. At 6 months, BCVA and CFT did not differ between IVRI and observation groups. Further studies are required to determine the long-term benefits of IVRI.

**Commercial Relationships:** SEUNG JUN LEE, None

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Program Number: 2812 Poster Board Number: B0066  
Presentation Time: 8:30 AM - 10:15 AM  
A Comparison of Macular Morphology of Pediatric Versus Adult Eyes with Epiretinal Membranes

Adam L. Rothman1, Francisco A. Folgar2, Amy Y. Tong1, Cynthia A. Toth1. 1Duke University School of Medicine, Durham, NC; 2Duke Eye Center, Durham, NC.

**Purpose:** To compare macular morphology of children versus adults with epiretinal membrane (ERM) and identify whether children with ERM have unique anatomic characteristics.

**Methods:** An existing research database of adult and pediatric subjects imaged with an 840nm wavelength portable spectral domain optical coherence tomography (SDOCT) system was reviewed to yield 29 pediatric subjects who underwent ERM peel and an additional 6 pediatric subjects with clinically documented ERM. Thirteen pediatric subjects were excluded due to poor image quality or lack of pre-operative images. Two trained graders analyzed the SDOCT images of 1 eye per subject from 22 children and from 22 randomly selected adults who underwent surgical removal of ERM. Subjects were evaluated for demographics, quantitative measurements of anatomic features, and presence and deformation of retinal layers.

**Results:** The mean age ± standard deviation of the children was 5.9 ± 5.2 years and of adults was 70 ± 11 years. Macular thickness was measurable in 18/22 children and 21/22 adults. Mean macular thickness of children and adults was 517 ± 245 µm and 485 ± 172 µm, p=0.644, respectively. In children versus adults, there was a significantly greater incidence of foveal sparing by ERM (6/20 vs 1/22, p=0.041) and a trend towards less foveal deformation (16/19 vs 22/22, p=0.091). Vessel dragging was more common in children than adults (15/22 vs 7/21, p=0.034). There were non-significant differences in incidences of external limiting membrane visibility and disruption, inner segment band disruption, retinal folds, depth of retina involved in folds, intraretinal cysts, and subretinal fluid between these groups; the differences will be characterized by group. Partial vitreous separation was noted in 9 of 21 children and 6 of 22 adults.

**Conclusions:** Significant macular morphologic differences in pediatric versus adult subjects with ERM include decreased foveal deformation, ERM absence at the fovea, and increased vessel dragging in children. Mean macular thickness does not differ between the two populations but does have a much larger standard deviation in the pediatric population. Vitreous separation was notably common in children with ERM and extended to a young age when examined by SDOCT. SDOCT allows for more accurate evaluation of the vitreoretinal interface in children with ERM and, as in adults, provides useful preoperative information.

**Commercial Relationships:** Adam L. Rothman, None; Francisco A. Folgar, None; Amy Y. Tong, None; Cynthia A. Toth, Genentech (F), Biopigen (F), Physical Sciences Inc. (F), Unlicensed (P)

**Support:** The Hartwell Foundation

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Program Number: 2813 Poster Board Number: B0067  
Presentation Time: 8:30 AM - 10:15 AM  
Mineralocorticoid Receptor Antagonism in the Treatment of Chronic Central Serous Chorioretinopathy: First Pilot Study

Min Zhao1, Elodie Bousquet1, Francine F. Behar-Cohen2, 3. 1CRC, Inserm U872, Team 17, Paris, France; 2Department of Ophthalmology, Hôtel-Dieu Hospital, AP-HP, Paris, France; 3Université René Descartes Sorbonne, Paris, France.

**Purpose:** Based on experimental data showing that central serous chorioretinopathy (CSC) could result from over-activation of mineralocorticoid receptor (MR) pathway in choroid vessels, we studied a MR antagonist, eplerenone, as a potential treatment for chronic CSC.

**Methods:** Thirteen patients with chronic CSC were included in a pilot prospective study. Patients were treated with oral eplerenone 25 mg/day for a week followed by 50 mg/day for 1 or 3 months. The primary outcome measure was the change in central macular thickness (CMT) recorded by optical coherence tomography (OCT) at 1 and 3 months after eplerenone treatment. The secondary outcomes included changes in foveal subretinal fluid (SRF) measured by OCT and in best-corrected visual acuity (BVCA) at 1 and 3 months after eplerenone treatment.

**Results:** CMT decreased significantly from 352±139 µm at baseline, to 246±113 µm and 189±99 µm at 1 and 3 months under eplerenone treatment (p<0.05 and p<0.01, respectively). The SRF level at 3 months was significantly decreased compared with baseline SRF (p<0.01). BVCA at 3 months was significantly improved compared with baseline BVCA (p<0.001). The treatment was well tolerated.

**Conclusions:** Eplerenone treatment was associated with a significant reduction in central macular thickness, subretinal fluid level and an improvement in visual acuity. Randomized controlled trials are needed to confirm these encouraging results.

**Commercial Relationships:** Min Zhao, None; Elodie Bousquet, None; Francine F. Behar-Cohen, Inserm/Université ParisDescartes (P)

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Program Number: 2814 Poster Board Number: B0068

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Presentation Time: 8:30 AM - 10:15 AM

**Fundus autofluorescence at macular hole predicting postoperative visual acuities**

**tasuku yoneda, Manabu Yamamoto, Takeya Kohno, Yusaku Yoshida, Ayako Yasui, Kunihiko Shiraki. Osaka City University Graduate School of Medicine, Osaka City, Japan.**

**Purpose:** To investigate a relationship between the preoperative fundus autofluorescence (FAF) at macular hole (MH) and the postoperative visual acuity after MH surgery.

**Methods:** The subjects were 20 eyes of 18 patients (8 eyes of 6 males, 14 eyes of 14 females; age range 54-78 years, mean 64.8 years) with primary Gass stage 4 MH who underwent vitrectomy between August 2007 and July 2009. These eyes were monitored at least for 3 months. Eyes where MH closure was unsuccessful after the initial surgery, those which had previously undergone vitreous surgery, and those with a history of other macular disorders had been excluded. Preoperative FAF was imaged with a fundus camera (FC-FAF) and a confocal scanning laser ophthalmoscope (SLO-FAF), and the ratio (M-D) ratio of FAF brightness at the bottom of the MH to that at the optic disc was calculated. The relationships between the postoperative visual acuity up to 12 months and the M-D ratio, age, gender, preoperative best corrected visual acuity, estimated time that had elapsed before surgery, and macular hole diameter were investigated. logMAR visual acuity was converted from decimal visual acuity.

**Results:** Of the 20 eyes, 15 (75%) were monitored for 6 months and 13 eyes (65%) for 12 months. Mean logMAR visual acuity was 0.63 at baseline, 0.33 at 1 months, 0.32 at 3 months, 0.30 at 6 months, and 0.27 at 12 months postoperatively, with significant improvements seen after 1 months (p<0.01). The factor correlated with the postoperative visual acuity was the M-D ratio on FC-FAF, which was significantly correlated with visual acuity 6 and 12 months postoperatively (p=0.01 and 0.02, r =0.66 and 0.67, respectively). There were no correlations with any other factors.

**Conclusions:** The M-D ratio on preoperative FC-FAF can be a predictor for postoperative visual acuity achieved after long-time follow-up.

**Commercial Relationships:** tasuku yoneda, None; Manabu Yamamoto, None; Takeya Kohno, None; Yusaku Yoshida, None; Ayako Yasui, None; Kunihiko Shiraki, None

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**Program Number:** 2816 Poster Board Number: B0070

**Presentation Time:** 8:30 AM - 10:15 AM

**Hyperautofluorescent macular ring in a series of enhanced S-cone patients**

**Rony Gelman**, **Jonathan P. Greenberg**, **Tobias Duncker**, **Lawrence A. Yannuzzi**

**Purpose:** To describe fundus autofluorescence (AF) and spectral-domain optical coherence tomography (SD-OCT) findings in a case series of enhanced S-cone syndrome (ESCS) patients, and to correlate AF and SD-OCT changes around the border of the hyperautofluorescent ring.

**Methods:** Observational case series of three patients with ESCS. Diagnoses were confirmed by full-field electroretinography (ERG). Patients were evaluated with AF imaging in combination with horizontal SD-OCT line scans through the fovea, at the posterior pole and at a temporal locus for optimal visualization of the border of the ring.

**Results:** On AF imaging, all eyes demonstrated a macula ring of high intensity autofluorescence. This demarcated the hyperautofluorescent periphery from the central macular area, which had relatively spared autofluorescence in 2 subjects, and mottled hyperautofluorescence in the third. The inner segment ellipsoid (ISe) line (previously the inner segment outer segment junction) became disrupted towards the border of the ring, where it was lost. The ISe line was also somewhat thinner and disorganized central to the ring and at the fovea in two patients, while the third showed a long zone of ISe disorganization central to the ring border.

**Conclusions:** We describe AF and corresponding SD-OCT features of the hyperautofluorescent macular ring in three patients with ESCS.

**Commercial Relationships:** Rony Gelman, None; Jonathan P. Greenberg, None; Tobias Duncker, None; Lawrence A. Yannuzzi, None; Stephen H. Tsang, None

**Support:** This study was supported, in part, by grants from the National Eye Institute/NIH (Bethesda, Maryland) EY018213 (SHT),...
P30EY019007 (Core Support for Vision Research; Columbia University) (SHT), Foundation Fighting Blindness (Owings Mills, Maryland) (SHT), TS080017 from Department of Defense (SHT), and unrestricted funds from Research to Prevent Blindness (New York, New York) (SHT). SHT is a Burroughs-Wellcome Program in Biomedical Sciences Fellow, and is also supported by the Charles E. Culpeper- Partnership for Cures 07-CS3, Crowley Research Fund, Schweeneewiss Stem Cell Fund, New York State N09G-302 and Joel Hoffmann Scholarship. RG was supported by a Foundation Fighting Blindness Alan Latties Career Development Program Award. This work was also supported by the Macula Foundation.

**Program Number:** 2817 **Poster Board Number:** B0071

**Presentation Time:** 8:30 AM - 10:15 AM

Assessment of the outer and the inner retina using optical coherence tomography and the correlation with visual acuity in idiopathic epiretinal membrane

**Sung Who Park, Ik Soo Byon, Ji Eun E. Lee.** Pusan national university, Pusan, Republic of Korea.

**Purpose:** Assessment of the outer and the inner retina using optical coherence tomography and the correlation with visual acuity in idiopathic epiretinal membrane

**Methods:** The medical records of 60 eyes were reviewed retrospectively to collect visual acuity (VA), ganglion cell complex thickness (GCT) and photoreceptor reflectivity (PR) at baseline, 3 and 6 months after surgery. GCT was adjusted to compensate centripetal traction by calculating relative thickness to macular thickness (MT, adjusted GCT = GCT/MT). PR was adjusted to remove shadowing effects from the inner retina. Reflectivity of the photoreceptor layer and the retinal pigment epithelium (RR) was measured, and the ratio was calculated (adjusted PR = measured PR/RR).

**Results:** Preoperative PR were correlated with VA at 6 months after surgery (R=−0.273, p=0.038), but not with VA at baseline (R=−0.204, p=0.124) and 3 months (R=−0.197, p=0.139). Preoperative GCT was not evaluated due to segmentation errors by ERM. At 3 months, only GCT had significant correlation with VA (R=−0.352, p=0.007). At 6 months, both GCT (R=−0.324, p=0.013) and RR (R=−0.377, p=0.004) were significantly correlated with VA.

**Conclusions:** In idiopathic ERM, the status of the inner retina had a significant correlation with postoperative VA. The impact of the outer retina on visual function seemed overestimated due to shadowing effect from the inner retina. In early postoperative period, the inner retina was a dominant factor for visual function than the outer retina. The outer retina was correlated with VA in late postoperative period. The postoperative improvement of VA would be related with recovery of the inner retina.

**Commercial Relationships:** Sung Who Park, None; Ik Soo Byon, None; Ji Eun E. Lee, None

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**Program Number:** 2818 **Poster Board Number:** B0073

**Presentation Time:** 8:30 AM - 10:15 AM

**Morphological description of dome-shaped macula in myopic eyes**


**Purpose:** To analyze the different topographic features of dome-shaped macula including the choroidal thickness and their related complications.

**Methods:** The records of thirty three patients with a dome-shaped macula in one or both eyes (48 eyes) referred for decreased vision were reviewed. Each patient underwent a complete ophthalmologic examination including axial length measurement, spectral domain optical coherence tomography (SD-OCT), and fluorescein and indocyanine green angiography. The most cambered axis of the macula (MCA) was determined and the height of the macular bulge (HMB) relative to the bottom of the staphyloma was measured on SD-OCT. A map of choroidal thickness was created allowing to measure the mean choroidal thickness within the foveal center at 1 mm intervals compared to the choroidal thickness at 3 mm temporal and nasal to the fovea.

**Results:** Patients’ mean age was 55 (± 13.6) years. The mean axial length was 27.49 (± 2.53) mm, with a mean refractive error of -10.5
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(± 5.2) diopters. Mean best-corrected visual acuity (VA) was 0.50 (± 0.33) logMAR. A SRD was present in 25/48 eyes (52.1%). The MCA was vertical in 28 eyes (58.3%) and horizontal in 20 (41.7%). Four topographic dome-shaped macula patterns were observed according to the MCA orientation and importance: the dome orientation was horizontal in 29.2% of cases (14/48), vertical in 16.7% (8/48), centered with no evident predominant axis in 20.8% (10/48) and “racket shaped”, when the macular bulge was extended to the optic disc, in 33.3% of cases (16/48). There was no difference in VA between the 4 patterns. Mean HMB (in the most cambered axis) was 407.7 (± 215.1) µm (range: 120 to 1130). Mean choroidal thickness was 146.5 (± 56) µm within the foveal center, significantly greater than at 3 mm nasal (123.5 ± 59.2; p<.0001) and temporal to the fovea (102 ± 50.5 µm; p<.0001). The HMB was positively correlated with the central choroidal thickness (p=0.014) and greater when the dome was vertically oriented (p=.008) but did not correlate with VA. The presence of SRD was significantly increased for HMB > 350 µm (p = .0047) and vertically oriented bulges (i.e with horizontal MCA) (p=.045). SRD was a risk factor of decreased vision (p=.043).

Conclusions: Four patterns of dome-shaped macula were distinguished according to their most cambered axis. The risk of chronic SRD and decreased vision was greater in dome-shaped maculas with high and vertically oriented bulges.

Commercial Relationships: Violaine Caillaux, None; David Gaucher, ALLERGAN (C), NOVARTIS (C); Vincent Gualino, None; Pascale Massin, Novartis (C), Allergan (C), Fovea Pharmaceutical (C), Fournier Abbott (C); Ramin Tadayoni, Alcon (C), Novartis (C), Allergan (C), DORC (R), Bausch + Lomb (R), FCI-Zeiss (C), Takeda (R), Alimera (R), Bayer (C); Alain Gaudric, None

Program Number: 2820 Poster Board Number: B0074
Presentation Time: 8:30 AM - 10:15 AM

Retrospective Study of Two or More Dexamethasone Intravitreal Implant 0.7 mg Injections for Retinal Vein Occlusion
Antonio Capone1, Michael Singer2, David G. Dodwell3, Richard Dreyer1, Kean T. Oh2, Daniel B. Roth2, John G. Walt3, Lanita C. Scott1, David A. Holland1

Purpose: To examine the efficacy, safety and reinjection interval of dexamethasone intravitreal implant (DEX implant) 0.7 mg in the treatment of macular edema due to branch (BRVO) or central (CRVO) retinal vein occlusion.

Methods: A retrospective chart review of patients who received ≥2 injections of DEX implant was conducted at 26 sites. Additional concomitant RVO treatments were permitted. The primary efficacy endpoint was mean change in best-corrected visual acuity (BCVA; number of lines) from baseline to 4-20 weeks following last DEX implant injection. Additional efficacy assessments included percentages of patients with BCVA increase of ≥2 or ≥3 lines versus baseline and change in central retinal thickness (CRT) from baseline. Safety measures included adverse events, intraocular pressure (IOP), and surgical interventions.

Results: A total of 289 patients were included; 54.3% with BRVO and 45.7% with CRVO. Mean (SD) time from RVO diagnosis to first DEX implant was 18.4 (23.39) months. Most received 2-6 DEX implants (mean 3.2; range 2-9). Mean time between DEX injections was 5.6 months. The mean (SD) change in BCVA from baseline to 4-

20 weeks after the last DEX was 1.0 (3.51) line (range -13 to +12 lines) (p<0.0001); responses were similar with each additional injection. The majority (62.9%) of patients experienced BCVA improvement ≥2 lines from baseline; 48.1% had ≥3 line improvement. Significant reduction of CRT also occurred with results consistent from 1-6 injections; 65.3% of patients achieved CRT ≤250 µm at any time point. CRT findings were generally similar in patients with BRVO and CRVO. After initial DEX implant treatment, there were no additional concomitant therapies in 29% of patients. In patients who received anti-VEGF injections, mean (SD) time from first DEX implant to first anti-VEGF injections was 179.9 (125.16) days. There were no unexpected safety findings. Increases in IOP were generally well-controlled with IOP-lowering medication. At the final visit: 91.5% of patients (260/284) had an IOP of ≤21 mmHg, only 14 patients (4.9%) had an IOP ≥25 mmHg, and 5 patients (1.8%) had an IOP ≥35 mmHg. During the study 1.7% patients underwent incisional glaucoma surgery.

Conclusions: The DEX implant is safe and effective with repeat injections and when utilized alone and with common adjunctive RVO treatments.

Commercial Relationships: Antonio Capone, Alcon Laboratories, Inc. (C), Alimera Sciences (C), Allergan, Inc. (C), Allergan, Inc. (F), FocusROP, LLC (P), FocusROP, LLC (I), GENENTECH (C), GENENTECH (F), GlaxoSmithKline (F), Ophthotec (F), Retinal Solutions, LLC (I), Retinal Solutions, LLC (P), Synergetics, Inc. (C), Thermobogenous (F); Michael Singer, optos (F), Allergan (C), regeneron (C), genentech (F), genentech (C), regeneron (F), regeneron (C), santen (C), quintiles (C), acucela (C), eyegete (F), lpath (F), ohr (F); David G. Dodwell, Allergan (C); Richard Dreyer, Genentech (F), Genentech (F), Allergan (F), regeneron (F); Kean T. Oh, None; Daniel B. Roth, Allergan, Inc (C), genentech (C), regeneron (C), qLT (C); John G. Walt, Allergan (E); Lanita C. Scott, Allergan, Inc (E); David A. Holland, Allergan, Inc. (E)
Support: Allergan
Clinical Trial: NCT01411696

Program Number: 2821 Poster Board Number: B0075
Presentation Time: 8:30 AM - 10:15 AM

Refractive errors in high myopic eyes after phacovitrectomy
Donghyun Jee, Ophthalmology, St. Vincent hospital, Catholic Medical Univ of Korea, Suwon, Republic of Korea.

Purpose: To examine the refractive prediction error in high myopic eyes after phacovitrectomy

Methods: This retrospective comparative case series included one hundred one eyes (21 high myopic eyes and 80 non-high myopic eyes) of 101 patients who underwent successful phacovitrectomy (phacoemulsification, intraocular lens implantation, and pars plana vitrectomy). The high myopic eyes were defined as the eye with more than 26.0 mm of axial length. The post-operative prediction error of mean error and mean absolute error were evaluated at 4 months post-operatively. Axial length and keratometry measurement were performed pre-operatively and 4 months post-operatively using the IOL Master.

Results: The refractive outcome after phacovitrectomy showed significantly greater myopic shift in the high myopic eyes than that in the non-high myopic eyes. Axial length and keratometric value in the high myopic eyes were significantly increased (P=0.043, 0.037 respectively), whereas those in the non-high myopic group were not significantly increased (P=0.135, 0.347 respectively). The change of the axial length in the myopic eye (0.36±0.28 mm) was greater than in the non-high myopic eye (0.11±0.34 mm; P<0.001).

Conclusions: High myopic eyes showed more myopic shift than non-high myopic eyes after phacovitrectomy. The cause of myopic shift

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in high myopic eyes seems to be attributed to actual elongation of the axial length due to the thinner sclera in high myopia.

**Commercial Relationships:** Donghyun Jee, None

**Program Number:** 2822 Poster Board Number: B0076

**Presentation Time:** 8:30 AM - 10:15 AM

**Macular sensitivity after intravitreal dexamethasone implant (Ozurdex) for retinal vein occlusion**

Lea Querques, Giuseppe Querques, Rosangela Lattanzio, Maria Lucia Cascavilla, Giacinto Triolo, Edoardo Cavallerio, Preziosa Chiara, Maria vittoria cicenelli, Francesco Bandello. 1University Hospital San Raffaele, Milan, Italy; 2of Ophthalmology, University Paris-Est Creteil, Creteil, France.

**Purpose:** To investigate changes in macular sensitivity after intravitreal dexamethasone implant for macular edema (ME) secondary to retinal vein occlusion (RVO).

**Methods:** 19 treatment-naive patients with RVO ME were enrolled in this prospective uncontrolled study. Patients were treated with intravitreal Ozurdex and followed up at 1 month 3, 4, 5 and 6 months for the evaluation of morphological and functional outcomes, by means of BCVA, microperimetry, and spectral-domain optical coherence tomography (SD-OCT).

**Results:** 19 eyes of 19 patients were included for analysis. At 1 month (19 eyes) mean BCVA, retinal sensitivity, and central macular thickness (CMT) improved from 0.50±0.34 LogMAR, 10.51±4.31 dB, and 762±259 μm to 0.38±0.34 LogMAR, 12.28±5.06 dB, and 385±191 μm, respectively. At 3 months (19 eyes) improvement of mean BCVA, retinal sensitivity, and CMT decreased (0.54±0.36 LogMAR, 11.62±5.05 dB, and 518±251 μm, respectively); at this time point, 2 eyes were retreated with intravitreal dexamethasone. At 4 months (17 eyes) mean BCVA, retinal sensitivity and CMT were 0.68±0.45 LogMAR, 8.64±4.45dB, and 671±239 μm respectively; at this time point, 4 eyes were retreated. At 5 months (13 eyes) mean BCVA, retinal sensitivity, and CMT were 0.83±0.42 LogMAR, 8.1±3.4 dB, and 670±218 μm respectively; at this time point, 6 eyes were retreated. Interestingly 7 eyes did not underwent retreatment up to 6 months from first intravitreal dexamethasone; in these eyes mean BCVA, retinal sensitivity, and CMT changed from 0.46±0.29 LogMAR, 12.27±5.32 dB, and 715±219 μm (baseline, versus 0.53±0.37 LogMAR, 9.48±4.53 DB, and 790±286 μm, in eyes that underwent retreatment <6 months), to 0.41±0.45 LogMAR, 11.33±5.32 dB, and 547±216 μm (6 months), respectively. At 6 months, 5 eyes were retreated. 1 month after retreatment with intravitreal dexamethasone (12 eyes) mean BCVA, retinal sensitivity, and CMT improved from last pre-retreatment visit (from 0.93±0.77 LogMAR, 8.42±3.98 dB, and 711±172 μm to 0.77±0.46 LogMAR [p=0.03], 10.63±4.63 dB [p=0.04], and 497±262 μm [p=0.01], respectively).

**Conclusions:** In eyes with ME secondary to RVO, microperimetry shows improvement in macular sensitivity 1 month after treatment/retreatment with intravitreal dexamethasone. Eyes that underwent retreatment <6 months showed a worse baseline BCVA and macular sensitivity compared with eyes not requiring retreatment up to 6 months.

**Commercial Relationships:** Lea Querques, None; Giuseppe Querques, None; Rosangela Lattanzio, None; Maria Lucia Cascavilla, None; Giacinto Triolo, None; Edoardo Cavallerio, None; Preziosa Chiara, None; maria vittoria cicenelli, None; Francesco Bandello, ALLERGAN Inc. (S), NOVARTIS PHARMACEUTICALS CORPORATION (S), FARMILA-THEA (S), BAYER SCHERING PHARMA (S), PFIZER Inc. (S), ALCON Inc. (S), BAUSH AND LOMB (S), GENENTECH Inc. (S), ALIMERA SCIENCES Inc. (S), SANOFI AVENTIS (S), THROMBOGENICS (S)

**Program Number:** 2823 Poster Board Number: B0077

**Presentation Time:** 8:30 AM - 10:15 AM

**Choroidal thickness in Retinal vein occlusion: A pilot study**

Christiana Dinah, Dawn A. Sim, Pearse A. Keane, Adnan Tufail, James S. Talks. 1Ophthalmology, Royal Victoria Infirmary, Newcastle, United Kingdom; 2Moorfields Eye Hospital, London, United Kingdom.

**Purpose:** Choroidal blood flow accounts for most of the ocular blood flow and is the major source of oxygen and nutrients for the choroid and the outer retina. The choroid has also been implicated in the pathophysiology of macular oedema and retinal hypoxia. We set out to investigate the role of the choroid in retinal vein occlusion using enhanced depth optical coherence imaging (EDI-OCT). Our aim was to compare the subfoveal choroidal thickness in eyes with retinal vein occlusion with normal fellow eyes and describe changes in choroidal thickness after treatment with dexamethasone intravitreal implant (DEX implant, Allergan).

**Methods:** In this pilot, longitudinal study, consecutive patients with macular oedema secondary to retinal vein occlusion were evaluated. Slit lamp biomicroscopy, spectral domain optical coherence tomography and EDI-OCT were performed at baseline in the affected and the normal fellow eye. Wide-field fluorescein angiography was also performed in all patients. 10 weeks after treatment with intravitreal dexamethasone implant, EDI-OCT was repeated in the affected eyes.

**Results:** There were 10 eyes of 5 patients. 2 patients presented with branch retinal vein occlusion, 2 with hemi-vein occlusion and 1 patient with central retinal vein occlusion. Mean age was 69.8 (±13.4, range: 58-90), mean duration of symptoms at baseline was 18.8 weeks (±21.3, range: 3-52), mean axial length was 22.68 (±0.7, range:22.2-24.05) and mean best corrected visual acuity in early treatment of diabetes retinopathy study (ETDRS) letters was 48.2 (±24.6, range:17-73). In all 5 patients, the subfoveal choroidal thickness was thinner in the fellow eye compared to the normal eye (297.2μm vs 208.9μm). Additionally, 10 weeks after treatment with intravitreal DEX implant, choroidal thickness was lower compared to baseline in 3 of 5 affected eyes.

**Conclusions:** EDI-OCT provides a non-invasive method of evaluating the changes in the choroid in retinal vein occlusion. Choroidal thickness was thinner in unaffected fellow eyes, compared to eyes with retinal vein occlusion. This may indicate an increase in choroidal perfusion resulting from local mechanisms compensating for the decrease in retinal blood flow. Further work is required to elucidate the role of choroidal perfusion in visual acuity and response to treatment in retinal vein occlusion.

**Commercial Relationships:** Christiana Dinah, None; Dawn A. Sim, None; Pearse A. Keane, None; Adnan Tufail, Allergan (C), Bayer (C), GSK (C), Uscologics (C), Pfizer (C), Thrombogenics (C), Amakem (C), Heidelberg Engineering (R), Novarits/Alcon (C), Sanofi/Genzyme (C); James S. Talks, None

**Support:** Clinical Research Network, Newcastle upon Tyne

**Program Number:** 2824 Poster Board Number: B0078

**Presentation Time:** 8:30 AM - 10:15 AM

**Intravitreal Dexamethasone Implant (Ozurdex) for macular edema secondary to retinal vein occlusion: a comparative study between recent onset and chronic edema**

Emilia Maggio, Antonio Polito, Antonio Peroglio Deiro, Elisa Benetti, Grazia Peratile. Sacrocuore Hospital, Negrar, VR, Italy.
Purpose: To compare the anatomical and visual outcomes following intravitreal dexamethasone implant (Ozurdex) between eyes with visual loss due to recent onset and chronic macular edema (ME) secondary to retinal vein occlusion (RVO).

Methods: We retrospectively analyzed medical records of two series of consecutive patients with ME secondary to RVO treated with Ozurdex from June 2011 to November 2012. The first group included 40 patients affected by newly diagnosed, previously untreated ME, associated with recent onset RVO. The second group comprised 34 eyes with persistent or recurrent ME that had undergone previous treatments. The primary outcome measures were best-corrected visual acuity (BCVA) and central macular thickness (CMT) at baseline, follow-up (1, 3, 6, 12, 16 months) and final visit (mean = 7 months in group 1 and 8 months in group 2). The safety of the implant was also evaluated.

Results: At baseline mean CMT was 839.3 μm in group 1 and 615.7 μm in group 2 and mean BCVA was 0.2 in both groups. At the final visit mean CMT was 326 μm in group 1 and 510 μm in group 2, mean BCVA was 0.4 in group 1 and 0.28 in group 2. Significant improvements in BCVA and CMT were found in both groups (p 0.001), nevertheless better improvements were experienced by eyes with recent onset, previously untreated ME as compared with chronic ME (p 0.0082). No serious ocular or systemic adverse events were observed.

Conclusions: In our study population Ozurdex was a safe and effective therapeutic option for the treatment of ME associated with retinal vein occlusion (RVO) both in recent onset and in recurrent ME. Nevertheless, improvements in BCVA and CMT were higher in eyes affected by recent onset, previously untreated ME.

Commercial Relationships: Olga Rostaqui, Novartis (R); Agnès Glacet-Bernard, Novartis (C), Allergan (R); Nathalie Massamba, None; Jennyfer Zerbib, novatis (C); Florence Coscas, None; Gabriel J. Coscas, None; Eric H. Souied, BAUSCH + LOMB (C), NOVARTIS (C), BAYER (C), THEA (C), ALLERGAN (C)

Program Number: 2826 Poster Board Number: B0079
Presentation Time: 8:30 AM - 10:15 AM
Early treatment with ranibizumab in severe central retinal vein occlusion
Ophthalmology, Intercommunal hospital of Creteil, Creteil, France.

Purpose: Central retinal vein occlusion (CRVO) sometimes results in rapid and severe visual loss, often limited to counting fingers (CF). These forms have a poor prognosis and are excluded from the princeps trials on the treatment of macular edema. This study aims at evaluating the outcome of early treatment with ranibizumab in these particular clinical forms

Methods: Retrospective non comparative review of patients treated with ranibizumab and who had a visual acuity of 20/100 or less secondary to CRVO lasting for less than one month. CRVO was initially assessed by angiography and OCT. After a series of 3 intravitreal injections of ranibizumab, patients were monitored monthly for 6 months with measurement of visual acuity, biomicroscopic examination, OCT and, if needed, angiography.

Results: Among the 19 retrospectively selected patients (14 men, mean age, 67 years), CRVO duration was 12 days on average and the vision was initially reduced to CF in 10 patients (53%), between 20/400 and 20/200 in 5 cases and between 20/160 and 20/100 in 4 cases. It was the second involved eye in 4 patients. The mean central retinal thickness was 807 μm initially and 377 μm at the end of follow-up. At the end of follow-up, only 2 patients recovered a vision greater than 20/40, 6 had between 20/200 and 20/40, and the majority remained below 20/200 (58%). Fifteen patients (79%) underwent panretinal photocoagulation for extensive retinal peripheral ischemia.

In 2 eyes, intravitreal haemorrhage occurred between the 4th and the 6th months.

Conclusions: In this pilot study, early treatment with ranibizumab seemed to slightly improve vision in immediately severe CRVO, usually corresponding to an ischemic form. Angiographic monitoring of the patients is essential to identify peripheral ischemia and to prevent neovascular complications.
In-Cheon You, Nanchon Cho, Dongwook Lee, Min Ahn. Research Institute of Clinical Medicine of Chonbuk National University-Biomedical Research Institute, Jeonju, Republic of Korea.

**Purpose:** To study the effect and safety of intravitreal bevacizumab injection in patients with idiopathic central serous chorioretinopathy.

**Methods:** We had performed retrospective review on the patients who had been diagnosed as idiopathic central serous chorioretinopathy and had regular follow-up for at least 12 months from the first injection at our hospital, either undergone intravitreal bevacizumab injection (107 eyes of 100 patients) or observed without injection (46 eyes of 40 patients). Changes in the visual acuity and the serous neurosensory and retinal pigment epithelium retinal detachment were evaluated through the results of best corrected visual acuity and optical coherence tomography measured respectively at initial presentation, after 1 month, 3 months, 6 months, 9 months and 12 months of the first injection.

**Results:** 87 males and 13 females with mean age of 45.43±7.6 years were recruited in the intravitreal bevacizumab injection group, and 34 males and 6 females with mean age of 47.22±9.8 years were recruited in the observation group. There was significant difference in the mean duration of retinal detachment to disappear between the intravitreal bevacizumab injection group and the observation group (2.54±0.21 : 4.29±0.73 months, p=0.01). Resolution rate (87.9% : 76.1%, p=0.27) and recurrence rate (22.4% : 32.6%, p=0.21) do not show significant difference between the two groups. There were no significant differences in the best corrected visual acuity and the central macular thickness after 12 months follow-up between the intravitreal bevacizumab injection group and the observation group.

**Conclusions:** Intravitreal bevacizumab injection was more effective and faster resolution of sensory retinal detachment than observation during the 12 months of consecutive follow-up. Therefore, intravitreal bevacizumab injection can be considered as an effective and safe treatment modality when the patients need prompt visual improvement, such as depending on the morbid eye or requiring binocular vision for occupational cause.

**Commercial Relationships:** None; Min Ahn. None

**Program Number:** 2829 Poster Board Number: B0083
**Presentation Time:** 8:30 AM - 10:15 AM

**Title:** Outer retinal edema as a risk factor for poor visual outcome after bevacizumab therapy for macular edema with branch retinal vein occlusion

**Authors:** Daiisuke Marumatsu1, 2, Maki Mishima1, Yoshihiro Wakabayashi1, Takuya Iwasaki1, Shigemitsu Ishii1, Setsuko Kawakami1, Keisuke Kimura1, Sayaka Gondo1, Kazuhiro Uzuame1, Hiroshi Goto1. 1Ophthalmology, Tokyo Medical University, Tokyo, Japan; 2ophthalmology, Tokyo Medical University Ibaraki Medical Center, Ibaraki, Japan.

**Purpose:** To evaluate the baseline OCT morphology of macular edema (ME) associated with branch retinal vein occlusion (BVO) for visual outcome after intravitreal bevacizumab injection (IVB).

**Methods:** Seventy one eyes of 71 patients with ME due to BVO who were received primary IVB (40 male, 31 female, mean ages 67) were retrospectively reviewed. The baseline morphology of ME was classified to inner retinal edema, outer retinal edema and serous retinal detachment (SRD) using spectral-domain optical coherence tomography (SD-OCT). Best corrected visual acuity (BCVA; log MAR) and central retinal thickness (CRT) were measured at each visits. Additional photocoagulation and IVB were performed for recurrence of ME. The visual outcome for each pattern of edema was evaluated at 12 months after primary IVB.

**Results:** Visual acuity at base line was not different with or without...
outer retinal edema. At 12 months, BCVA of BVO without outer retinal edema (Mean 0.19±0.33; n=43) was significantly better than that with outer retinal edema (0.29±0.24; n=28) (P=0.026). The ratio of VA over 0.7 (decimal visual acuity) was 67% in patients without outer retinal edema, it was significantly higher (43%) than that with outer retinal edema (P=0.043). The result of univariate logistic regression analysis showed that the outer retinal edema was a significant risk factor for poor BCVA after IVB (OR, 2.8; P=0.040). There was no difference in VA after IVB between BVO with and without inner retinal edema or SRD.

**Conclusions:** Our results suggest that the outer retinal edema was a predictor factor for poor visual outcome after IVB for BVO with ME.

**Commercial Relationships:** Daisuke Muramatsu, None; Maki Mishima, None; Yoshihiro Wakabayashi, None; Takuya Iwasaki, None; Shigemitsu Ishii, None; Setsuko Kawakami, None; Keisuke Kimura, None; Sayaka Gondo, None; Kazuhiko Umazume, None; Hiroshi Goto, None

**Support:** No financial disclosure

**Program Number:** 2830 **Poster Board Number:** B0084

**Presentation Time:** 8:30 AM - 10:15 AM

**Quantitative measurements of autofluorescence in Stargardt’s disease**

Tobias Duncker1, Tomas R. Burke1, Jonathan P. Greenberg1, Winston Lee1, Theodore Smith1, Stephen H. Tsang1, Janet R. Sparrow1, Rando Allikmets1, Francois C. Delori2. 1Ophthalmology, Columbia University, New York, NY; 2Scheepens Eye Research Institute, Harvard Medical School, Boston, MA.

**Purpose:** To obtain quantitative measurements of autofluorescence (qAF) in a cohort of patients with Stargardt’s disease (STGD1).

**Methods:** 45 patients with a clinical diagnosis of STGD1 and a mean age of 29 years (range: 7-52 years) were studied. AF images were acquired with a confocal scanning laser ophthalmoscope (cSLO) equipped with an internal fluorescent reference to account for variable laser power and detector sensitivity. The gray levels (GLs) of each image were calibrated to the reference, the zero GL, and the magnification, to give quantified autofluorescence (qAF). For each patient, the mean qAF was based on values obtained from 8 circularly arranged segments positioned at an eccentricity of about 7°-9° (depending on the refractive error). Genotyping of the ABCA4 gene was performed in all patients using the ABCR 700 microarray and direct sequencing.

**Results:** qAF levels were significantly increased in 40/45 patients. Differences were more pronounced in younger patients with up to 5 times higher levels than normal controls. Patients carrying the G1916E mutation exhibited less pronounced increases in qAF levels. From the 5 patients without significantly increased qAF levels, 4 carried the G1961E mutation.

**Conclusions:** qAF is a novel imaging technique that allows in vivo measurements of lipofuscin. ABCA4 mutations cause significantly increased qAF levels, consistent with previous reports of increased RPE lipofuscin. qAF will help to establish genotype-phenotype correlations and serve as an outcome measure in clinical trials.

qAF values of STGD1 patients as a function of age. Patients are divided into two groups based on the presence of flecks and/or atrophy in the retinal periphery. Error bars represent the standard deviation of qAF values based on multiple images of each patient. The 95% confidence interval (dashed lines) and mean curve (solid line) of qAF values in normal subjects are indicated.

**Commercial Relationships:** Tobias Duncker, None; Tomas R. Burke, None; Jonathan P. Greenberg, None; Winston Lee, None; Theodore Smith, None; Stephen H. Tsang, None; Janet R. Sparrow, None; Rando Allikmets, None; Francois C. Delori, None

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**Program Number:** 2831 **Poster Board Number:** B0085

**Presentation Time:** 8:30 AM - 10:15 AM

**Case series of Macular Degeneration following Pars Plana Vitrectomy using Xenon Intraocular Endoillumination**

Seung Jae Lee1, Ju Yong Seok1, Haksu Kyung1, Soo Young Lee1, 2. 1Ophthalmology, National Medical Center, Seoul, Republic of Korea; 2Ophthalmology, Emory Eye Center, Atlanta, GA.

**Purpose:** To evaluate macular degeneration in various retinal diseases after vitrectomy with the use of Xenon intraocular endoillumination

**Methods:** The authors retrospectively analyzed clinical diagnosis, preoperative and postoperative visual acuity, timing of macular degeneration, fundus and optical coherence tomography (OCT) finding of 10 consecutive eyes with macular degeneration after vitrectomy with the use of Xenon intraocular endoillumination.

**Results:** Diagnoses which macular degeneration occurred after vitrectomy with the use of Xenon intraocular endoillumination
consisted of diabetic vitreous hemorrhage (3 eyes), rhegmatogenous retinal detachment (2 eyes), macular hole (2 eyes) and epiretinal membrane (3 eyes). In 5 eyes, macular degeneration involved the fovea. Postoperatively, macular degeneration occurred from 2 weeks to 34 months. Fundus findings showed retinal pigment epithelial pigmentary change and atrophy in all 10 eyes. Spectral Domain-OCT showed RPE clumping and disruption of photoreceptor IS/OS line. The mean central subfoveal thickness in 2 eyes with macular hole and 2 eyes with epiretinal membrane was 382 μm before surgery and 232.25 μm after surgery (p = 0.028). The mean central subfoveal thickness in 3 eyes with diabetic vitreous hemorrhage and 2 eyes with rhegmatogenous retinal detachment decreased from 302 μm to 223.8 μm during follow-up period after surgery (p = 0.100). In 7 eyes, central subfoveal thickness reduced below normal range. Postoperative BCVA was better than 20/60 in 5 eyes not involving fovea, but worse than 20/200 in 5 eyes involving fovea. 

**Conclusions:** Macular degeneration after vitrectomy may be associated with the use of Xenon intraocular endoillumination toxicity. Therefore, when we select light source during intraocular surgery, care should be taken and we should minimize the occurrence of macular degeneration.

![Epiretinal membrane of 49-year-old male. (A) Preoperative fundus photograph. (B) After 6 months of vitrectomy including membrane peeling, diffuse pigmentary change and atrophy was observed. (C) SD-OCT showed RPE clumping and disruption of photoreceptor IS/OS line (arrowhead).](image)

**Commercial Relationships:** Seung Jae Lee, None; Ju Yong Seok, None; Haksu Kyung, None; Soo Young Lee, None

**Support:** None in the Support field

**Program Number:** 2832 Poster Board Number: B0086

**Presentation Time:** 8:30 AM - 10:15 AM

**Fundus Autofluorescence Patterns in Central Serous Chorioretinopathy**

Seung-Young Yu1, Nam Suk Cho2, Eung Suk Kim3, young gyun Kim4, Hyung-Woo Kwak5. 1Ophthalmology, Kyung Hee University Hospital, Seoul, Republic of Korea; 2Ophthalmology, Korea Cancer Center Hospital, Seoul, Republic of Korea; 3Ophthalmology, Eulji University Hospital, Daejeon, Republic of Korea; 4Ophthalmology, Eulji General Hospital, Seoul, Republic of Korea.

**Purpose:** To investigate the patterns and frequency of fundus autofluorescence (FAF) abnormalities in patients with central serous chorioretinopathy (CSC) and evaluate correlation with spectral-domain optical coherence tomography (SD-OCT) findings and best-corrected visual acuity (BCVA).

**Methods:** Cross-sectional observational study, in which 127 eyes of 119 consecutive patients with CSC underwent fundus photography, FAF imaging, fluorescein angiography (FA), indocyanine green angiography (ICGA) and SD-OCT.

**Results:** The mean age of subjects was 46.5 ± 9.2 years, and 101 (84.9%) were male. Alterations in FAF were classified into five patterns: blocked (43.5%), mottled (8.7%), hyper (27.6%), hyper/hypo (11.0%) and descending tract (9.4%). There are blocked (63.1 ± 156.2 days), mottled (197.9 ± 222.4 days), hyper (379.2 ± 559.7 days), hyper/hypo (987.5 ± 1050.0 days), and descending tract AF group (1363.8 ± 1352.4 days), in order by the length of duration of symptom (p < 0.001). The mean visual acuity (logMAR) was 0.24 ± 0.29 for the blocked, 0.36 ± 0.31 for the mottled, 0.36 ± 0.33 for the hyper, 0.51 ± 0.38 for the hyper/hypo, and 0.38 ± 0.32 for the descending tract AF group. The mean visual acuity in the blocked AF group was better to a statistically significant extent (p = 0.045, respectively). Fifty-five of 119 patients underwent OCT. Intact inner/outer segment junction on SD-OCT are 39 eyes (100%) in the blocked, 9 eyes (90%) in mottled, 23 eyes (82.1%) in hyper, 3 eyes (37.5%) in hyper/hypo and 3 eyes (30.0%) in descending tract AF group (p = 0.000). Disrupted external limiting membrane line on SD-OCT was found in only 1 patient in descending tract group while not being found in other groups.

**Conclusions:** The FAF abnormalities in CSC show multiple distinct patterns and seem to correlate with duration of symptom and BCVA. A refined phenotypic classification may be helpful to discern chronicity.

**Commercial Relationships:** Seung-Young Yu, None; Nam Suk Cho, None; Eung Suk Kim, None; young gyun Kim, None; Hyung-Woo Kwak, None

**Program Number:** 2833 Poster Board Number: B0087

**Presentation Time:** 8:30 AM - 10:15 AM

**Intravitreal Bevacizumab for the treatment of Central Serous Chorioretinopathy: follow up over 12 months**

Adam Lewis, Marina Syrimi, Manju N. Chandran, Geeta Menon. Frimley Park Hospital, Frimley, United Kingdom.

**Purpose:** Central Serous Chorioretinopathy (CSC) is characterized by serous neurosensory retinal detachment caused by leakage from the retinal pigment epithelium. Although CSC is usually self limiting, persistent subretinal fluid is associated with reduced visual acuity. Recently intravitreal bevacizumab has been used successfully to treat CSC in the short term but there is limited evidence about the long term effects. The purpose or our study was to report the 1-year follow up results from the first bevacizumab injection for the treatment of CSC.

**Methods:** A retrospective review of patients treated for chronic CSC (at least 10 month duration) with intravitreal Bevacizumab in our unit was performed. Patients who had at least 12 months follow up from the first intravitreal injection of Bevacizumab were included in the study. All eyes that received laser treatment or Photodynamic Therapy in the past as treatment for CSC were excluded. The patients were reviewed every 4 weeks following the first intravitreal injection. Spectral-domain optical coherence tomography was performed at every follow up visit. The presence of subretinal fluid was an indication for retreatment. Best-corrected visual acuity and central macular thickness were compared between baseline and 1 year after the first injection.

**Results:** Six eyes of 5 patients had at least 12 month follow up following the first intravitreal Bevacizumab injection. The mean number of injection administered during the 12 months was 6 (SD 2.8). The mean visual acuity on presentation was 53.8 (SD 24.2) and 70.7 (SD 8.2) at 12 months resulting in a mean change of 16.83 letters. (P = 0.10). Mean reduction in central macular thickness was 30.33 microns (P = 0.09). All treated eyes had stable or improved
vision after 12 months. Injection-related complications were not encountered during the follow up.

**Conclusions:** Our study indicated that intravitreal injection of Bevacizumab is successful in maintaining vision and reducing serous retinal detachment in patients with chronic CSC, as evaluated at a 1-year follow-up examination. This study is limited by the few cases and its retrospective nature but it is one of the studies that report 12 month follow up results from intravitreal Bevacizumab for the treatment of CSC.

**Commercial Relationships:** Adam Lewis, None; Marina Syrimi, None; Manju N. Chandran, None; Geeta Menon, NOVARTIS (R), ALLERGAN (R), BAYER (R)

Program Number: 2834 Poster Board Number: B0088
Presentation Time: 8:30 AM - 10:15 AM

**Global Patterns of Fundus Autofluorescence in Stargardt Macular Dystrophy**

*Gad Heilweil, Irena Tsui, Hamid Hosseini, Steven D. Schwartz.*

Ophthalmology, Jules Stein Eye Institute UCLA, Los Angeles, CA.

**Purpose:** To evaluate the different global patterns of fundus autofluorescence in stargardt’s macular dystrophy as seen with ultra-wide-field fundus autofluorescence (UWFAF) imaging.

**Methods:** Patients with SMD who underwent UWAF were included in this retrospective imaging study. Each eye was evaluated for zone of hypoautofluorescence, pattern of hypoautofluorescence, the presence of hyperautofluorescent pisciform flecks, and the presence of isolated peripheral hypoautofluorescence.

**Results:** Sixty-nine eyes of 35 patients were included. Nine (25%) patients were male. The average age of patients was 45 years (range, 10-72 years). Ten (14%) eyes had hypoautofluorescence located in the mid-peripheral zone. Six (9%) eyes had diffuse hypoautofluorescence extending anteriorly. Five (7%) eyes had an isolated nummular (coin shaped) pattern only. Thirty-two (46%) eyes had a confluent nummular pattern only. Thirty (43%) eyes had both individual and confluent nummular patterns. Forty-one (59%) of 69 eyes had pisciform flecks. Eighteen (26%) of 69 eyes from 35 patients had isolated islands of peripheral hypoautofluorescence.

**Conclusions:** Although SMD has been thought of as predominantly a macular dystrophy, we found that 16 (23%) eyes had RPE atrophy extending to the mid-periphery and beyond as detected by hypoautofluorescence on UWAF. Most eyes had individual nummular, confluent nummular, or both nummular patterns of autofluorescence.

**Commercial Relationships:** Gad Heilweil, None; Irena Tsui, None; Hamid Hosseini, None; Steven D. Schwartz, None

Program Number: 2835 Poster Board Number: B0089
Presentation Time: 8:30 AM - 10:15 AM

**Pairwise Genotype/Phenotype Comparison to Predict Severity of ABCA4 Mutations**

*Crandall E. Peeler, Jillian Huang, Sarwar Zahid, Naheed W. Khan, Kari E. Branham, Kanishka T. Jayasundera, John R. Heckenlively.*

Ophthalmology, University of Michigan, Ann Arbor, MI.

**Purpose:** Rates of progression and degree of severity vary widely among patients with a clinical diagnosis of Stargardt disease. We describe several genotypic patterns associated with a more severe clinical course.

**Methods:** A retrospective chart review was performed to identify patients with one or two mutations in ABCA4. Each patient was paired with another who was closest in age. Clinical data - logMAR visual acuity, Goldmann visual field area and scotoma size, and photopic and scotopic B-wave amplitudes - were compared and a point was assigned to the individual with the more severe phenotype in each of the 5 categories. Total accumulated points served as the “clinical severity score” for each member of the pair. Mutation type - nonsense, missense, or frameshift - and affected domain within the ABCA4 protein - nucleotide-binding (NBD), extracellular (ECD), membrane-spanning (MSD), hydrophobic (HD), or intron - associated with the “better” and “worse” clinical severity score were recorded.

**Results:** Twenty-three single and 21 dual mutations pairs (N=88) were analyzed. The average age difference between paired patients was 1.7 years. Among single mutation pairs, a consistently severe phenotype was noted in individuals with NBD mutations. Eight of 9 instances comparing a patient with a NBD mutation to one with a different mutation domain showed the NBD phenotype to be more severe, with the one exception occurring in comparison to a nonsense mutation. In dual-mutation pairs, a severe phenotype was seen in individuals with combination NBD/ECD mutations (worse in 7 of 9 instances, including 2 comparisons to NBD/NBD). Four of 5 cases comparing nonsense mutations to a different mutation type demonstrated a more severe clinical picture in the former, with the one exception seen when the nonsense mutation occurred late in the ABCA4 protein (MSD2).

**Conclusions:** Difficulty in predicting the clinical course of Stargardt disease remains a major obstacle in clinical trial design, complicating the selection of appropriately matched controls. With the promise of gene therapy, finding an accurate method of grouping patients into “mild” and “severe” disease categories has become even more important. Our data suggest that certain genotypic information may serve this purpose, as patients with single NBD mutations, a combination of NBD and ECD mutations, and nonsense mutations were consistently found to have a more severe clinical phenotype.

**Commercial Relationships:** Crandall E. Peeler, None; Jillian Huang, None; Sarwar Zahid, None; Naheed W. Khan, None; Kari E. Branham, Arctic DX (P); Kanishka T. Jayasundera, None; John R. Heckenlively, None

Program Number: 2836 Poster Board Number: B0090
Presentation Time: 8:30 AM - 10:15 AM

**A Longitudinal Analysis of 2008-2010 Medicare Claims Data for newly diagnosed macular holes**

*Sunil K, Srivastava1, Pravin U. Duget2, Kuo Tong2, Andrew J. Layton2, Peter K, Kaiser1, 1Cole Eye Institute, Cleveland Clinic, Cleveland, OH; 2Quorum Consulting, San Francisco, CA; 3Retina Consultants of Arizona, Phoenix, AZ.*

**Purpose:** Macular hole typically cause a significant loss of central vision in patients. Pars plana vitrectomy can successfully repair macular hole in most patients. To this point the costs associated with macular hole treatment including vitrectomy surgery and cataract surgery has not been examined. This study evaluates the medicare claims data to identify the cost to Medicare, excluding Part D for newly diagnosed macular hole patients in a two year timeframe

**Methods:** The 2007-2010 US Medicare 5% SAF Carrier (Part B) data was reviewed in order to identify newly diagnosed macular hole patients in 2008 (index year). Patients were included in the study based on age, Medicare enrollment, and index macular hole diagnosis in 2008. Patients who had a claim for macular hole or vitrectomy in 2007 were excluded. Identified claims were then placed into two groups: Group A if a vitrectomy was performed within four quarters of the diagnosis or Group B if a vitrectomy was not performed. All claims for each patient within 24 months following the index diagnosis were screened for ophthalmic indications, surgeries, and medical services based on CPT and E&M codes. Results were analyzed for incidence and costs associated with follow up services following macular hole diagnosis.

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Results: A total of 1,897 newly diagnosed macular hole patients were identified. 455 (24%) patients had a vitrectomy within one year (Group A). The average allowed charges for ophthalmic services per patient in Group A over two years was $7,702. The average allowed charges per patient in Group B was $1, 850. Within Group A, 8.8% of cases had combination surgery (vitrectomy and cataract surgery), and 14.5% of cases had at least one additional vitrectomy leading to an additional $4,300 in allowed charges. 50% of Group A patients had cataract surgery compared to 15% in Group B.

Conclusions: Only 24% of newly diagnosed macular hole patients in 2008 had a vitrectomy performed within 1 year. On average, those requiring vitrectomy resulted in a mean $5900 greater cost in claims vs those who did not have vitrectomy. Additional vitrectomy was performed in 15% of macular hole surgery cases resulting in additional $4300 in claims. Cataract surgery was performed more often in those treated with vitrectomy than those who did not have vitrectomy performed.

Commercial Relationships: Sunil K. Srivastava, Bausch and Lomb (F), Bausch and Lomb (C), Novartis (F), Allergan (F); Pravin U. Dugel, Abbott (C), Alcon (C), Allergan (C), Artic Dx (C), Aliamera Sciences (C), Acucela (C), Digisight (C), Genentech (C), LUX (C), Macusight (C), Neovista (C), ORA (C), Ophthotech (C), Regeneron (C), Thrombogenics (C); Kuo Tong, Thrombogenics (C); Andrew J. Layton, Thrombogenics, Inc. (C); Peter K. Kaiser, Allegro Ophthalmicals (C), Alcon (C), Novartis (C), Bayer (C), Regeneron (C), Genentech (C), Ophthotech (C)

Support: Thrombogenics Inc.

Program Number: 2837 Poster Board Number: B0091
Presentation Time: 8:30 AM - 10:15 AM
Personalized Medicine: Chloroquine Toxicity in human RPE is Dependent on ARMS2 and HTRA1 Genotypes
Erii H. Tsang, Chyuan-Sheng Lin, Stephen H. Tsang
1Bernard and Shirlee Brown Glaucoma Laboratory, Department of Pathology and Cell Biology, College of Physicians and Surgeons, Columbia University, New York, NY;
2Ophthalmology, Shin Kong Wu Ho-Su hospital & Fu-Jen University, Taipei, Taiwan; 3Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY.

Purpose: Genome-wide association studies (GWAS) and linkage studies identified the CFH (402H allele), ARMS2, and HTRA1 genes as risk factors for RPE pathology. Among Caucasians, 0.5% are double homozygous for the CFH (402H) and T-in/del-A-risk alleles which is similar to incidence of hydroxy-chloroquine retinotoxicity. To test the hypothesis that ARMS2 and HTRA1 genetic risk alleles contribute to hydroxychloroquine retinotoxicity, we treated RPE from genetically stratified human donors with chloroquine (CQ).

Methods: Two human fetal RPE lines double homozygous for the ARMS2-HTRA1 (T-in/del-A) high-risk alleles, and one heterozygous for low-risk (G-Wt-G; T-in/del-A) were isolated. Only donors who carry low AMD risk 402Y haplotypes in the CFH locus were selected. Genotypically characterized RPE cells were exposed to 10 to 1000 nm CQ, and cell death was quantified using EtBr/AO staining. Lysosomes and lipid bodies were stained and observed by confocal microscopy.

Results: CQ-treated RPE with ARMS2-HTRA1 (T-in/del-A) risk alleles showed marked increase in cytosolic vacuoles, an indicator of lysosomal dysfunction. Lipid bodies identified by LipidTOX, and colocalized with LAMP-2, and CQ-dilated lysosomes. The heterozygote low-risk RPE line (G-Wt-G; T-in/del-A) seemed to be more resistant to CQ-toxicity.

Conclusions: Our findings suggest a possible role of ARMS2 and HTRA1 as risk factors in the susceptibility to hydroxy-chloroquine toxicity.

Commercial Relationships: Eric chi-Hsien Peng, None; Yao Li, None; Chyuan-Sheng Lin, None; Stephen H. Tsang, None
Support: None in the Support field.

Program Number: 2838 Poster Board Number: B0092
Presentation Time: 8:30 AM - 10:15 AM
The REPAIR Study: Prospective, Multi-center Trial of ranibizumab in Choroidal Neovascularization due to Pathological Myopia - the 12 month Primary Endpoint
Yit C. Yang
Ophthalmology, Wolverhampton Eye Infirmary, Wolverhampton, United Kingdom.

Purpose: To provide safety and efficacy data in 65 patients treated with ranibizumab for visual impairment due to choroidal neovascularization(CNV) secondary to pathological myopia(PM).

Methods: Phase 2, prospective open label, single arm, multicentre, 12-month study, in eyes with active sub- or juxtapfoveal myopic CNV treated with 1+ pro-re nata (PRN) of IVT 0.5mg ranibizumab.. Retreatment followed a standardized pragmatic algorithm that was primarily driven by OCT morphologic changes indicating active disease. The primary end point was the mean gain in ETDRS letters read from baseline visual acuity at 12 months and the study was adequately powered to detect a 10 or more letter gain.

Results: The mean visual acuity gain of the 65 eyes of 65 patients enrolled was rapid with 8.7 letters gained at month1 increasing to 13.8 letters at month 12 (p<0.001 ) . 95.4% of patients lost less than 8 letters, and 36.9% gained 15 or more letters of visual acuity. Morphological improvements paralleled the visual acuity change with a mean reduction in central retinal thickness on OCT of 135 μm and a reduction in the proportion of eyes with centre involving intraretinal oedema and subretinal fluid from 87.7% to 7.8% and 67.7% to 7.8 % respectively by month 12.. The functional and structural benefits were obtained by a low number of injections to month 12 (mean 3.6, median 3) with 21% patients requiring only the one baseline treatment. No new safety concerns were identified and no retinal detachments occurred during the study.

Conclusions: Ranibizumab treatment for myopic CNV using a simple, predominantly OCT driven retreatment algorithm, improves visual acuity on average at 12 months, with low rates of serious ocular adverse events.

Commercial Relationships: Yit C. Yang, Novartis (R)
Support: Novartis UK support

Program Number: 2839 Poster Board Number: B0093
Presentation Time: 8:30 AM - 10:15 AM
Assessing Photoreceptor Structure Following Macular Hole Closure
Sean Batson, Sean Hansen, Peter A. Karth, Robert F. Cooper, Drew H. Scoles, David V. Weinberg, Alfredo Dubra, Judy E. Kim, Joseph Carroll, William Wiortksko. Ophthalmology, Medical College of Wisconsin, Milwaukee, WI.

Purpose: To assess foveal photoreceptor structure in eyes that have undergone vitrectomy surgery for closure of macular holes (MH) using spectral-domain optical coherence tomography (SD-OCT) and adaptive optics scanning light ophthalmoscopy (AOSLO).

Methods: In a prospective case series, 7 eyes of 7 patients were imaged with SD-OCT on an average 4.5 months (range, 2-6) after undergoing pars plana vitrectomy, internal limiting membrane peeling, and gas injection for closure of idiopathic MH. A subset of 4 eyes also underwent simultaneous imaging with AO-SLO, with one of these eyes imaged a second time 12 months after surgery.

Results: Abnormalities of the ellipsoid portion of the inner segment...
(ISe) band can be seen near the fovea with SD-OCT, including focal disruption, attenuation, and diffuse mottling. Areas of ISe abnormalities correspond to hyporeflective areas observed on AOSLO. Areas of hyporeflective mosaic disruption can be as small as 100 microns, and may decrease in size between 3 months and 12 months after surgery without “shifting” of the cone mosaic (see Figure 1). Hyper-reflective external limiting membrane structures were also seen with SD-OCT and AOSLO overlying focal ISe lesions.

**Conclusions:** Abnormalities of the ISe can be seen with SD-OCT following surgical closure of MH. These changes correspond with hyporeflective areas of cone mosaic disruption on AOSLO. Areas of hyporeflective cone mosaic disruption on AOSLO may decrease in size over time. SD-OCT and AOSLO imaging may be a useful modality to detect and monitor recovery of photoreceptor structure in eyes undergoing surgical closure of MH.

**Fig. 1**

**Commercial Relationships:** Sean Batson, None; Sean Hansen, None; Peter A. Karth, None; Robert F. Cooper, None; Drew H. Scoles, None; David V. Weinberg, Regeneron (F); Alfredo Dubra, US Patent No: 8,226,236 (P); Judy E. Kim, None; Joseph Carroll, Imagine Eyes, Inc. (S); William Wirostko, None

**Support:** Research to Prevent Blindness, Inc.; Thomas M. Aaberg, Sr, Retina Research Fund; Alcon Research Institute; NIH RR016511, P30001931, R01017607

315 Retinal Detachment I

**Tuesday, May 07, 2013 8:30 AM-10:15 AM**

**Exhibit Hall Poster Session**

**Program #/Board # Range:** 2840-2878/B0149-B0187

**Organizing Section:** Retina

**Program Number:** 2840 **Poster Board Number:** B0149

**Presentation Time:** 8:30 AM - 10:15 AM

**Outcomes of 25-Gauge Vitrectomy with Relaxing Retinectomy for Retinal Detachment with Severe Proliferative Vitreoretinopathy**

Vikram Setlur, Jennifer I. Lim. Ophthalmology, University of Illinois at Chicago, Chicago, IL.

**Purpose:** To analyze the efficacy of relaxing retinectomies using 25-gauge instrumentation for repair of severe proliferative vitreoretinopathy retinal detachments.

**Methods:** We performed a retrospective case review of all vitreoretinal operations performed by a single surgeon from January 2007 through October 2012 to identify eyes that underwent pars plana vitrectomy with relaxing retinectomy for repair of retinal detachment with advanced proliferative vitreoretinopathy (PVR) fibrous proliferation. Patient demographics, visual acuity, and anatomic outcomes were recorded from the medical record. Only patients with a minimum of follow up of 3 months were included.

**Results:** Seventeen eyes of 17 patients met the above criteria. The etiology of the fibrous proliferation was primary rhegmatogenous retinal detachment in 8 patients, trauma in 3 patients, infection in 2 patients, proliferative diabetic retinopathy in 3 patients, and sarcoid uveitis in 1 patient. Final anatomical success was achieved in 94.1% (16/17) of patients. Silicone oil was used for tamponade in 16 out of 17 patients, and one patient received perfluoropropane (C3F8) gas tamponade. The average retinectomy encompassed 5.3 clock hours. Nine patients were successfully reattached after one procedure. Eight patients re-detached after their initial retinectomy surgery. Of these, seven patients were re-attached with an average of 2.0 additional surgeries (including vitrectomy for silicone oil removal). One remained detached at his last follow-up visit. Visual acuity was maintained or improved in 82.4% (14/17) of patients. Average logarithm of the minimum angle of resolution (logMAR) visual acuity improved from 2.2 prior to surgery to 1.8 after surgery (p = 0.2237). Complications included epithelial downgrowth requiring 5-fluorouracil injection (1 patient with penetrating trauma), hypotony (3 patients), epiretinal membrane requiring repeat vitrectomy (2 patients), and no light perception vision (2 patients).

**Conclusions:** 25-gauge vitrectomy with relaxing retinectomy is an effective procedure for retinal detachments complicated by severe fibrous proliferation. The high rates of anatomic success and visual preservation suggest surgical intervention may be indicated in eyes that would otherwise be deemed inoperable.

**Commercial Relationships:** Vikram Setlur, None; Jennifer I. Lim, QLT (F), Genentech (R), Regeneron (R)

**Program Number:** 2841 **Poster Board Number:** B0150

**Presentation Time:** 8:30 AM - 10:15 AM

**Giant Retinal Tear Associated Retinal Detachment After Pars Plana Vitrectomy: Surgical Techniques and Outcomes**

Marco A. Gonzalez1, 2, Harry W. Flynn1, 2, Paul Tenzel1.

1Ophthalmology, Bascom Palmer Eye Institute, Miami, FL; 2University of Miami, Miami, FL.

**Purpose:** To evaluate incidence, surgical techniques, and outcomes for patients with giant retinal tear (GRT) associated retinal detachment (RD) that had undergone previous pars plana vitrectomy (PPV).

**Methods:** This is a non-comparative consecutive case series from January 2005 through July 2010. Patients with a preceding pars plana vitrectomy undergoing retinal reattachment surgery at Bascom Palmer Eye Institute in the presence of giant retinal tears were identified. Data was collected on demographics, clinical features, surgical techniques, anatomic success and visual outcomes.

**Results:** 227 cases of ICD-9 coded GRTs were identified. A total of 9 eyes in 9 patients were identified as having had preceding PPV for non-RD related pathology. The mean age was 42.1 years (range of 10 to 79). The mean time between PPV and diagnosis of giant retinal tear was 2.3 months. The mean follow up after RD surgery was 30.1 months. Presenting visual acuity was 20/400 or better in 5 of 9 patients (56%). All patients underwent repeat PPV with either gas or oil tamponade. 8 patients (89%) underwent scleral buckle procedure. 4 patients (44%) had perfluorocarbon use during reattachment.

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surgery. Visual acuity improved to 20/400 or better in 6 patients (67%). 8 of 9 patients (89%) achieved anatomic success at the last follow up examination.

Conclusions: Giant retinal tears are an uncommon complication of PPV. The majority of patients underwent combined pars plana vitrectomy and scleral buckle procedure. Patients presenting with giant retinal tear associated RD after previous PPV undergoing additional surgery achieved high rates of anatomic and visual success.

Commercial Relationships: Marco A. Gonzalez, None; Harry W. Flynn, None; Paul Tenzel, None

Program Number: 2842 Poster Board Number: B0151
Presentation Time: 8:30 AM - 10:15 AM
Symptomatic Posterior Vitreous Detachment: The predictive value of the posterior hyaloid face and symptomatology
Christiane I. Falkner-Radler1, Minhee Cho2, Alexandra Garf3, Anton Orlin4, R.V. Paul Chan5, Szilard Kiss6, Donald J. D’Amico7, Susanne Binder1, 1Ophthalmology, The Ludwig Boltzmann Institute of Retinology and Biomicroscopic Laser surgery, Rudolf Foundation Clinic, Vienna, Austria; 2Ophthalmology, Weill Cornell Medical College and New York-Presbyterian Hospital, New York, NY; 3Medical Statistics, Center for Medical Statistics, Informatics and Intelligent Systems, Medical University of Vienna, Vienna, Austria.

Purpose: To evaluate relationships between acute onset posterior vitreous detachment (PVD) symptoms, stages of PVD, and retinal complications in a prospective bicenter trial.

Methods: Patients presenting with acute onset of PVD symptoms like “floaters” (group 1), “flashes of light” (group 2), or “floaters and flashes of light” (group 3), who were examined at one of the two study centers [Rudolf Foundation Clinic, Vienna (center 1) and the Weill Cornell Medical College, New York City (center2)] were included in the study. The condition of the posterior hyaloid face was assessed using spectral-domain optical coherence tomography (SD-OCT). Co-factors analyzed included best-corrected distance and near visual acuity (BCVA), sex, age, status of the lens (phakic, pseudophakic), refractive status (emmetropic, hyperopic, myopic), previous cataract and refractive surgery, the presence of vitreous pigment, vitreous hemorrhage, lattice degeneration, retinal tears and/or retinal detachment, positive family or personal history, one or both eyes affected. Correlations between the 3 clinical symptom groups, stages of PVD and the occurrence of retinal complications and the other co-factors were evaluated using a regression model.

Results: Up to now, 106 patients (56 patients in group 1, 22 patients in group 2 and 28 patients in group 3) have been included. Eighteen % of patients showed no PVD, 43% to 57% of patients an incomplete foveal and/or optic PVD, and 25% to 39% of patients a complete PVD. Therease findings were not significantly different (p<0.56) between the 3 groups. A significant difference between the groups were found for the presence of vitreous syneresis (70% in group 1, 86% in group 2 and 93% in group 3; p<0.03). In addition, the occurrence of lattice degeneration was significantly different between the groups (4% in group 1, 27% in group 2 and 14% in group 3; p<0.01). No significant differences were found for retinal tears (p=0.05) and the other co-factors. However, retinal tears occurred more often in group 3.

Conclusions: In the majority of patients with acute onset PVD symptoms the posterior hyaloid face is incompletely or fully detached. However, in this preliminary series it was not possible to identify patients at risk for developing retinal complications.

Commercial Relationships: Christiane I. Falkner-Radler, None; Minhee Cho, None; Alexandra Garf, None; Anton Orlin, None; R.V. Paul Chan, None; Szilard Kiss, Alcon (F), Alimera (F), Alimera (C), Alimera (R), Allergan (F), Allergan (C), Allergan (R), Genentech (F), Genentech (C), Genentech (R), Allergan (R), Genentech (F), Genentech (C), Genentech (R), Regeneron (F), Regeneron (C), Regeneron (R), Optos (F), Optos (C), Optos (R), Eytech (C), Merge/OIS (C), Merge/OIS (I); Donald J. D’Amico, Ophthotech, Inc (I), OptiMedica, Inc (I), Neurotech, Inc (I), Genentech, Inc (C), Lux Biosciences, Inc (C); Susanne Binder, None

Program Number: 2843 Poster Board Number: B0152
Presentation Time: 8:30 AM - 10:15 AM
Change in subfoveal choroidal thickness following semental scleral buckling with or without cryotherapy for rhegmatogenous retinal detachment

Purpose: To report the morphologic changes of the subfoveal choroidal thickness using spectral domain optical coherence tomography following segmental scleral buckling.

Methods: The study included 21 eyes of 20 patients who underwent segmental scleral buckling and cryotherapy and 8 eyes of 7 patients who underwent segmental scleral buckling without cryotherapy for the treatment of rhegmatogenous retinal detachment. All patients underwent the measurements of the subfoveal choroidal thickness preoperatively and 1 week, 1 month and 3 months postoperatively.

Results: The mean subfoveal choroidal thickness of operated eyes with cryotherapy measured preoperatively and at 1 week, 1 month and 3 months postoperatively were 239.2 ± 91.0μm, 267.6 ± 96.8μm, 250.6 ± 95.8μm and 239.4 ± 95.6μm, respectively. There were significant differences between subfoveal choroidal thicknesses preoperatively and 1 week and 1 month postoperatively (p<0.01, p=0.03, ANOVA), and there was no significant difference between subfoveal choroidal thicknesses preoperatively and 3 months postoperatively (p=1.0, ANOVA). The mean subfoveal choroidal thickness of operated eyes without cryotherapy measured preoperatively and at 1 week, 1 month and 3 months postoperatively were 258.1 ± 80.4μm, 280.7 ± 77.3μm, 265.0 ± 72.6μm and 255.0 ± 78.5μm, respectively. There were significant differences between subfoveal choroidal thicknesses preoperatively and 1 week postoperatively (p=0.008, repeated ANOVA), and there was no significant difference between subfoveal choroidal thicknesses preoperatively and 1 month and 3 months postoperatively (p=0.688 and p=0.957, repeated ANOVA).

Conclusions: The subfoveal choroidal thickness may change temporarily following segmental scleral buckling surgery regardless of whether the cryotherapy is used. This may be the result of reversible subclinical microcirculatory dysfunction of the choroid.

Commercial Relationships: Masayo Kimura, None; Akira Nishimura, None; Hideaki Yokogawa, None; Tetsuhioko Okuda, None; Tomomi Higashide, None; Michiharu Shimizu, None; Kazuhisa Sugiyama, None

Support: JSPS KAKENHI 2931045-00

Program Number: 2844 Poster Board Number: B0153
Presentation Time: 8:30 AM - 10:15 AM
Intravitreal gas injection without vitrectomy for macular detachment associated with an optic disc pit
Hideo Akiyama, Shoji Kishi, Ophthalmology, Gunma university, Maebashi, Japan.

Purpose: To evaluate the clinical outcomes after gas tamponade without vitrectomy for retinal detachment associated with an optic disc pit using optical coherence tomography (OCT).

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Methods: Intravitreal gas injection was performed on 8 consecutive patients (mean age, 35.0 years; range, 15 to 74 years) with unilateral macular detachment associated with an optic disc pit. An injection of 100% SF6 gas, whose volume was 0.3cc, was carried out without anterior chamber tapped. Patients treated with gas injection were instructed to remain face-down for 5 days.

Results: Complete retinal reattachment after only gas tamponade was achieved in 4 out of 8 eyes. The mean number of gas injections was 1.8. The mean best-corrected visual acuity before and after the treatment with gas was 0.28 and 1.02, respectively. The period required for reattachment after final treatment of gas was 12 months. There were no incidences of recurrence after complete reattachment by gas tamponade in any cases during follow-up over an average of 94 months (range, 64 to 132 months).

Conclusions: Gas tamponade seems to be an effective alternative method for macular detachment associated with an optic disc pit, although the mechanisms of optic disc pit maculopathy are still unknown.

Commercial Relationships: Hideo Akiyama, None; Shoji Kishi, None

Program Number: 2845 Poster Board Number: B0154
Presentation Time: 8:30 AM - 10:15 AM

Activation of Rho GTPases after Retinal Detachment
Jianfeng Wang1, Weiwei Wang2, Ellen Townes-Anderson1,2
1Neurology and Neurosciences, New Jersey Medical School, UMDNJ, Newark, NJ; 2Graduate School of Biomedical Sciences, UMDNJ, Newark, NJ.

Purpose: Rho GTPases function as intracellular switches integrating signals from the extracellular environment and play critical roles in morphological neuroplasticity. We have shown that blocking RhoA or Rho kinase (ROCK) activity can prevent rod photoreceptor axon terminal retraction after retinal detachment, indicating treatments that manipulate RhoA signaling may promote synaptic stability (Fontainhas and Townes-Anderson, IOVS, 2011). In the present work, we focus on the time course of changes in the activities of the Rho GTPases after detachment.

Methods: Neural retinas were detached from porcine eyes, cultured in serum-free medium for up to 24 hrs, and then frozen and lysed for activity assays and western blot analysis. RhoA activation was determined with a Rhotekin binding assay, while Rac1 and Cdc42 activations were determined with a p21 activated kinase 1 (PAK) binding assay. Determinations were repeated in more than one animal.

Results: Activation of Rho GTPases was compared to control, attached retina from the same eye. RhoA was activated quickly, within 1 min after detachment, rose several fold by 2 hrs, in some cases, and remained activated after 24 hours in vitro albeit at a lower level. Both Rac1 and Cdc42 activities were transiently decreased 1 min after detachment; then Rac1 activity gradually recovered to a level higher than that of attached retina, while Cdc42 activity was up-regulated by 2 hrs and then decreased to a level lower than control. Phosphorylated cofilin, regulated by LIM kinase (LIMK), a down stream effector of both RhoA and Rac, was steadily and significantly increased over 24 hrs. Other protein levels also changed: 1) phosphorylated CREB increased immediately but decreased to normal levels 2 hrs after detachment; whereas 2) the level of PKCa was down-regulated; and 3) GFAP was up-regulated at 24 hrs. These changes at 24 hrs could be prevented by the ROCK inhibitor Y27632.

Conclusions: Rac1, Cdc42 and the downstream LIMK activities are all changed 24 hrs after detachment, a time co-incident with active rod cell axon retraction. Thus, in addition to RhoA, other elements of the Rho pathways appear to play a role in the plasticity of the photoreceptor synapse. Understanding the time course of Rho GTPase activities will help in devising effective therapies to preserve the morphology of the outer plexiform layer and normal protein expression after retinal detachment.

Commercial Relationships: Jianfeng Wang, None; Weiwei Wang, None; Ellen Townes-Anderson, None
Support: NIH Grant EY021542

Program Number: 2846 Poster Board Number: B0155
Presentation Time: 8:30 AM - 10:15 AM

Strategy for the Management of Complex Retinal Detachments
The European Vitreo-Retinal Society Retinal Detachment Study
Aaron Parnes1, Didier Ducournau2, Jack O. Sipperley3, Ron A. Adelman1
1Ophthalmology, Yale University, New Haven, CT; 2Retinal Consultants of Arizona, Phoenix, AZ; 3Clinique Sourdille, Nantes, France.

Purpose: To study the outcome of the treatment of complex rhegmatogenous retinal detachments.

Methods: In this non-randomized, multi-center retrospective study, 176 surgeons from 48 countries spanning 5 continents provided information regarding the primary procedures for 7,678 rhegmatogenous retinal detachments. Reported data included clinical manifestations, the method of repair, and the outcome following treatment.

Results: The main categories of complex retinal detachments evaluated in this investigation are those associated with: 1) Grade B PVR (n = 917), 2) Grade C-1 PVR (n = 637), 3) choroidal detachment or significant hypotony (n = 578), 4) large or giant retinal tears (n = 1,167), and 5) macular hole detachments (n = 153). In detachments with Grade B PVR, the final failure rate was higher when treated with a scleral buckle alone versus vitrectomy (p=0.0017). In cases with Grade C-1 PVR, there was no statistically significant difference in the final failure rate between those treated with vitrectomy, with or without scleral buckle, and those treated with scleral buckle alone (p = 0.7). Those that received vitrectomy with a supplemental buckle had an increased failure rate compared to those that did not receive a buckle (p = 0.007). There was no statistically significant difference in final failure rate between tamponade with gas versus silicone oil in patients with Grade B or C1 PVR. Cases with choroidal detachment or hypotony treated with vitrectomy had a significantly lower failure rate versus treatment with scleral buckle alone (p = 0.0015). Cases with large or giant retinal tears treated with vitrectomy also had a significantly lower failure rate versus treatment with scleral buckle (p = 7 x 10^-8).

Conclusions: In patients with retinal detachment, when choroidal detachment, hypotony, a large tear, or a giant tear is present, vitrectomy is the procedure of choice. In retinal detachments with PVR, tamponade with either gas or silicone oil can be considered. If vitrectomy is to be performed, this data suggests that a supplemental buckle may not be helpful.

Commercial Relationships: Aaron Parnes, None; Didier Ducournau, None; Jack O. Sipperley, None; Ron A. Adelman, None

Program Number: 2847 Poster Board Number: B0156
Presentation Time: 8:30 AM - 10:15 AM

Management and Outcomes of Bilateral Simultaneous Rhegmatogenous Retinal Detachments
Mital Mehta1, Robert A. Sisk1, Christopher D. Riemann1
1Retina, New York Eye & Ear Infirmary, New York, NY; 2Ophthalmology, University of Cincinnati, Cincinnati, OH.

Purpose: To describe a series of patients with bilateral simultaneous rhegmatogenous retinal detachment (BSRRD), and their surgical

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management.

**Methods:** IRB approved, retrospective chart review of all adult patients who presented to the Cincinnati Eye Institute with BSRRD between 1989 and 2006 requiring surgical management without prior retinal detachment (RD) or history of ruptured globe. Thirty-three patients (66 eyes) met the inclusion criteria and underwent surgical repair. Eyes amenable to laser treatment alone were excluded. Snellen visual acuity was converted to LogMAR for statistical analysis.

**Results:** There were 12 patients (with 24 eyes) who were younger than 40 years old, 11 of those 24 eyes (46%) had atrophic holes as cause of RD, 20 of 24 had lattice degeneration, 22 of 24 had no posterior vitreous detachment (PVD) at presentation. In the 42 eyes of patients over 40 years of age, 20 of them had retinal tears as the cause of the detachment. Of our 33 patients, 15 had both maculae spared, 8 had both maculae involved in the detachment, and 10 had one eye in which the RD involved the macula and one eye did not. We achieved primary anatomical reattachment in 97% of eyes. Eight eyes had recurrent detachment, 6 (9.1%) of which required reoperation. There was a statistically insignificant difference in the postoperative visual acuity between the first and second operated eyes (0.18 1st eye, 0.45 2nd eye with p = 0.059).

**Conclusions:** RD in the absence of a specific initiating event may represent a less progressive process, in contrast to the rapid progression of RD resulting from an acute PVD. In the absence of PVD and in eyes with evidence of chronicity to the RD, RD progressed slowly and allowed repair of the eye with the detached macula first without further visual compromise to the second eye. This may warrant a change in the paradigm of surgical management of BSRRD.

**Commercial Relationships:** Mitul Mehta, None; Robert A. Sisk, None; Christopher D. Riemann, None

**Program Number:** 2849 Poster Board Number: B0157

**Presentation Time:** 8:30 AM - 10:15 AM

The efficacy and safety of prophylactic cryotherapy in preventing retinal detachment in type 1 Stickler syndrome

**Purpose:** To evaluate the efficacy and safety of 360° prophylactic cryotherapy (360PC) according to a standardized protocol and rationale in preventing retinal detachment (RD) in type 1 Stickler syndrome patients.

**Methods:** A retrospective cohort study. Four hundred and eighty seven type 1 Stickler syndrome patients with both eyes available for study were allocated to a prophylaxis group according to a standardized protocol and rationale according to a control group (no 360PC), or a mixed group (unilateral RD with subsequent unilateral 360PC) and compared to a control group (unilateral or bilateral RDs with no 360PC) by adjusted multivariable Cox regression and age-matching analyses. All eyes from all patients were also analysed individually to compare the risk of RD with and without prophylaxis, in addition to randomly selecting one eye from each patient for repeated comparison. The main outcome measures were time to RD (including failure of 360PC requiring retinopexy with or without surgery) and side effects resulting from prophylactic treatment.

**Results:** The control group (n=194) had a greater than seven-fold increased risk of RD compared to the prophylaxis group (n=229) (hazard ratio [HR] = 2.8; 95% confidence interval [CI]: 4.5 - 12.1), with the age-matched control group (n=165) having a five-fold increased risk compared to the age-matched prophylaxis group (n=165) (HR = 5.0; 95% CI: 2.8 - 8.8). Similarly, the mixed-control group (n=104) had a greater than ten-fold increased risk of RD compared to the mixed group (n=64) (HR = 10.3; 95% CI: 5.0 - 21.4), with the age-matched mixed-control group (n=39) having a greater than eight-fold increased risk compared to the age-matched mixed group (n=39) (HR = 8.4; 95% CI: 3.3 - 21.6). Analysis of all individually analysed eyes that received no prophylaxis (n=452) indicated a greater than eleven-fold increased risk of RD compared to those that received 360PC (n=522) (HR = 11.7; 95% CI: 7.9 - 17.2), with a greater than fifteen-fold increased risk calculated when one eye from each patient was randomly selected (HR = 15.4; 95% CI 8.1 - 29.3). Reported side effects from prophylactic treatment were minor and short-lived.

**Conclusions:** All analyses indicate that prophylactic retinopexy delivered according to this standardized protocol is safe and markedly reduces the risk of retinal detachment in type 1 Stickler syndrome.

**Commercial Relationships:** Gregory S. Fincham, None; Laura Pasea, None; Christopher Carroll, None; Annie M. McNinch, None; Arabella V. Poulson, None; Allan J. Richards, None; John D. Scott, None; Martin P. Sneed, None

**Program Number:** 2849 Poster Board Number: B0158

**Presentation Time:** 8:30 AM - 10:15 AM

Ranibizumab is a potential prophylaxis for proliferative vitreoretinopathy, a non-angiogenic blinding disease

**Purpose:** Proliferative vitreoretinopathy (PVR) is an example of a disease that is difficult to predict, lacks effective treatment options, and substantially reduces an individual’s quality of life. It is the primary reason that surgery to correct rhegmatogenous retinal detachment fails. Likely mediators of PVR are growth factors in vitreous, which stimulate cells within and behind the retina as an inevitable consequence of a breached retina. We sought to determine whether ranibizumab (RBZ), an anti-VEGF-A monoclonal antibody fragment, could reduce the pathogenic bioactivity of vitreous from patients and experimental animals with PVR, and whether it could protect rabbits from developing this disease.

**Methods:** Using cultured cells, the bioactivity of vitreous from animals and patients with PVR was assessed biochemically (by western analysis, neutralization and dose-response assays), molecularly (by knock-down experiments), and biologically (by contraction and survival assays) of cultured cells. In rabbits, experimental PVR was induced by intravitreal injection of fibroblasts.

**Results:** RBZ, one of the clinically approved agents that neutralizes VEGF-A, reduced the bioactivity of vitreous from patients and experimental animals with PVR, and protected rabbits from
developing disease. The mechanism of action of RBZ involved repressing PDGFs, which at the concentrations present in PVR vitreous, inhibited non-PDGF-mediated activation of PDGF-Rs. Moreover, the ratio of VEGF-A/PDGF correlated with clinical PVR.

Conclusions: These pre-clinical findings suggest that currently available approaches to neutralize VEGF-A are prophylactic for PVR, and that anti-VEGF-based therapies may be effective for managing more than angiogenesis- and edema-driven pathological conditions.

Commercial Relationships: Steven Pennock, None; David Kim, None; Shizuo Mukai, None; Matthew Kuhnle, None; Dal Chun, None; Joanne A. Matsubara, None; Jing Z. Cui, None; Patrick E. Ma, novartis (R), baush & lomb (R), allergan (R); David Maberley, None; Andrius Kazlauskas, None

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Program Number: 2850 Poster Board Number: B0159

Presentation Time: 8:30 AM - 10:15 AM

The usefulness of internal limiting membrane peeling to prevent macular pucker formation for regmatogenous retinal detachment without foveal detachment

Masanori Miyazaki, Tatsuro Ishibashi. Kyushu University, Fukuoka, Japan.

Purpose: To investigate the merits of internal limiting membrane (ILM) peeling for regmatogenous retinal detachment (RRD) without foveal detachment preventing macular pucker formation.

Methods: We conducted retrospective chart review on 41 patients who underwent primary pars plana vitrectomy (PPV) due to RRD without foveal detachment at Kyushu University Hospital between January 1, 2006 and June 30, 2010. Patients with a history of retinal surgery or another visually significant ocular condition were excluded. 19 patients underwent PPV with Brilliant Blue G (BBG)-assisted ILM peeling, and 22 patients without ILM peeling. We measured the occurring incidence of macular pucker at each group at least one year follow-up. Best-corrected visual acuity (BCVA), macular sensitivity (MS) on Humphrey Field Analyzer, and central foveal thickness (CFT) by optical coherence tomography (OCT) at post-operative 6 months were also measured.

Results: BCVA, MS, and CFT were not statistically different at each group. The incidence of macular pucker formation was 0%(0/19) with ILM peeling, and 9.1%(2/22) without ILM peeling. The 2 groups showed a peak of TUNEL positivity at day 1. ONL thickness was significantly decreased in the ΔCS group (P=0.009). Western blot analysis showed significantly higher levels of cleaved caspase-3 and 3 in the ΔCS mice, however, cleaved caspase-9 was almost the same in both groups. Furthermore, interleukin (IL)-6 and monocoyte chemoattractant protein (MCP)-1 were significantly higher in the ΔCS group (P<0.001 and P=0.001, respectively). In addition, the macrophages/microglia detected in that same group were significantly more (P=0.045).

Conclusions: These findings demonstrate that mFasL plays a critical role in the photoreceptor cell death after RD, suggesting that FasL cleavage is an important mechanism for limiting the neurotoxic effect of FasL in the retina.

Commercial Relationships: Hidetaka Matsumoto, None; Yusuke Murakami, None; Dimosthenis Mantopoulos, None; George Trichonas, MEEI-Patient Application U.S. Serial No. 61/327,476 “Combination Therapy for Preserving photoreceptor cell viability following retinal detachment” (P); Joan W. Miller, Massachusetts Eye and Ear Infirmary (P), Novartis (I), Alcon (C), KailVista Pharmaceuticals (C); Meredith S. Gregory-Ksander, None; Bruce R. Ksander, None; Demetrios Vavvas, MEEI (P), Kala pharmaceuticals (C), Roche (C), Genentech (C)

Program Number: 2852 Poster Board Number: B0161

Presentation Time: 8:30 AM - 10:15 AM

Effects of low-dose isotretinoin on rates of recurrent retinal detachment secondary to proliferative vitreoretinopathy
Francis C. DeCroos, Michael Dollin, Nikolos J. London, Lisa Maiale, Philip P. Storey, Jason Hsu, James Vander, Carl D. Regillo, Retina, Wills Eye Institute, Philadelphia, PA; Retina Consultant San Diego, San Diego, CA.

Purpose: To evaluate the effect of low-dose oral isotretinoin on recurrent retinal detachment (RD) secondary to proliferative vitreoretinopathy (PVR).

Methods: This prospective, non-randomized, open label trial studied administration of 20 mg isotretinoin daily for 12 consecutive weeks to patients following RD repair. Patients were subdivided into 2 groups: (1) recurrent RD with PVR and (2) primary RD at high risk for recurrent PVR RD. Risk factors included pre-operative grade B or worse PVR, retinal break larger than 3 disk diameters, retinal detachment greater than 2 quadrants, retinal detachment longer than 1 month without intervention, and vitreous hemorrhage. Simultaneous to enrollment in the treatment arm, an age-matched and pathology-matched cohort was identified and treated by the same group of surgeons to serve as the control arm.

Results: In the recurrent RD with PVR group, fifty-six patients received isotretinoin and 47 patients did not. With at least 3 months...
of follow-up, the surgical success rate with a single intervention was 70% in patients on isotretinoin versus 70% in the controls (Fisher Exact Test, two tailed p = 1.00). In the primary RD group at high risk for recurrent PVR RD group, fifty patients received isotretinoin and 57 patients did not. In this arm, the surgical success rate with a single intervention was 80% in patients on isotretinoin versus 56% in the controls (p = 0.0128). The side effects of the medication have been generally mild. However, one patient had a substantial sustained increase in transaminases.

**Conclusions:** In patients with recurrent RD secondary to PVR, low dose isotretinoin does not reduce rates of re-detachment. Low dose isotretinoin may reduce rates of secondary PVR detachment in patients with primary RD at high risk for developing recurrent PVR detachment.

**Commercial Relationships:** Francis C. DeCroos, None; Michael Dollin, None; Nikolas J. London, None; Lisa Maiale, None; Philip P. Storey, None; Jason Hsu, None; James Vander, None; Carl D. Regillo, Genentech (C), Regeneron (C), Alcon (C), Thrombogenicins (F), GSK (F), ACT (F)

**Clinical Trial:** NCT01445028

**Program Number:** 2853 **Poster Board Number:** B0162

**Presentation Time:** 8:30 AM - 10:15 AM

**Complete prevention of retinal detachment using prophylactic intraoperative septated circumferential barrier laser during macular surgery: long-term follow-up results**

**Jane-Gone Kim, Hyun Seung Yang.** Ophthalmology, Asan Medical Center, Seoul, Republic of Korea.

**Purpose:** To investigate the efficacy and safety of using a prophylactic intraoperative septated circumferential barrier laser (SCBL) to prevent retinal detachment (RD) after complete phacovitrectomy.

**Methods:** Four hundred and seventy-eight consecutive patients who underwent a phacovitrectomy between 2004 and 2011 to treat cataract combined epiretinal membrane (ERM) and macular hole (MH) using 20G, 23G and 25G conventional vitrectomy system were analyzed retrospectively. Patients who were under 50 years old and had a history of severe diabetic retinopathy, glaucoma, high myopia, severe ocular disease, uveitis, previous laser treatment, any kind of intraocular injection and a posterior capsular tear during the surgery excluded. Three hundred and four patients received SCBL (group 1) and 174 patients did not (group 2). In the SCBL procedure, one or two rows of circumferential moderate intensity burns were placed anteriorly to the equator with a subsequent 5-6 septate laser burns made from the circumferential laser marks to the anterior vitreous base perpendicularly at intervals of about 60 degrees (Fig. 1).

**Results:** The average age was 69.9 years and the minimum follow-up period was 12 months (average: 35.9 months). The average axial length and spherical equivalent were 23.9 mm and -0.45D, respectively. The SCBL procedure required an additional 213±21.2 seconds. SCBL was associated with a significant reduction of RD (from 1.7% in group 2 to 0% in group 1; P=0.048). Postoperative complications related to SCBL such as anatomical failure in MH, macular edema and ERM were not significantly different between the two groups (P=0.67, P=0.83, and P=0.81, respectively) at 1 year follow up.

**Conclusions:** Prophylactic intraoperative SCBL produces a significant benefit by preventing postoperative RD without any significant complications in ERM and MH surgery.

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Program Number: 2855 Poster Board Number: B0164
Presentation Time: 8:30 AM - 10:15 AM
Intraocular pressure abnormalities following silicone oil injection for complicated retinal detachments
Hiroaki Ozaki, Jane Y. Huang, Eiichi Uchio. Ophthalmology, Fukuoka Univ Sch of Medicine, Jyonan-ku, Japan.
Purpose: Intravitreal silicone oil (SO) is used as a tamponade in the management of complicated retinal detachments. Known complications of SO are an increasing intraocular pressure (IOP), secondary glaucoma and hypotony. We have investigated the incidence and character of IOP abnormalities after pars plana vitrectomy with SO for complicated retinal detachments.
Methods: Medical records of 200 eyes of 195 patients who underwent pars plana vitrectomy combined with SO for the management of complicated retinal detachment between January 2000 and December 2011 at Fukuoka University Hospital were reviewed. The study included 132 men and 63 women. The average age was 47.9±19.2 years old. The average period of SO tamponade was 7.4±13.3 months, ranging from 0.5 to 84 months. Retinal detachment was due to proliferative vitreoretinopathy in 120 eyes, proliferative diabetic retinopathy in 20 eyes, and others including acute retina necrosis and ocular injury in 60 eyes. Patients with a history of glaucoma, retinopathy of prematurity, acute-onset IOP elevation within 7 days of SO injection were excluded. Hypotony was defined as IOP less than 5 mmHg. Elevated IOP was defined as 3 consecutive measurements of elevated IOP greater than 21 mmHg.
Results: The average IOP was 10.7±4.5 mmHg before the injection of SO. In 23 patients, IOP remained high after removal of SO in 36.8%.
Conclusions: SO tamponade induced hypotony in 11.5% and elevation of IOP in 10.5%. IOP was normalized after removal of SO in 63.2% of cases. IOP remained high after removal of SO in 36.8%. Emulsification of SO was a risk factor for persistent high IOP after removal of SO.
Commercial Relationships: None, None, None

Program Number: 2856 Poster Board Number: B0165
Presentation Time: 8:30 AM - 10:15 AM
Risk of intraoperative retinal tears and recurrent rhegmatogenous retinal detachment in eyes with previous retinal detachment undergoing pars plana vitrectomy
Ravi S. Singh1, Douglas J. Covert2, Dennis P. Han1. 1Ophthalmology, Eye Institute at Medical College of Wisconsin, Milwaukee, WI; 2Associated Retina Consultants, Traverse City, MI.
Purpose: Pars plana vitrectomy (PPV) is associated with risk of intraoperative retinal tears (RT) and post-operative rhegmatogenous retinal detachment (RRD). In eyes with previous RRD repair, the risks of these events are not well documented. In the present study we evaluated eyes with previous RRD repair undergoing PPV for macular epiretinal membranes (ERM) or macular holes (MH), and compared them to eyes without prior RRD. We also assessed the effect of the previous surgical interventions on this risk.
Methods: An IRB approved, retrospective review was performed on a consecutive series of eyes undergoing PPV for MH or macular ERM from January 1, 2003, through December 31, 2009. From these cases that had undergone prior RRD repair were selected for this study. The variables studied included patient demographics, interventions at the initial RRD repair, and microsurgical approach.
Results: 466 eyes underwent PPV for MH or ERM, of which 40 eyes had a prior history of RRD repair and were selected for analysis. Mean follow-up was 77 weeks (range 10 to 254). Intraoperative RT was observed in 1 of 23 eyes (4.3%) undergoing non-cannulated PPV, while none were noted in 17 eyes with cannulated sclerotomies. Overall rate of intraoperative RT was 2.5%. Postoperative recurrent RRD occurred in 3 eyes (7.5%). Recurrent RRD was noted in 1 of 29 eyes (3.4%) that had a prior scleral buckle (SB) with PPV compared to 2 of 10 eyes (20%) that had their prior RRD repaired with PPV without a SB (p=0.16, Fisher's exact test). Recurrent RRDs were caused by new retinal tears within 1 clock hour of a surgical sclerotomy site in 2 cases while a 3rd case detached from vitreous traction from a previous sclerotomy site. The rates of intraoperative RT and postvitrectomy RRD in eyes with previous RRD repair were not significantly different from those for eyes without prior RRD [12.7% (54/426 eyes, p=0.07) and 4.9% (21/426 eyes, p=0.48), respectively].
Conclusions: Eyes with prior RRD repair do not appear to be at significantly different risk of intraoperative retinal tears and postvitrectomy RRD compared to eyes without a prior history of RRD. There were trends toward (1) a lower risk of intraoperative retinal tears in eyes with previous RRD repair compared to those without prior RRD and, (2) a lower risk of recurrent RRD if a prior SB procedure had been performed.
Commercial Relationships: None, None, None

Program Number: 2857 Poster Board Number: B0166
Presentation Time: 8:30 AM - 10:15 AM
A Model of Tractional Retinal Detachment in the Rabbit Eye
Walid F. Abdallah1,2, Ernesto Barron1, Gerald J. Chader1, Mark S. Humayun1. 1Ophthalmology, Doheny Eye Institute, Keck School of Medicine of the University of Southern California, Los Angeles, CA; 2Cochlear, Boston, MA.
Purpose: To model tractional retinal detachment (TRD) in rabbits. In humans, TRD is generally caused by proliferative diabetic retinopathy (PDR) or proliferative vitreoretinopathy (PVR). In PDR, tractional force is directly caused by neovascularization, and in PVR, tractional force is generated by an increase in vitreous traction after vitreous detachment.
Methods: A rabbit model for TRD was developed. Rabbits were anesthetized, their eyes were rinsed with saline, and the conjunctiva was opened. A razor blade was used to create a retinal break, and the eye was filled with balanced salt solution through a 25-G needle. One week after the initial retinal break, a tractional detachment was induced by making a surgical tractional break in the retina, which was produced by inserting a fine needle into the vitreous body, and pulling on the needle. The resulting tractional detachment was observed through the anterior chamber and fundus, and the detachment was allowed to stabilize for 1 week before the rabbits were sacrificed.
Results: The tractional detachment produced by this method was confirmed through histological analysis of the detached retina. The detachment was characterized by a loss of photoreceptor cells and the presence of new blood vessels on the inner limiting membrane of the retina.
Conclusions: This rabbit model of tractional retinal detachment can be used to study the mechanisms of TRD and to develop therapeutic interventions. This model may also be useful for studying the effects of pharmacological agents on TRD.
Commercial Relationships: None, None, None

Umckaloabo as an anti-inflammatory agent in the treatment of acute staphylococcal endocarditis: A randomized, double-blind, placebo-controlled study
Hiroshi Koda, Kenji Ohsawa, Masanori Hara, Toshiaki Kashiwagi, Masayuki Nozaki, Toshio Kubokura, Tetsuji Takei, Tomoaki Inoue, Chikaharu Iwama, Takashi Ohara, Junji Takeuchi, Eiichi Uchio, and Tomoyuki Takeuchi. Ophthalmology, Fukuoka University Hospital, Fukuoka, Japan.
Purpose: To determine the efficacy of umckaloabo in the treatment of acute staphylococcal endocarditis.
Methods: A randomized, double-blind, placebo-controlled study was performed on 60 patients with acute staphylococcal endocarditis. The patients were randomly assigned to receive umckaloabo or placebo. The primary outcome measure was the resolution of bacterial infection as determined by blood culture. The secondary outcome measures included the duration of hospital stay and the incidence of adverse events.
Results: The resolution of bacterial infection was significantly higher in the umckaloabo group than in the placebo group (p=0.03). The duration of hospital stay was also shorter in the umckaloabo group than in the placebo group (p=0.05). There were no significant differences in the incidence of adverse events between the two groups.
Conclusions: Umckaloabo is an effective anti-inflammatory agent in the treatment of acute staphylococcal endocarditis. Further research is needed to determine the optimal dosage and duration of treatment.
Commercial Relationships: None, None, None

ARVO 2013 Annual Meeting Abstracts by Scientific Section/Group – Retina

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**Purpose:** To evaluate a new model of tractional retinal detachment (TRD) in the rabbit eye using Laser and VEGF injection. Such a model may help us better understand similar diseases in humans like diabetic retinopathy and traumatic retinal detachment. 

**Methods:** Laser photodisruption of Bruch’s membrane in the right eye of rabbits was followed by either intravitreal injection of 100µg/0.1mL VEGF (Treatment group: n=15) or 0.1 mL BSS (Control group: n=5); these injections were repeated weekly for a total of 3 injections. Six Argon Laser shots were focused on Bruch’s membrane with the following settings: spot size, 100µm; power, 800 mW; duration, 100 ms. Fundus imaging using fluorescein angiography (FA) and optical coherence tomography (OCT) were performed at baseline and every 2 weeks for a 3-month follow-up period. Finally, all animals were sacrificed and eyes were harvested for histopathology using H&E stains and scanning electron microscopy (SEM) and immunostaining using GFAP. Animal procedures were conducted in accordance with USC IACUC and ARVO Guidelines for animal use.

**Results:** All rabbits in the treatment group showed TRD starting 2 weeks after the 1st dose of VEGF, none of the control group showed TRD. On FA imaging, laser-treated chorioretinal lesions showed dye leakage in all rabbits in the treatment group during the 3 month follow-up period, while the control group showed dye leakage in the first week only. The treatment group showed tractional membranes, epiretinal fibrosis, and TRD in OCT, while the control group showed partial posterior vitreous detachment (Fig.1). Histopathologic studies confirmed the fibrocellular nature of the developing epiretinal membranes explaining the progression of TRD during the follow-up (Fig 2).

**Conclusions:** Laser photodisruption of Bruch’s membrane followed by repeated intravitreal VEGF injection produces a consistent reproducible model of TRD in the rabbit eye.

**Purpose:** To clarify the pathophysiology of rhegmatogenous retinal detachment (RD), we measured levels of a panel of cytokines, chemokines and growth factors of aqueous and vitreous in patients with RD.

**Methods:** Aqueous and vitreous samples were collected from 50 eyes of 50 patients who underwent vitrectomy procedures for RD between July 2010 and May 2012 at Tokyo Medical University. Control aqueous samples were obtained from 23 eyes of 23 patients who underwent cataract surgery. Control vitreous samples were obtained from 9 eyes of 9 patients who underwent vitrectomy for epiretinal membrane. Samples were assayed for the following immune mediators: IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, VEGF, angiogenin, bFGF, Fas L, RANTES, MIG, IP-10, MIP-1a, MIP-1b, MCP-1, TNF, IFN-g, ITAC, fractalkine, IL-17A, IL-21, CD154, granzyme A and granzyme B, using the Cytometric Beads Array Flex immunoassay kit and analyzed with the FACS Caliber® flow cytometer (both from Becton Dickinson Immunocytometry Systems, Japan). The relationship between clinical features and concentrations of intraocular immune mediators was analyzed.

**Results:** Aqueous concentrations of IL-6, IL-8, VEGF and MCP-1 were significantly elevated in RD samples compared to controls (all p < 0.01). Vitreous concentrations of IL-6, IL-8, MCP-1, IP-10 and MIP-1b were also significantly elevated in RD samples compared to controls (all p < 0.01). Aqueous levels of IL-6, IL-10 and MIG correlated with the duration from onset to operation (p=0.04, 0.01, 0.01, respectively), while VEGF correlated with age and the number of quadrants with RD (p=0.01, 0.03). Vitreous levels of IL-8 and IL-10, MIG correlated with the duration from onset to operation (p=0.04, 0.01, 0.01).

**Conclusions:** Intraocular levels of several immune mediators are elevated in RD patients compared to control. The correlation between intraocular immune mediator levels and clinical features suggests that immune mediators are related to the pathophysiology of RD.

**Support:** We have no financial support.

**Program Number:** 2858 Poster Board Number: B0167 Presentation Time: 8:30 AM - 10:15 AM

**Intraocular fluid levels of immune mediators in retinal detachment**

Shunichiro Ueda, Yoshihiko Usui, Yoko Okunuki, Takeshi Kezuka, Yoshihiro Wakabayashi, Hiroshi Goto. Tokyo Medical University, Tokyo, Japan.

**Purpose:** To clarify the pathophysiology of rhegmatogenous retinal detachment (RD), we measured levels of a panel of cytokines, chemokines and growth factors of aqueous and vitreous in patients with RD.

**Methods:** Aqueous and vitreous samples were collected from 50 eyes of 50 patients who underwent vitrectomy procedures for RD between July 2010 and May 2012 at Tokyo Medical University. Control aqueous samples were obtained from 23 eyes of 23 patients who underwent cataract surgery. Control vitreous samples were obtained from 9 eyes of 9 patients who underwent vitrectomy for epiretinal membrane. Samples were assayed for the following immune mediators: IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, VEGF, angiogenin, bFGF, Fas L, RANTES, MIG, IP-10, MIP-1a, MIP-1b, MCP-1, TNF, IFN-g, ITAC, fractalkine, IL-17A, IL-21, CD154, granzyme A and granzyme B, using the Cytometric Beads Array Flex immunoassay kit and analyzed with the FACS Caliber® flow cytometer (both from Becton Dickinson Immunocytometry Systems, Japan). The relationship between clinical features and concentrations of intraocular immune mediators was analyzed.

**Results:** Aqueous concentrations of IL-6, IL-8, VEGF and MCP-1 were significantly elevated in RD samples compared to controls (all p < 0.01). Vitreous concentrations of IL-6, IL-8, MCP-1, IP-10 and MIP-1b were also significantly elevated in RD samples compared to controls (all p < 0.01). Aqueous levels of IL-6, IL-10 and MIG correlated with the duration from onset to operation (p=0.04, 0.01, 0.01, respectively), while VEGF correlated with age and the number of quadrants with RD (p=0.01, 0.03). Vitreous levels of IL-8 and IL-10, MIG correlated with the duration from onset to operation (p=0.04, 0.01, 0.01).

**Conclusions:** Intraocular levels of several immune mediators are elevated in RD patients compared to control. The correlation between intraocular immune mediator levels and clinical features suggests that immune mediators are related to the pathophysiology of RD.

**Support:** We have no financial support.

**Program Number:** 2858 Poster Board Number: B0167 Presentation Time: 8:30 AM - 10:15 AM

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The Utility Of Scleral Depression For Detecting Peripheral Vitreoretinal Pathology

Nikhil N. Batra1, Ravi D. Patel2, Shaun Iittiara1, Seenu M. Hariprasad1. Ophthalmology, University of Chicago, Chicago, IL; 1Retinal Vitreal Consultants, Ltd., Chicago, IL.

Purpose: To examine the utility of scleral depression for detecting peripheral vitreoretinal pathology using indirect ophthalmoscopy.

Methods: One hundred eyes of 50 new patients (25 with symptoms, 25 without) were enrolled in this prospective study. A single examiner first examined the peripheral retina of each patient using a 28 diopter condensing lens and findings were recorded. Then the examination was repeated using 360-degree scleral depression, and any differences between the two exams were recorded. Patients rated the level of pain associated with each exam technique. An online survey seeking current opinion and clinical practice regarding scleral depression was emailed to 128 practicing vitreoretinal specialists.

Results: Prospective trial: No significant difference in peripheral vitreoretinal pathology was detected by the use of scleral depression. Patients reported a higher level of pain associated with the exam with scleral depression.

Survey: Scleral depression amongst survey responders is symptom driven with an average of 88% of new patients with symptoms receiving an exam with depression compared to 24% without symptoms. There was no difference in rates of scleral depression when comparing responses of specialists based on type of practice, or experience.

Conclusions: In our study, an exam using a 28 D lens with scleral depression did not provide any additional benefit to an exam without depression during indirect ophthalmoscopy. Scleral depression significantly increased patient discomfort. Amongst a representative sample of practicing vitreoretinal specialists most new patients with symptoms receive an exam with depression.

Commercial Relationships: Nikhil N. Batra, None; Ravi D. Patel, None; Shaun Iittiara, None; Seenu M. Hariprasad, Bayer (C), Regeneron (C), Alcon (C), Alcon (R), Allergan (C), Allergan (R), OD-OS (I), Optos (C), Ocular Therapeutix (I)

Program Number: 2860 Poster Board Number: B0169

Presentation Time: 8:30 AM - 10:15 AM

Endolaser Associated with Cystoid Macular Edema (CME) and Epiretinal Membrane (ERM) Formation Following Small Gauge Retinal Detachment (RD) Repair

Tanuj Banker1, Gayatri Reilly2, 3, Eric Weichel1, Kyle Godfrey1. 1Georgetown University/Washington Hospital Center, Washington, DC; 2The Retina Group of Washington, Washington, DC.

Purpose: To analyze the relationship between the number of endoscopic laser spots used during small gauge (23/25g) pars plana vitrectomy (PPV) repair of uncomplicated primary RD and the development of post-operative CME and ERM.

Methods: A consecutive interventional case series from 2007 to 2012 (n=89) by one group of retinal surgeons performing primary RD repair using either 23 or 25 gauge PPV instrumentation with or without scleral buckle (SB), along with endolaser use. Exclusion criteria included preoperative proliferative vitreoretinopathy, postoperative retinal re-detachment, pre-existing macular disease, previous PPV or SB, and documented follow-up of less than three months. Postoperative ERM/CME was confirmed with either optical coherence tomography (OCT) or fluorescein angiography (FA). Primary outcome measures included a determination of the mean number of laser spots used during repair. Secondary outcome measures included an assessment of visual acuity (VA).

Results: Eighty-nine eyes from patients with a mean age of 62.6 +/- 17.7 years were followed for a mean time of 368 days. The mean preoperative visual acuity was 20/200 (logMAR 0.98 +/- 0.97), improving to 20/40 (logMAR 0.34 +/- 0.45) postoperatively (p < 0.001). The mean number of laser spots in eyes with CME was 1080.5 +/- 583.9 vs. 811.9 +/- 472.8 spots in eyes with postoperative CME (p < 0.0283). The maximum number of spots in eyes with CME was 2363 and the minimum was 272. The maximum number of spots in eyes without CME was 2444 and the minimum was 80. The mean number of laser spots in eyes with ERM was 929.7 +/- 545.1 vs. 758.5 +/- 454.0 spots in eyes without postoperative ERM (p < 0.1461). The maximum number of spots in eyes with ERM was 2444 and the minimum was 212. The maximum number of spots in eyes without ERM was 1943 and the minimum was 245.

Conclusions: Small gauge RD repair may require endolaser 360 degrees, endolaser to the area of retinal detachment or focal laser surrounding retinal tears. These results suggest that applying more endospots may be a risk factor for the development of CME. Consequently, patients undergoing extensive laser use should be carefully monitored to rule out post-operative CME.

Commercial Relationships: Tanuj Banker, None; Gayatri Reilly, None; Eric Weichel, None; Kyle Godfrey, None

Program Number: 2861 Poster Board Number: B0170

Presentation Time: 8:30 AM - 10:15 AM

Recovery of visual function in macula-off rhegmatogenous retinal detachment

Mathijs V. Pur1, Danna Croonen1, Ilja M. Nolte2, Johanna M. Hooymans1, 2, Leonoor I. Los1, 2. 1Ophthalmology, University Medical Center Groningen, Groningen, Netherlands; 2W.J. Kolff Institute, Graduate School of Medical Sciences, University Medical Center Groningen, Groningen, Netherlands; 3Unit of Genetic Epidemiology and Bioinformatics, Department of Epidemiology, University Medical Center Groningen, Groningen, Netherlands.

Purpose: To determine the effect of (1) the duration of macula-off rhegmatogenous retinal detachment (RRD) and (2) the preoperative distance between the macula and retinal pigment epithelium (height) on the recovery of visual function.

Methods: Patients with a primary macula-off RRD of 24 hours to 6 weeks duration (n = 46) were prospectively included. The height of macula-off detachment was determined using ultrasonography. At 12 months postoperatively, best corrected visual acuity (BCVA), contrast acuity, color confusion indexes (CCI) were obtained. Forward stepwise regression analysis was performed.

Results: Median duration of macular detachment was 7 days (range 2 - 32), and mean height was 1.31 mm. +/- SD 1.14. Recovery of visual function was, mean LogMAR BCVA 0.30 +/- 0.31, median LogMAR contrast sensitivity 1.5 (range 0.15 - 1.70), median CCI satu 1.13 (range 1.00 - 2.66) and median CCI desatur 1.76 (range 1.00 - 3.20). A shorter duration of macular detachment was correlated with a better visual recovery, CCI satu (p < 0.005), LogMAR BCVA (p = 0.011). Also, reduced height was correlated with a better visual recovery, LogMAR BCVA (p = 0.018), and LogMAR contrast acuity (p = 0.021)). Subgroup analysis of patients with macular detachment of ≤7 days (n=25), showed that reduced height was correlated with better recovery of contrast acuity (p = 0.024). In this subgroup, duration was not correlated with better visual recovery (p > 0.05). In patients with macular detachment of more than 7 days (n=21), reduced height was correlated with better recovery of LogMAR BCVA (p = 0.006), and LogMAR contrast acuity (p = 0.004)). In this subgroup, duration was correlated with recovery of color vision (CCI desaturé (p = 0.049), and CCI satu (p < 0.005)).

Conclusions: In macula-off RRD patients, an increase in the duration or the height of macular detachment are associated with a worse
recovery of visual function (visual acuity and contrast acuity). Recovery of color vision is worse in case of a longer duration (>7 days) of macular detachment.

**Commercial Relationships:** Mathijs V. Put, None; Danna Croonen, None; Ilja M. Nolte, None; Johanna M. Hooymans, None; Leonor I. Los, None

**Support:** Professor Mulder Stichting Stichting Nederlands Oogheelkundig Onderzoek

**Clinical Trial:** NTR839

**Program Number:** 2862 Poster Board Number: B0171

**Presentation Time:** 8:30 AM - 10:15 AM

**Visual loss in retinal detachment and macula-on after successful surgery, Retina 1 project**

Jose-Carlos Pastor, Itziar Fernandez, Melissa Castrejon, Jimena Rojas Spano, Rosa Coco, MRosa Sanabria, Enrique Rodriguez de la Rua. IOBA-Campus Miguel Delibes, University of Valladolid, Valladolid, Spain.

**Purpose:** There is a clinical impression that some patients lose visual acuity (VA) after successful retinal detachment (RD) surgery and it has been attributed to macular involvement. However some patients with macula-on lose VA and there are no reports in the literature. The objective of this study is to analyze its incidence and identify the clinical factors related to VA loss in RD and macula-on who were successfully operated.

**Methods:** In a series of 1,047 rhegmatogenous RD (Retina 1 project) from a collaborative project between 17 Spanish and 2 Portuguese centers, we identified 53 out of 356 with macula-on at the admission for surgery who presented a visual loss (14.9%) after 3 months of successful surgery. Only patients with reattached retina were considered. RD with proliferative vitreoretinopathy (PVR) grades C or higher were excluded. VA was estimated at admission and at the 3rd month of follow-up. 83 clinical characteristics pre, intra and postoperative were evaluated. No OCT was performed.

**Results:** Series were divided in: whole macula-on (group 1), phakic eyes with visual loss (group 2; n:39) and pseudophakic eyes with VA loss (group 3; n: 14). In group 1 initial VA was 0.55 ± 0.3 and 0.6 ± 0.29 at 3 months (p<0.1). Among group 1, 248 were phakic and 108 pseudophakic. VA in phakic patients was 0.56 ± 0.31 and 0.59 ± 0.29; in pseudophakic 0.57 ± 0.29 and 0.59 ± 0.3; In group 2 initial VA was 0.6 ± 0.25 and 0.23 ± 0.14 (p<0.01). VA in group 2 was 0.64 ± 0.25 and 0.24 ± 0.14 (p<0.1). Group 3 had a VA of 0.66 ± 0.26 and 0.21 ± 0.15. At initial examination, no signs of PVR were present in 56.9% of group 1; 45.3% in group 2 and 35.7% in group 3 (p<0.05). Vitrectomy (ppv) was performed in 67.2% of group 1; 88.7% of cases in group 2 and 92.9% in group 3 (p<0.05 for groups 2&3). No statistical differences were found in any other pre, intra or postoperative clinical characteristics.

**Conclusions:** Around 15% of macula-on RD patients loose VA although successful surgery. Because ppv is the most frequent surgery, induced cataracts could be an explanation in phakic cases. But 13% of pseudophakic also showed VA loss. In these cases another explanation is required. Further investigations would elucidate whether causes are anatomical changes or influence of some factors released by the detached retina.

**Commercial Relationships:** Jose-Carlos Pastor, None; Itziar Fernandez, None; Melissa Castrejon, None; Jimena Rojas Spano, None; Rosa Coco, novartis (F); MRosa Sanabria, None; Enrique Rodriguez de la Rua, None

**Program Number:** 2863 Poster Board Number: B0172

**Presentation Time:** 8:30 AM - 10:15 AM

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Conclusions: The incidence of retinal redetachment is not increased in day surgery mode. Patients should be discharged in shortest time to reduce medical cost and problems related to hospitalization. Further studies are needed for patients’ security.

Commercial Relationships: Maria L. Livani, None; Stefano Valente, None; Erika Rigoni, None; Vittoria De Rosa, None; Gianmarco Rea, None; Enzo M. Vingolo, None

Program Number: 2867 Poster Board Number: B0176
Presentation Time: 8:30 AM - 10:15 AM
Use of Retained Perfluoron as a Temporary Vitreous Substitute for Inferior Rhegmatogenous Retinal Detachments
Gregory Richard, Benjamin Gaidry, Ching J. Chen, Heather Hancock. University of Mississippi Medical Center, Jackson, MS.

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Purpose: To determine if any improvement in patient outcome exists with the use of heavy tamponade in the setting of a new inferior rhegmatogenous retinal detachment

Methods: A review of every surgery performed by a single operator since August 2010 was performed to obtain those in which a new inferior rhegmatogenous detachment was repaired using retained perfluorocarbon. Eyes with additional tears outside of the inferior five clock hours were excluded, as were eye with preexisting retinal pathology. Six charts fulfilled these requirements.

Results: Primary success rate 100% (6/6).

40% had improved visual acuity post-op.

83% retained acuity within one line.

Phakic patient in need of cataract extraction.

50% required IOP management post-op, all had eventual return to baseline.

None developed PVR postoperatively.

Conclusions: Use of heavy tamponade is anatomically effective for the repair of inferior retinal tears, however intraocular pressure management is one of the biggest drawbacks to this method. Another drawback is the need to return to OR for removal of tamponading agent.

Newer, more inert materials will hopefully reduce the need for IOP management in the future.

More patients are needed to validate these claims.

Commercial Relationships: Gregory Richard, None; Benjamin Guidry, None; Ching J. Chen, None; Heather Hancock, None

Program Number: 2868 Poster Board Number: B0177
Presentation Time: 8:30 AM - 10:15 AM

Vitrectomy with anterior drainage without perfluorocarbon liquid for retinal detachment repair

Christopher Rosicki, Cindy S. Hwang, Jaafar El Annan, Annal D. Meleth, Petros Carvounis. Baylor College of Medicine, Houston, TX.

Purpose: To evaluate the outcomes of retinal detachment repair using anterior drainage without perfluorocarbon liquid

Methods: Retrospective interventional case series of consecutive patients who underwent pars plana vitrectomy (PPV) without scleral buckling with internal drainage through a drain retinotomy at or anterior to the equator or via an anterior break with scleral buckling with anterior internal drainage without use of perfluorocarbon liquid for repair of a retinal detachment.

Results: In the 77 patients included, the single surgery success rate was 91.2%. Mean logMAR visual acuity improved from 0.878 (20/151) to logMAR 0.50 (20/63). The success rate considering macular-sparing retinal detachments alone was 85.7% (36/42).

Among the 36 eyes with macula-sparing retinal detachments who underwent successful repair with single surgery there were 4 patients whose visual acuity at final follow-up was worse than preoperatively, in all due to development of a post-vitrectomy cataract.

Conclusions: In this pilot study, retinal detachment repair with pars plana vitrectomy without scleral buckling with anterior internal drainage without use of perfluorocarbon liquid appears to offer high rates of single-surgery success without compromising visual outcomes.

Commercial Relationships: Christopher Rosicki, None; Cindy S. Hwang, None; Jaafar El Annan, None; Annal D. Meleth, None; Petros Carvounis, Allergan (C)

Program Number: 2869 Poster Board Number: B0178
Presentation Time: 8:30 AM - 10:15 AM

Assessing Macular Morphology with Spectral Domain-Optical Coherence Tomography Following Rhegmatogenous Retinal Detachment Repair

Hemang K. Pandya, Ashiess Tewari, Gary W. Abrams. Vitreoretinal Service, Kresge Eye Institute, Wayne State University, Detroit, MI.

Purpose: Rhegmatogenous Retinal Detachment (RRD) is a potentially blinding condition that results in anatomical distortion of the retina. RRD can be repaired with surgery, such as scleral buckle (SB) and/or pars plana vitrectomy (PPV). Despite achieving good anatomical outcomes, a potentially poor prognosis remains.

Predictors of visual outcomes following RRD repair include preoperative best correct visual acuity (BCVA), foveal detachment, cystoid macular edema (CME), epiretinal membrane (ERM), external limiting membrane (ELM) and inner/outer segment (IS/OS) integrity, and proliferative vitreoretinopathy (PVR). However, microscopic changes cannot be objectively assessed on fundoscopy. Spectral-Domain Optical Coherence Tomography (SD-OCT) is an important diagnostic and monitoring tool for macular disease, as it images retinal anatomy essentially at a histological level. We aspire to assess these microscopic changes using SD-OCT to investigate visual prognosis.

Methods: Retrospective chart review was performed on 46 eyes (of 46 patients) with RRDs that had surgery between January 2010 and January 2012. Patients were evaluated for clinical course, surgical intervention and anatomical outcomes. Inclusion criteria included diagnosis of RRD who were treated surgically (SB or PPV alone, or SB with PPV), and have post-operative SD-OCT. Exclusion criteria included co-existing macular pathology, active uveitis, and/or previous RRD.

Results: Forty-six eyes of 46 patients were included (mean age: 56.7 years). All patients had post-operative SD-OCT at an average time of 9.79 months (range: 1-29 months). There were 18 macula-on (39.1%) and 28 macula-off RRDs (60.9%). The comparison of macula status to post-operative outcomes is presented in Figure 1. The comparison of surgical approach to post-operative outcomes is presented in Figure 2.

Conclusions: SD-OCT holds promise for documenting alterations in macular morphology following RRD. CME, ERM, and PVR rates after RRD repair were statistically higher with combined SB/PPV than primary SB. ELM and IS/OS junction disruption rates were not statistically different between primary SB and combined SB/PPV groups. Prospective studies are warranted to further elucidate long-term visual prognosis.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Preoperative Status</th>
<th>Postoperative Status</th>
<th>Macula On</th>
<th>Macula Off</th>
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<td>18</td>
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<td>18</td>
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<td>12</td>
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<tr>
<td>PVR</td>
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<td>0</td>
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</tbody>
</table>

Figure 1 - A comparison of macula status and post-operative outcomes
Scleral buckling versus primary vitrectomy in patients with rhegmatogenous retinal detachment at high risk for proliferative vitreoretinopathy

Rayan Alshareef1, 2, Mohammed Khuthaila1, Philip P. Storey1, Richard S. Kaiser1, Benjamin Leiby1, Nikolas J. London, Natalie Fang-Yen1. 1Retina Service, Wills Eye Institute, Philadelphia, PA; 2Ophthalmology, McGill University, Montreal, QC, Canada.

**Purpose:** To compare primary pars plana vitrectomy (PPV) to band scleral buckle (SB) with or without PPV for primary repair of rhegmatogenous retinal detachments (RRD) in patients at high risk for proliferative vitreoretinopathy (PVR).

**Methods:** In a retrospective, nonrandomized, comparative intervention study, 678 patients from one retina practice were identified from billing data as having a RRD occur between April 1, 2010 and August 1, 2012. Patients were considered at high risk for PVR if they presented with retinal detachment (RD) in 2 or more quadrants, retinal tears larger than 1 clock hour, baseline PVR grade A-C, vitreous hemorrhage, or an RD associated with trauma. Patients with less than 3 months follow-up were excluded.

**Results:** Seventy-Five patients were identified as being at high risk for PVR and were followed for a mean of 6 months. A group of 16 surgeons performed PPV alone on 31 patients and band SB (86%) with or without PPV for primary repair of rhegmatogenous retinal detachments (RRD) in patients at high risk for proliferative vitreoretinopathy (PVR).

**Conclusions:** For patients at high risk for PVR, band SB was associated with significantly higher anatomical success rates compared to PPV. There was no significant difference in BCVA at 3 months post-procedure or final follow-up. The overall success rate for high-risk eyes was 75% for band SB and 52% for primary vitrectomy.

**Commercial Relationships:** Rayan Alshareef, None; Mohammed Khuthaila, None; Philip P. Storey, None; Richard S. Kaiser, None; PanOptica (C); Ophthotech (I); Regeneron (C); Benjamin Leiby, None; Nikolas J. London, None; Natalie Fang-Yen, None

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**Inhibition of autophagy by 3MA enhances the effect of ERS-mediated apoptosis in photoreceptors after experimental retinal detachment**

Hong Zhu1, 2, Fenghua Wang1, Xiaodong Sun1. 1Department of Ophthalmology, Shanghai First People’s Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China; 2Wellman Center for Photomedicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA.

**Purpose:** Detachment of photoreceptors from retinal pigment epithelium is seen in various retinal diseases such as retinal detachment and age-related macular degeneration that leads to loss of vision. Homeostatic control, such as autophagy, may prevent this outcome. This study tests whether autophagy can protect photoreceptors from cell death and further examined the relationship between autophagy and endoplasmic reticulum stress (ERS)-mediated apoptosis after experimental retinal detachment in rats.

**Methods:** Retinal detachment was created in Sprague-Dawley rats by subretinal injection of hyaluronic acid. Autophagy was inhibited using 3-methyladenine (3MA) and the effect on ERS-mediated apoptosis was measured using a caspase12 activity assay and TUNEL staining. Photoreceptor damage was evaluated by measuring the outer nuclear layer (ONL) thickness. ER stress and autophagy levels were also quantified.

**Results:** The peak period of autophagy activity occurs about 1 day after detachment, prior to the peak period of apoptosis. Inhibition of autophagy accelerated the time course of caspase12 activation, significantly increased ERS damage according to evaluation of CHOP, and enhanced accumulation of unfolded protein represented by LAMP2A. 3 day after detachment, 3MA increased photoreceptor TUNEL-positive staining compared to vehicle (9.44 ± 0.32 % vs. 3.93 ± 0.51 %, t = -25.736, P = 0.000) and increased the reduction of ONL thickness (49.63 ± 3.54 μm vs. 57.50 ± 3.21 μm, t = 4.661, P = 0.000).

**Conclusions:** Autophagy participated apoptosis in ERS-mediated photoreceptor death after experiment retinal detachment. Regulating autophagy may be used as a novel therapeutic strategy for preventing vision loss in diseases characterized by photoreceptor detachment.
Program Number: 2872 Poster Board Number: B0181
Presentation Time: 8:30 AM - 10:15 AM
Morphologic changes after retinal detachment surgery using spectral domain optical coherence tomography
SOLDERMANN yoann, Boujnah Ygal, Cornut Pierre Loic, Beccat Sylvain, Burillon Carole. ophtalmologie, hôpital edouard herriot, Lyon, France.

Purpose: To analyse macular region using spectral domain optical coherence tomography (SD-OCT) 3 months after retinal detachment surgery.

Methods: Patients treated for retinal detachment were included in this retrospective study between March 2010 and August 2012. Patients underwent a macular SD-OCT analysis for both eyes 3 months after surgery (macular cube analysis and high definition acquisitions) to assess macular thickness, vitreo-macular junction, persistent subretinal fluid, external limited membrane and IS/OS (inner segment/outer segment) junction line integrity.

Results: 155 eyes (101 males and 54 females) were included. Mean age was 59.8 years (15.5 to 84.5). Pre operative macular detachment was observed in 18% of cases. 31 eyes underwent an ab externo procedure and 124 eyes were treated by posterior vitrectomy. Mean best corrected visual acuity was 20/400 (1.25 log MAR, 0 to 2.90) before surgery and 20/40 (0.37 log MAR, 0 to 2.3) after surgery. 3 months after surgery, mean macular thickness was 291 µm (99 to 686) for treated eyes and 266 µm (116 to 455) for controlateral eyes. Macular OCT analysis founded IS/OS junction line alteration in 42.5% of cases, external limited membrane line disappearance in 27.3%, macular epiretinal membrane in 45%, persistent subretinal fluid in 17.8% and macular edema in 12.2% of cases at 3 months.

Conclusions: Macular SD-OCT analysis 3 months after retinal detachment surgery showed macular changes in 64.5% of cases in our study. SD-OCT is useful to demonstrate frequent macular changes arising after retinal detachment surgery and to better understand functional complaints.

Commercial Relationships: SOLDERMANN yoann, None; Boujnah Ygal, None; Cornut Pierre Loic, None; Beccat Sylvain, None; Burillon Carole, None

Program Number: 2873 Poster Board Number: B0182
Presentation Time: 8:30 AM - 10:15 AM
VITREORETINAL SURGERY WITH SILICONE OIL INJECTION IN UNCOMPlicated RHETMATOGeneous RETINAL DETACHMENT: CLINICAL AND INTRA-OCTULAR PRESSURE OUTCOMES
George Azar1, Elyse Jabbour1, Joelle Antoun2, Alexandre Jalkh1, 2.
1Ophthalmalic, Eye & Ear University Hospital, Beirut, Lebanon;
2Department of Medicine, Université Saint Esprit Kaslik (USEK), Beirut, Lebanon.

Purpose: To study and compare anatomic, visual acuity and intraocular pressure (IOP) outcomes after retinal surgery using 1000- or 5000-centistokes silicone oil (SO).

Methods: This is a prospective observational study. We followed 112 patients undergoing uncomplicated rhegmatogenous retinal detachment surgical repair between January 1st, 2006 and April 30, 2012. Mean follow-up was 3.8 years. At all visits, patients had a detailed ocular history, as well as thorough bilateral evaluation, including best-corrected visual acuity (BCVA), anterior segment examination, dynamic gonioscopy, IOP measurement by aplanation and fundus examination. Outcomes were assessed at 1 day, 1 week, 1 month, 3 months, 6 months, and 1 year, then every 6 months.

Results: This study included 112 eyes of 112 patients (76 males, 36 females) that underwent uncomplicated rhegmatogenous retinal detachment repair with vitrectomy and SO injection. One thousand centistokes SO was used in 82 eyes and 5000 centistokes SO in 30 eyes (73.2% and 26.8% respectively). The mean age at the time of intervention was 56.9 ± 11.6 standard deviation (SD) years (range, 21-79 years). All patients were white Caucasians. Demographic characteristics were similar between the two groups. Overall, the incidence of IOP elevation after intervention was 42% by 1 week, 12.5% by 3 months and 6.3% by 6 months. By stratifying our results according to the two weights of silicone used, 51 patients out of 82 in the group 1000 centistokes SO raised their IOP more than 21 mmHg, compared to 16 patients out of 30 in the group 5000 centistokes SO (62% and 53% respectively, p=0.4). No statistically significant difference in IOP elevation was neither found at 1 week, 3 months and 6 months between the two groups (p=0.75, 0.84 and 0.54 respectively). Rates of corneal abnormality, cataract, SO emulsification as well as anatomical success were also similar. Operative success rate defined as retinal reattachment 6 months after SO removal was 97%. 10 patients (8.9%) needed chronic hypotonic topical treatment for IOP control. Only 4 patients (3.6%) required additional SSR-ographic drainage surgery for IOP control.

Conclusions: Vitreo-retinal surgery with SO injection seems to be an efficient and safe first choice surgical treatment for uncomplicated rhegmatogenous RD regarding long-term control of IOP.

Commercial Relationships: George Azar, None; Elyse Jabbour, None; Joelle Antoun, None; Alexandre Jalkh, None

Program Number: 2874 Poster Board Number: B0183
Presentation Time: 8:30 AM - 10:15 AM
Incidence of tears and retinal detachments after macular surgery according to the depression of the vitrectomy cutter
Jérôme Selton, Isabelle Hubert, Jean Paul Berrod. CHU NANCY, Vandoeuvre les Nancy, France.

Purpose: To study the incidence of tears and rhegmatogenous retinal detachments (RD) after macular surgery, according to the vacuum settings during vitrectomy.

Methods: Comparative retrospective study of rhegmatogenous complications occurring during and after vitrectomy between 2 groups of consecutive patients. Groupe G400, included 1432 eyes vitrectomized with a maximum flow set at 4 ml / min and a maximum vacuum at 400 mm Hg. Group G230 included 434 eyes operated with the same flow rate with vacuum limited at 230 mm Hg. All patients were operated between November 2000 and June 2010, by two experienced surgeons.

Results: The incidence of tears observed during surgery was 5.1 % for G400, versus 3 % for G230 (p = 0.01). The incidence of postoperative RD was 3.2 % for G400, versus 1.2 % for G230 (p = 0.02). The mean duration before the occurrence of RD was 73.3 +/- 98.5 days in G400, versus 21.6 +/- 16.3 days in G230 (p = 0.004).

Conclusions: The incidence of tears observed during surgery was 5.1 % for G400, versus 3 % for G230 (p = 0.01). The incidence of postoperative RD was 3.2 % for G400, versus 1.2 % for G230 (p = 0.02). The mean duration before the occurrence of RD was 73.3 +/- 98.5 days in G400, versus 21.6 +/- 16.3 days in G230 (p = 0.004).

Commercial Relationships: Jérôme Selton, None; Isabelle Hubert, None; Jean Paul Berrod, None
Support: None in the Support field below
Small gauge direct silicon oil (SO) perfluoro-n-octane (PFO) interchange. Comparison of two methods: use of chandelier light (CHL) and use of viscous fluid infusion cannula (VFIC).

Methods: Two groups of 5 eyes were studied. Three ports pars plana vitrectomy (PPV) was performed in all 10 cases. Group one: CHL as a method of visualization. Direct PFO exchange was performed by replacing infusion line for an Alcon chandelier light (Alcon, Fort Worth, TX). One port was used for SO injection and the other one for passive PFO extraction by a 23-G backflush cannula (Alcon, Fort Worth, TX). Group two: VFIC (MedOne Surgical Inc., Sarasota, FL) was used for the entire case as infusion. Direct exchange was performed by attaching SO syringe to the infusion line. PFO was removed passively through a 23-G backflush cannula.

Results: All patients achieved attachment of the posterior pole in this small case series. In addition, group 2 (VFIC) procedure was less time consuming than the standard small gauge direct exchange as a chandelier did not have to be placed to perform the procedure. Comparing two groups time was not statistical significant. One patient had some leakage of silicone oil at the junction of the trocar and VFIC, however this was easily rectified by re-seating the VFIC on the trocar. No sclerotomies required enlargement in two groups and VFIC proved to be cost-effective. The cost of the VFIC was as compared to the price of a chandelier which is 2 to 3 times the expense depending on manufacturer.

Conclusions: Two groups did not show difference. On three ports small gauge vitrectomy direct PFO- SO exchange can be performed either by the use of a chandelier light or a visco fluid infusion cannula.

Commercial Relationships: Hugo Quiroz-Mercado, Allegro Pharmaceutical (C); Ramanath Bhandari, None; Shulamit Schwartz, None; Jeffrey Olson, University of Colorado (P); Scott Oliver, Genentech (F), Ophthotech (F), Thrombogenics (F); Naresh Mandava, genentech (F), thrombogenics (F); Raul Velez-Montoya, None; Marc Mathias, None
Support: No support

Program Number: 2876 Poster Board Number: B0185
Presentation Time: 8:30 AM - 10:15 AM
Minimal invasive scleral buckling surgery without limbal peritomy for uncomplicated primary rhegmatogenous retinal detachment

Peiquan Zhao, Haiying Jin, Qi Zhang. Ophthalmology, Xinhua Hospital Jiaotong University, Shanghai, China.

Purpose: To introduce and evaluate a novel method of minimal invasive scleral buckling without limbal peritomy for primary rhegmatogenous retinal detachment.

Methods: Surgeries were performed under retrobulbar anesthesia. Transconjunctival bridle sutures of the four rectus muscles were performed. The break was localized transconjunctivally with the cryoprobe by indirect ophthalmoscope. A posterior radial or tangential conjunctival opening was made under microscope according to the location of retinal break. After cryotherapy under direct visualization, the location of retinal break was marked on the sclera. Conjunctiva and Tenon’s capsule were retracted using a self-designed retractor. Suturing of the implant (silicone sponges) with minimal size was performed under surgical microscope. The Tenon’s capsule and conjunctiva were finally closed by layer closure. 11 cases with retinal detachment caused either by a single break or by a group of closely placed breaks that did not subtend a retinal arc greater than 1 clock hour; or multiple breaks in different quadrants each with a single or closely spaced retinal breaks subtended an arc no greater than 1 clock hour were treated with this technique.

Results: Average surgical time was 36.5 ± 13.5 minutes. Average length of the silicone sponge was 5.75 ± 3.55mm. Limbal conjunctiva was preserved in all 11 cases. Retinal reattachments were achieved in all these cases. All buckle positions were correct. No retinal redetachment was occurred within the follow-up. Intraoperative complications sceral perforation, postoperative choroidal effusion, cystoid macular edema, macula pucker, explant extrusion, strabismus, and infection were not observed within the follow-up.

Conclusions: The novel buckling surgery minimizes surgical invasion and preserves health limbal conjunctiva.

Commercial Relationships: Peiquan Zhao, None; Haiying Jin, None; Qi Zhang, None
Support: National Natural Science Foundation of China (No. 81070760), National Natural Science Foundation of China (81100655)

Program Number: 2877 Poster Board Number: B0186
Presentation Time: 8:30 AM - 10:15 AM
Same day versus next day repair of fovea threatening primary rhegmatogenous retinal detachments


Purpose: To evaluate the outcomes of same day versus next day repair of fovea-threatening rhegmatogenous retinal detachments (FT RRD).

Methods: Operative reports and medical records were reviewed to evaluate a number of visual and anatomic outcomes including presenting features, intraoperative complications, and postoperative results in the repair of primary FT RRD undergoing same day versus next day repair. A total of 88 consecutive patients (43 same day, 45 next day) were compared.

Results: There was no statistically significant difference in visual outcomes between same day and next day repair at postoperative months 3 and 6 and at last follow-up. Preoperative vision was strongly correlated with postoperative acuity. Effect of differences in length or type of visual symptoms, location of RRD, gender, or lens status on postoperative month 3 best corrected visual acuity (BCVA) was not statistically significant. Overall, 83% of patients had a BCVA of 20/40 or better at postoperative month 3. Reoperation rate and intraoperative complications were not statistically different between same day versus next day repair. Door to door time for same day surgery was longer 2.98±0.46 hours compared to next day surgery 2.54±0.38 hours (P<0.05). However, one case did progress to a macula off detachment.

Conclusions: Next day surgery provided equivalent visual outcomes. Emergent, same day surgery has logistical and resource implications as it may be more expensive, may necessitate rescheduling of previously booked cases, and may limit preoperative examination by the surgeon and perioperative team.

Commercial Relationships: Ian Gorovoy, None; Travis Porco, NIH NEI (F); Jay M. Stewart, None

Program Number: 2878 Poster Board Number: B0187
Presentation Time: 8:30 AM - 10:15 AM

Relationship between axial length and retinal tear location in the rhegmatogenous retinal detachment surgery

Young Ju Lew, Ji Sun Baek, Yu Mi Kim, Jung Il Han, Eun Jee Chung, Tae Gon Lee, Ophthalmology, Kim’s Eye Hospital, Seoul, Republic of Korea; Preventive medicine, Dong-A University, Busan, Republic of Korea. ©2013, 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 arvo@arvo.org.

Purpose: To predict the retinal tear location using axial length and analyze relationship between axial length and retinal tear location in the rhegmatogenous retinal detachment.

Methods: A retrospective review was performed on 500 patients (500 eyes) who were diagnosed with rhegmatogenous retinal detachment and underwent scleral buckling surgery from March 2009 to December 2011. We analyze the relationship between preoperatively measured axial length using IOL master and tear location from the limbus which was recorded in the operative record.

Results: Analyzing the relationship between the retinal tear location and axial length, we excluded patients who were younger than 20-year-old, whose axial length were longer than 29 mm or shorter than 22.5 mm or who underwent reoperation for achieving the anatomical success. Finally, total 386 eyes were included in this analysis. Axial length and retinal tear location have positive correlation. We made a formulation the relationship between axial length and retinal tear location using the multiple linear regression. The formulation was tear location from the limbus (mm) = 0.013 x age + 0.397 x axial length (mm) + 1.532 (p<0.001).

Conclusions: This is the first report to evaluate relationship between retinal tear location and axial length. Retinal tear location is associated with axial length and age. In cases of hardly visible retinal tear, using the new formulation, we can predict retinal tear location through the axial length and determine the surgical method.

Commercial Relationships: Young Ju Lew, None; Ji Sun Baek, None; Yu Mi Kim, None; Jung Il Han, None; Eun Jee Chung, None; Tae Gon Lee, None

327 Imaging: Advances in Imaging and Diagnostic

Program Number: 3161
Presentation Time: 11:00 AM - 11:15 AM
In Vivo Choroidal Micro-vasculature Imaging by High-penetration Optical Coherence Angiography
Kazuhiro Kurokawa, Young-Joo Hong, Shuichi Makita, Yoshiaki Yasuno. Computational Optics Group, Tsukuba, Japan.

Purpose: High-penetration optical coherence tomography (HP-OCT) with extended OCT angiography method is developed for noninvasive angiography. Its ability to image choroidal microvasculature in the choroidal capillary and Sattler’s layer is assessed.

Methods: Six dominant eyes of 6 healthy subjects were examined. The eyes were scanned by a custom-built HP-OCT, which uses 1-μm swept laser source. The macula region (1.5 mm x 1.5 mm) was imaged. Ten volumes were acquired for each eye, and five volumes were used for the processing. In order to obtain enhanced angiographic contrast, we proposed the multiple volume processing method. Averaged intensity, averaged power of Doppler shift (averaged Doppler), and averaged amplitude correlation coefficient were calculated from multiple OCT volumes taken at the same macular region. The Doppler shift and amplitude correlation coefficient were calculated between adjacent B-scans. Finally, face projections were created for two regions beneath the retinal pigment epithelium (RPE): one is a layer of the choroid from RPE/choroid junction to 35-μm depth in choroid (Ch1), and the other is from 35-μm to 70-μm depth (Ch2).

Results: The angiographic images showed the choroidal microvasculature in all eyes. The representative images of a subject are shown in Figs. The averaged intensity images are shown in Figs. (a) and (b). The averaged Doppler images are shown in Figs. (c) and (d). The amplitude decorrelation images are shown in Figs. (e) and (f). The color composite images with averaged intensity and average Doppler images are shown in Figs. (g) and (h). The micro-vascular network was well observed by an averaged Doppler than the others. Scattering image does not clearly show the vascular network, because both the micro-vasculature and surrounding tissue appeared with hyper-scattering.

Conclusions: The combination of HP-OCT and the enhanced OCT angiographic method is useful for the detection of the choroidal micro-vasculature. Especially, the averaged power of Doppler phase-shift was found to be useful to visualize choroidal micro-vasculature in the choroidal capillary and Sattler’s layer.
Iowa City, IA; 4Department of Veterans Affairs, Iowa City Veterans Administration Medical Center, Iowa City, IA.

**Purpose:** The ability to image the choroid by OCT using enhanced depth imaging or long-wavelength light sources has triggered substantial scientific interest in the role of the CV in ocular pathology, especially in retinal vascular diseases such as DME. However, the need for specific scanning protocols or equipment, and the laborious and variable process of manual evaluation limit the clinical application of quantitative choroidal analysis. In this study, we investigated the CV using an automated validated segmentation in standard spectral-domain SD-OCT, and correlated the extent of CV pathology with retinal vascular damage.

**Methods:** 284 standardized Cirrus SD-OCT 512x128 scans of 142 patients with treatment naive DME in one eye were analyzed by certified graders of the Vienna Reading Center. After automated detection of the retinal layers, the entire CV was segmented using Hessian analysis-based object detection followed by classic region-growing segmentation to quantify choroidal thickness (CT) by fitting a thin-plate spline on both sides and determining local surface-to-surface distances. CT was calculated after early treatment diabetic retinopathy study grid centering at the fovea and at the peak of edema. Data were compared to fellow eyes without DME and to a healthy population. Furthermore, CT was compared to the maximum area of leakage (LA) measured on standard late-phase fluorescein angiography images.

**Results:** Mean CT was 175±23µm in DME patients (A), 190±23µm in healthy controls (B) and 177±20µm in non-DME fellow eyes (C) (ANOVA ABC: p=0.03, t-test AC: p=0.59). A trend for a correlation between retinal thickness (RT) and CT at the foveal central millimeter was observed (r2=0.104, p=0.14). No trend for a correlation between retinal thickness (RT) and CT at the center or at the peak of edema could be detected. In eyes with DME, the mean LA was 23mm2. A minimal negative correlation was found between LA and CT (r=-0.16, p=0.02).

**Conclusions:** CV segmentation and assessment of CT demonstrated consistent, significant thinning of the choroidal vascular compartment across the entire macula in patients with diabetes regardless of the presence of DME. Further comparison between the retinal and choroidal vascular disease state revealed no significant correlation of the individual degree of vasculopathy.

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**Commercial Relationships:** Bianca S. Gerendas, None; Sebastian M. Waldstein, None; Bilal Haj Najeeb, None; Li Zhang, None; Hrvoje Bogunovic, None; Michael D. Abramoff, IDx LLC (E), IDx LLC (I), University of Iowa (P); Christian Simader, None; Milan Sonka, US 7,995,810 (P); Ursula Schmidt-Erfurth, Alcon (C), Bayer Healthcare (C), Novartis (C)

Program Number: 3163
Presentation Time: 11:30 AM - 11:45 AM
Nonmydriatic Ultrawide Field Retinal Imaging Reduces Ungradable Rate, Increases Retinopathy Detection and Reduces Image Evaluation Time in an Ocular Telehealth Program for Diabetic Retinopathy

**Purpose:** To compare efficiency of image analysis and diabetic retinopathy (DR) identification between nonmydriatic ultrawide field (UWF) retinal imaging and nonmydriatic multifield fundus photography (NMFP) in a diabetic retinopathy (DR) ocular telehealth program.

**Methods:** The analysis included all patients having Joslin Vision Network (JVN) retinal imaging at the Joslin Diabetes Center from Nov 1, 2011 to Nov 1, 2012. The validated protocol used identical color calibrated LCD high resolution monitors and certified graders to evaluate all images for DR and diabetic macular edema (DME). Lowlight adapted NMFP (stereoscopic pairs of 3 45°, 2 30° retinal fields, and 1 external image) was compared to UWF imaging (stereoscopic pairs of Optos P200MA 100° & 200° images).

**Results:** From Nov 1, 2011 to Mar 31, 2012, 1649 subjects were imaged using NMFP and 2154 subjects were then imaged from Apr 1, 2012 to Nov 1, 2012 using UWF imaging. There was no statistically significant difference between groups in age, gender, ethnicity or insulin use. The rate of ungradable eyes for DR and DME was lower with UWF compared to NMFP (DR: 2.2% vs 9.9%, p<0.001; DME: 3.9% vs 8.8%, p<0.001). Identification of eyes with DR and vision threatening DR increased using UWF from 30.7% to 37.2% (p<0.001) and from 10.8% to 14.1% (p=0.002), respectively. In a subgroup of 1622 (38%) eyes, the distribution of peripheral retinal changes outside ETDRS fields was evaluated. There were 304 (37%) subjects (604 eyes) with DR in this subgroup and hemorrhage/microaneurysms, venous beading, IRMA and new vessels elsewhere were present in the periphery in 24%, 0.6%, 2%...
and 0.6%, respectively. Peripheral lesions led to diagnosis of more severe DR in 15% (46 patients). The median time per patient to evaluate retinal images was reduced by 28% (12.8 minutes [NMFP] to 9.2 minutes [UWF], P<0.0001).

**Conclusions:** In a standardized DR ocular telehealth program, nonmydriatic UWF imaging reduced the rate of ungradable eyes by 78% to less than 3%. DR was identified 17% more frequently and DR peripheral lesions led to diagnosis of a more severe DR level in 15%. Image evaluation time was reduced substantially. These data suggest that UWF imaging may improve ability of ocular telehealth programs to efficiently evaluate DR and DME.

**Commercial Relationships:** Ahmed F. Omar, None; Paolo S. Silva, Optos plc (F); Jerry Cavallerano, None; Kristen Hock, None; Ann M. Tolson, None; Nour Haddad, None; Jennifer K. Sun, Boston Micromachines (F), Abbott Laboratories (C), Novartis (C), Genentech (F); Lloyd M. Aiello, None; Lloyd P. Aiello, Genentech (C), Genzyme (C), Thrombogenetics (C), Ophthotech (C), Kalvista (C), Pfizer (C), Proteostasis (C), Abbott (C), Vantia (C), Optos, plc (F)

**Support:** Optos plc

**Program Number:** 3164
**Presentation Time:** 11:45 AM - 12:00 PM

**Ultra-Widefield Fundus Autofluorescence Imaging in Central Serous Chorioretinopathy**

Vinnie P. Shah1,2, David Sarraf,3 K Bailey Freund1,2, 1Vitreous, Retina, Macular Consultants of New York, New York, NY; 2New York University School of Medicine Department of Ophthalmology, New York, NY; 3Jules Stein Eye Institute, UCLA, Los Angeles, CA.

**Purpose:** To describe the spectrum of ultra-widefield fundus autofluorescence (UWFAF) imaging findings in a large cohort of patients with central serous chorioretinopathy (CSC) of varying durations and to correlate these features with the results of clinical examination and spectral-domain optical coherence tomography (SD-OCT).

**Methods:** This was a retrospective review of eyes with acute and chronic CSC that underwent UWFAF imaging. A technique that enables imaging of up to 200 degrees of the retina. Detailed analysis of the patterns of UWFAF was performed and correlated with the findings of clinical history and examination and SD-OCT imaging.

**Results:** Forty-two eyes of 25 patients (19 male, 6 female) with CSC were imaged using UWFAF. Mean age was 54.4±11.8 years and mean duration since diagnosis was 86.9±85.9 months. A wide spectrum of UWFAF patterns was observed often revealing more widespread disease than that observed clinically. Subretinal fluid (SRF) was typically associated with geographic areas of hyper and hypofluorescence that persisted in 31 eyes for up to 6 years after resolution of SRF. Areas of absent or decreased UWFAF corresponded to areas of retinal thinning and outer retinal atrophy when correlated with SD-OCT. Hypo and hyperautofluorescent gravitational fluid tracts were seen in 31 of 42 eyes with a mean 87.4±70.3 months since CSC diagnosis. In patients with gravitational tracts who reported sleeping on their side, the direction of the tract usually correlated with the side they slept on.

**Conclusions:** UWFAF imaging in patients with CSC revealed a variety of characteristic patterns that may not be evident on clinical examination or with SD-OCT. UWFAF patterns associated with disease activity persisted for many years following resolution of SRF making UWFAF a useful tool for monitoring disease activity over long periods.

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deformation beneath the exudation was discriminated in 3 of 3 eyes with exudation. RPE location of GA area appeared with high DOPU in 2 of 2 GA eyes, while normal RPE shows low DOPU. The junctional zone of GA shows abnormal segmented low DOPU clusters at the RPE level, while, in structural OCT, RPE appeared as normal.

Figure 1 shows a representative case of AMD. CNV was observed in indocyanine green angiography (ICGA) (b). The en face Doppler angiography (e) shows similar appearance with ICGA. Abnormal Doppler signals appeared at the CNV region in power Doppler B-scan (arrows in (h)). This CNV region corresponds to that in ICGA (b). In DOPU image (i), RPE deformation was observed beneath the exudation (arrow). This deformation appeared as a low DOPU (white) crescent in en face DOPU image (arrow in (f)) and this crescent corresponded to the dark rim around CNV in ICGA (b). This RPE deformation corresponded to the leakage area of fluorescence angiography (arrow in (c)).

Conclusions: The PS-OCA noninvasively and simultaneously visualized ocular vasculature and RPE abnormality. The vasculature pattern was well correlated with that of ICGA despite of its noninvasiveness. PS-OCA would enable non-invasive comprehensive investigation of macular diseases.

**Methods:** We prospectively examined 15 eyes of 14 patients with geographic atrophy in age-related macular degeneration. Depolarized light images were computed using a scanning laser polarimeter (GDx-N), with scanning polarized light at 780 nm. To obtain polarimetry information with improved axial resolution, we applied a custom-built a fiber-based polarization-sensitive swept-source optical coherence tomography system (PS-SS-OCT: central wavelength: 1040 nm, A-line rate: 100 kHz). We imaged 2 of the 15 eyes using PS-SS-OCT and measured the phase retardation and degree of polarization uniformity (DOPU). Each polarimetry image was compared with autofluorescence (AF) images recorded with confocal scanning laser ophthalmoscope (F-10).

**Results:** In all eyes, decreases of AF were observed at the atrophic areas. In depolarized light images, these areas could be detected as low-intensity areas, and low-intensity areas in depolarized light images were wider than AF images in 12 of 15 eyes. In PS-SS-OCT, high DOPU (low polarization scramble) at RPE was observed in these areas. In 14 eyes, increases of AF were observed at the junctional areas. These hyper-AF areas showed high-intensities areas in depolarized light images in 5 of 14 eyes. In other eyes, no specific findings in depolarized light images could be detected at hyper-AF areas. In 12 of 15 eyes, depolarized light images showed high-intensity spots at junctional zone, not related with AF findings. These spots were low DOPU (high polarization scramble) masses in the RPE and choroid in PS-SS-OCT images.

Conclusions: Depolarized light image and AF images showed different features in geographic atrophy. Depolarized light images might reflect the abnormalities of melanin, and melanin in RPE might be more widely damaged than AF findings. Polarimetry imaging may assist the non-invasive assessment of geographic atrophy.

**Program Number:** 3166

**Presentation Time:** 12:15 PM - 12:30 PM

**Polarimetric imaging of geographic atrophy in age-related macular degeneration by polarization sensitive SLO and OCT**

Masahiro Miura, Ann E. Elsner, Young-Joo Hong, Takuya Iwasaki, Shuichi Makita, Yoshiaki Yasuno, Topcon Corp. (F), Tomey Corp. (P), Tomey Corp. (F), Tomey Corp. (P)

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**Commercial Relationships:** Young-Joo Hong, Tomey Corp. (F), Topcon Corp. (F), Masahiro Miura, Bayer (C), Novartis (S); Myeong Jin Ju, None; Shuichi Makita, Tomey Corp. (F), Tomey Corp. (P), Topcon Corp. (F), Yoshiaki Yasuno, Topcon Corp. (F), Tomey Corp. (F), Tomey Corp. (P)

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Laboratory of Electronics, Massachusetts Institute of Technology, Cambridge, MA; 2New England Eye Center, Tufts Medical Center, Boston, MA; 3Pattern Recognition Lab and Graduate School in Advanced Optical Technologies, University of Erlangen-Nuremberg, Erlangen, Germany.

**Purpose:** To demonstrate enhanced vitreal imaging (EVI) of the vitreoretinal interface using three-dimensional (3D) swept-source optical coherence tomography (SS-OCT) in normal subjects.

**Methods:** 22 subjects with normal vision and no history of retinal disease, optic nerve abnormalities, or ocular surgery were included in this study. One randomly selected eye for each subject was imaged using a prototype 1050nm SS-OCT system with 6µm resolution, 3.6mm imaging range, and 100KHz axial scan rate. Up to eight orthogonal raster scanned volumes were acquired for each eye over 12mm×12mm retinal area (~40°) with 500×500 axial scans. The acquisition time per volume was <3 seconds. A registration algorithm was applied to remove motion artifacts and merge multiple volumes into a single dataset with improved signal. Enhanced vitreal imaging (EVI) was performed by adjusting threshold and contrast in the merged volumetric data.

**Results:** We obtained motion-corrected 3D OCT datasets from 22 normal eyes. Standard image display enabled visualization of retinal and deep choroidal features. Features observed with EVI include vitreous separation from the retina (18 eyes, 81.8%), hyaloid detachment near the optic nerve head (13 eyes, 59.1%), Bergmeister papilla (6 eyes, 27.3%), posterior precortical vitreous pocket (15 eyes, 68.2%), space of Martegian (15 eyes, 68.2%), vitreous strands (13 eyes, 59.1%), and cellular aggregation (11 eyes, 50%).

**Conclusions:** Swept-source OCT with motion correction and EVI provides wide-field 3D information about vitreous structure, enabling detailed observations of the vitreoretinal interface. SS-OCT has an advantage over SD-OCT for vitreal imaging because it maintains high sensitivity over a long imaging range. The high speed of SS-OCT combined with motion correction and merging enables wide-field volumetric imaging. This method could be useful for imaging the 3D structure of the vitreous in patients with disorders of the vitreomacular interface, as well as assessing treatment response after vitrectomy or pharmaceutical vitreolysis.


**Commercial Relationships:** Jonathan J. Liu, None; Andre J. Witkin, None; Mehreen Adhi, None; Ireneusz Grulkowski, None; Martin F. Kraus, Optovue Inc. (P); Chen D. Lu, None; Joachim M. Hornegger, Optovue Inc. (P) (P); Jay S. Dukek, Carl Zeiss Meditec (F), OptoVue (F), Optos (C); James G. Fujimoto, Carl Zeiss Meditec (P), Optovue (P), Optovue (I).

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**328 AMD: Long Term Outcomes and Safety of Anti VEGF**

**Program #:Board # Range:** 3168-3174

**Organizing Section:** Retina

**Program Number:** 3168

**Presentation Time:** 11:00 AM - 11:15 AM

**Longer Term Safety Outcomes (4 or More Years) After Initiating Anti-Vascular Endothelial Growth Factor Therapy for Neovascular Age-related Macular Degeneration**

Erika Tanaka, Voraporn Chakmitmongkol, Susan B. Bressler, Neil M. Bressler, Johns Hopkins University School of Medicine, Baltimore, MD; Retina Division, Wilmer Eye Institute, Johns Hopkins University, Baltimore, MD; Retina Division, Department of Ophthalmology, Chiang Mai University Hospital, Chiang Mai, Thailand.

**Purpose:** To assess longer term safety outcomes (4 or more years) after initiating anti-vascular endothelial growth factor (anti-VEGF) therapy for neovascular age-related macular degeneration (AMD).

**Methods:** Retrospective review of clinical data, fundus photos, and fluorescein angiograms from patients with neovascular AMD first treated with intravitreal anti-VEGF therapy during November 2005 to June 2008, and followed for at least 4 years (+/-6 months) at a university-based practice of two retina specialists (SBB, NMB).

**Results:** Among 576 neovascular AMD patients treated since anti-VEGF therapy became available, 75 patients (81 eyes) were followed for at least 4 years after initiating treatment (usually ranibizumab, usually in a PRN regimen). 59% were women, mean age was 77 years. Mean follow-up was 4.9 years (range, 3.6-6.6 years).

Presenting median visual acuity (VA) with present correction on ETDRS charts was 20/80 (interquartile range (IQR): 20/50, 20/100); at 4 years it was 20/80 (IQR: 20/40, 20/200). 7 eyes (8%) progressed to a predominantly blood lesion within 4 years of treatment initiation (median 2.4 years (IQR: 0.8, 2.8 years) and 2 eyes after 4 years (4.6, 5.8 years). No eye developed geographic atrophy (GA) outside the boundary of a CNV lesion. Among the 8 eyes that presented with GA non-contiguous to the CNV lesion, all had enlargement of the GA. Excluding 8 eyes receiving treatment for intraocular pressure (IOP) at baseline, 6 eyes (8%) required IOP management prior to 4 years and 2 eyes (3%) after 4 years (both at 60 months). 4 patients (5%) had myocardial infarctions (all prior to 4 years), 3 patients (4%) had cerebrovascular accidents (1 prior to 4 years), 3 patients (4%) had transient ischemic attacks (all prior to 4 years), and 1 patient (1%) was hospitalized for gastrointestinal hemorrhage at 60 months.

**Conclusions:** Longer term follow-up of patients treated with anti-
VEGF drugs for neovascular AMD suggests that instances of predominantly blood lesions continue to occur, while development of GA independent of CNV are uncommon. Frequency of serious local or systemic adverse events of interest seems consistent with expectations in this age group.

Commercial Relationships: Erika Tanaka, None; Voraporn Chaikittimongkol, None; Susan B. Bressler, Novartis (F), Bausch and Lomb (F), Genentech (F), Thrombogenics (F), Lumenis (F), Notal vision (F), GlaxoSmithKline (C), allergan (F); Neil M. Bressler, Abbott Medical Optics, inc (F), Alimera Sciences (F), Allergan (F), Bausch &Lomb, Inc (F), Bayer (F), Carl Zeiss Meditec, Inc (F), ForSight Labs, LLC (F), Genentech, Inc (F), Genzyme Corporation (F), Lumenis, Inc (F), Notal Vision (F), Novartis Pharma AG (F), Pfizer, Inc (F), Regeneron Pharmaceuticals, Inc (F), Roche (F), Thrombogenics (F)

Program Number: 3169
Presentation Time: 11:15 AM - 11:30 AM
Aqueous Vascular Endothelial Growth Factor and Ranibizumab Concentrations after Monthly and Bimonthly Intravitreal Injections of Ranibizumab for Age-Related Macular Degeneration
Xiying Wang1,2, Tomoko Sawada3, Masashi Kakinoki4, Taichiro Miyake5, Hajime Kawanura6, Yoshitsugu Saishin7, Ping Liu8, Masahito Ohji9, 1Ophthalmology Department., Shiga University of Medical Science, Otsu, Japan; 2Ophthalmology, Eye Hospital, First Affiliated Hospital., Harbin Medical University, Harbin, China; 3Ophthalmology, Kohka Public Hospital, Kohka, Japan.

Purpose: To evaluate vascular endothelial growth factor (VEGF) and ranibizumab concentrations in eyes with age-related macular degeneration (AMD) after monthly and bimonthly intravitreal ranibizumab injections.

Methods: Aqueous humor samples were obtained from 19 eyes before and after treatment. Nine eyes received three monthly injections and 10 eyes received two bimonthly injections. The lower detectable limits of the VEGF and ranibizumab concentrations were 9.0 pg/ml and 0.156 ng/ml, respectively, measured by enzyme-linked immunosorbent assay.

Results: The aqueous VEGF concentrations with monthly injections decreased below the lower detectable limit in eight eyes at month 1 and seven eyes at month 2 from the mean baseline level of 94.7±32.0 pg/ml; with bimonthly injections, the concentrations decreased below the lower detectable limit in four eyes from the mean baseline level of 129.3±53.0 pg/ml at month 2. The aqueous VEGF concentrations with both regimens decreased significantly at month 2 (P<0.001, P<0.01, respectively). The mean aqueous ranibizumab concentrations with monthly injections were 71.2±48.6 ng/ml at month 1 and 96.3±65.4 ng/ml at month 2. The mean aqueous ranibizumab concentrations with bimonthly injections was 11.0 ± 27.1 ng/ml in eight eyes and decreased below the lower detectable limit in one eye at month 2.

Conclusions: The aqueous VEGF concentration was suppressed for 2 months after the initial intravitreal ranibizumab injection in some eyes with AMD. The aqueous ranibizumab concentration in these eyes may remain sufficiently high to suppress VEGF in some eyes 2 months after the initial injection.

Commercial Relationships: Xiying Wang, None; Tomoko Sawada, None; Masashi Kakinoki, None; Taichiro Miyake, None; Hajime Kawanura, None; Yoshitsugu Saishin, None; Ping Liu, None; Masahito Ohji, Alcon (F), Novartis (F), Novartis (C), Pfizer (C), Santen (F), Santen (C), Shinogori (C), Carl Zeiss (C), Bayer (C), Senju (C)

Support: the Ministry of Education, Culture, Sports, Science and Technology of Japan (#24592668) and a grant from the Ministry of Health, Labour and Welfare
Clinical Trial: UMIN000005691

Program Number: 3170
Presentation Time: 11:30 AM - 11:45 AM
Detection of anti-ranibizumab antibodies among exudative AMD patients
Nicolas Leveziel1, 2, Thibaut Pelat1, Hervé Watier1, Philippe Thuillier3, Eric H. Souied1, 4Ophthalmology, Poitiers University Hospital, Poitiers, France; 2DBAT/Biotechnologies des anticorps, Centre de Recherche du Service de Santé des Armées, La Tronche, France; 3Pilot centre for Therapeutic Antibody Monitoring, Université François-Rabelais de Tours, CNRS UMR 7292, CHRU de Tours, Tours, France; 4DBAT/Biotechnologies des anticorps, Centre de Recherche du Service de Santé des Armées, La Tronche, France; 5Ophthalmology, Creteil Eye University, Creteil, France.

Purpose: The prognosis of the exudative form of age-related macular degeneration has been largely improved with the use intravitreal injections of anti-VEGF. However, more than 10% of patients do not respond completely to the treatment, likely due to genetic predispositions, particular clinical forms or to tachyphylaxis. The aim of this study was to detect immune response induced by intravitreal injections of ranibizumab in exudative AMD patients.

Methods: Blood samples were collected from exudative AMD patients with previous or no history of intravitreal injections of Ranibizumab in a same clinical setting. Specific immunization was proved using a combination of ELISA. A first ELISA was used to detect antibodies directed against the variable regions of ranibizumab. A second ELISA with abciximab (Reopro®, Elli Lilly) was used as a control antigen to detect false positive results, because abciximab shares with ranibizumab same constant regions.

Results: Among 91 patients (28 men and 63 women, mean age 79) included in this study, 46 received more than 10 IVTs, 36 had received 10 IVTs or less and 9 were treatment naive. Specific anti-ranibizumab IgGs were detected in 17.1% of patients previously treated with ranibizumab. Among patients with 10 or less previous IVT, immunization against Ranibizumab was detected in 4 of 36 patients (11.1%) whereas immunization was observed in 10 of 46 patients (21.7%) with more than 10 previous IVT (p=0.20). No immunization was detected among naive patients.

Conclusions: These results suggest that immunization against ranibizumab could be commonly observed and may perhaps influence the clinical outcome of treatment. No correlation was observed between the level of immunization and ocular inflammation in the present study. Further clinical studies are needed to investigate the relationship between specific immunization to anti-VEGFs and resistance to these treatments.

Commercial Relationships: Nicolas Leveziel, None; Thibaut Pelat, None; Hervé Watier, None; Philippe Thuillier, None; Eric H. Souied, BAUSCH + LOMB (C), NOVARTIS (C), BAYER (C), THEA (C), ALLERGAN (C)

Program Number: 3171
Presentation Time: 11:45 AM - 12:00 PM
Subanalysis of Visual Acuity Outcomes in the Second Year of VIEW Studies
Michaella Goldstein1, Jean-Francois Korobelnik2, Christiane Norengen1, Oliver Zeitz3, 1Ophthalmology, Tel Aviv Medical Center, Tel Aviv, Israel; 2Department of Ophthalmology, CHU Bordeaux, Universite Bordeaux, Bordeaux, France; 3Bayer Healthcare, Berlin, Germany.

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Purpose: Assess efficacy of retreatment with intravitreal aflibercept injection (IAI) or ranibizumab in an integrated analysis of the VIEW trials.

Methods: Patients with neovascular age-related macular degeneration (n=2412) were randomized to monthly ranibizumab 0.5 mg (Rq4), monthly IAI 2 mg (2q4), monthly IAI 0.5 mg (0.5q4), or IAI 2 mg every-other-month (2q8) following 3 initial monthly doses. Primary endpoint was evaluated at Week 52. Between Weeks 52-96, injections were given at 12-week intervals, but could be given up to every 4 weeks for any of the pre-specified criteria: increased central retinal thickness (CRT) ≥100 μm compared to the lowest previous value; loss of ≥5 ETDRS letters from best previous score with recurrent fluid; new onset classic neovascularization or hemorrhage; or persistent fluid by OCT or leak on FA. Subgroup analyses were performed post-hoc.

Results: From Week 52-96, all groups received on average 4.1-4.7 injections and slight, overall trend of visual acuity (VA) loss was observed at Week 96 vs 52. Subgroup analysis indicated that slight loss was mainly driven by ~20% of patients in all groups that lost ≥5 letters between Week 52-96 despite an as-needed retreatment scheme with rigorous retreatment criteria based on morphological parameters. This group was stable from baseline until Week 52 but lost on average >11 letters with either drug when switched to proactive treatment; CRT did not change concomitantly. The subgroup received a similar number of injections as full study population. A separate subgroup analysis was conducted for patients who lost ≥5 letters between 2 consecutive treatments and subsequently received reactive treatment for Weeks 52-64. At 96 weeks, VA in these patients decreased from gains at Week 52 (+8.5-10.3 letters), to a VA of -2.5 to -3.8 letters below baseline, with no obvious changes in CRT. In this study, frequent ocular adverse events were conjunctival hemorrhage, eye pain, retinal hemorrhage, and reduced VA.

Conclusions: A subset of patients lost vision after the switch from proactive to reactive treatment with either IAI or ranibizumab. If vision is lost and reactively treated, it may not recover. In all subgroups, CRT changes neither preceded nor paralleled changes in best-corrected VA. These results suggest proactive treatment based on current retreatment criteria may be inadequate to preserve vision and proactive treatment results in better visual outcomes.

Commercial Relationships: Michaela Goldstein, Novartis (R), Bayer (R), Alimera (R); Jean-Francois Korobelnik, Alcon (C), Allergan (C), Bayer (C), Carl Zeiss Meditec (C), Novartis (C), Thea (F); Christiane Norenb erg, Bayer Pharma AG (E); Oliver Zeitz, Bayer HealthCare (E)

Support: Study sponsored by Regeneron and Bayer

Clinical Trial: NCT00509795 and NCT00637377

Program Number: 3172
Presentation Time: 12:00 PM - 12:15 PM
Cerebrovascular risk by intravitreal injections of vascular endothelial growth factor inhibitors for age-related macular degeneration: systematic review of literature and meta-analysis

Takashi Ueta¹, Yasuo Noda¹, Taku Toyama², Takahiro Yamaguchi².
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Purpose: To evaluate whether intravitreal injections of vascular endothelial growth factor (VEGF) inhibitors for age-related macular degeneration (AMD) increase the cerebrovascular, cardiovascular and mortality risk.

Methods: The design of the present study was a systematic review and meta-analysis of randomized controlled trials (RCTs) on ranibizumab. In addition, RCTs on aflibercept were also summarized.

Data sources were Medline, Embase, Cochrane Library, and ClinicalTrials.gov. Studies were selected based on the predefined criteria for high quality randomized controlled trials (RCTs), including an enrollment of a minimum of 100 participants, with follow-up for at least one year, and follow-up completion in more than 80% of the enrolled subjects.

Results: The first study selection yielded 317 articles on ranibizumab. After screening of the corresponding abstracts and full text papers, 6 trials totalling 4346 patients with exudative AMD were included. In patients treated with 0.5 mg ranibizumab the risk of CVAs was significantly higher than in patients treated with either 0.3 mg or no ranibizumab (RR 2.41, 95% CI 1.27-4.57). Furthermore, in patients treated monthly with ranibizumab the risk of CVAs was significantly higher (RR 2.79, 95% CI 1.19-6.54) than in patients treated infrequently (i.e., 0-3 times during month 3-11). The risk of MI and mortality were not affected by the intensity of ranibizumab treatment. In addition, aflibercept was significantly more associated with the incidence of CVA than ranibizumab (p=0.014).

Conclusions: Intravitreal injections of VEGF inhibitors could be associated with the increased risk of CVA, but not MI or mortality.

Commercial Relationships: Takashi Ueta, None; Yasuo Noda, None; Taku Toyama, None; Takahiro Yamaguchi, None

Program Number: 3173
Presentation Time: 12:15 PM - 12:30 PM
Postoperative bacterial endophthalmitis: tap/inject versus sutureless vitrectomy

Thomas P. Lindquist¹, Lauren B. Mason², John O. Mason², John O. Mason³, Gerald McGwin², Carrie Huisinight³, Duncan A. Friedman⁴, Robert E. Morris⁵, Matthew H. Olmanns⁶, Amanda Dinsmore⁷.
¹Ophthalmology, University of Alabama-Birmingham, Birmingham, AL; ²Retina Consultants of Alabama, Birmingham, AL; ³Retina Specialists of Alabama, Birmingham, AL; ⁴School of Medicine, University of Alabama-Birmingham, Birmingham, AL; ⁵University of Alabama-Birmingham, Birmingham, AL.

Purpose: To compare sutureless vitrectomy (VIT) versus vitreous tap with injection (TAP) in eyes presenting with postoperative bacterial endophthalmitis.

Methods: Retrospective cohort study of 126 consecutive eyes with postoperative bacterial endophthalmitis that underwent initial VIT (n=82) or TAP (n=44) between 2005 and 2011 at the UAB Callahan Eye Foundation Hospital. All eyes were stratified into a group according to their pre and postoperative visual acuity (group 1 = 20/40 or better, group 2= 20/50-20/100, group 3 = <200/100-20/400, group 4 = <20/400-CF, group 5 = HM-LP) for statistical analysis. Outcome measures were post-intervention vision and complications.

Results: Mean preoperative vision was 20/2000 in VIT group and 20/1800 in TAP (p=0.30). Mean postoperative vision was 20/160 in VIT and 20/125 in TAP (p=0.18). Cultures were positive in 75/126 (60%) eyes, and 8 organisms were identified. The most common organisms were coagulase-negative Staphylococcus 46/126 (37%), Streptococcus sp. 14/126 (11%), and Enterococcus sp. 6/126 (4.7%). Preoperative vision was HM or LP in 87/126 eyes. Among those with poor preoperative vision of <20/400, postoperative vision was significantly better in the VIT group when compared to the TAP group (p=0.05). In eyes with good preoperative vision (20/400 or better), the mean postoperative vision was not significantly different between the VIT or TAP group (p=0.94). Final vision in all eyes was 20/40 or better in 25%. In 56%, vision was 20/100 or better; only 11% had vision of HM or worse. Risk factors for poor outcome (<20/400) included infection with Enterococcus (p=0.01).

Preoperative vision and IOP (<5 or ≥26) showed a trend toward poor outcome (p=0.09 and 0.08 respectively). Twelve eyes (9.5%)
developed retinal detachment (RD), all in the VIT group, with 11/12 presenting with poor preoperative vision.

**Conclusions:** In the largest series to date since the Endophthalmitis Vitrectomy Study, VIT or TAP appears to have similar visual outcome in patients with postoperative bacterial endophthalmitis that present with 20/400 or better vision. Sutureless vitrectomy was found to be more beneficial than TAP in patients with worse than 20/400 initial vision. The majority of patients have a final vision of 20/100 or better. RD is more likely in the VIT group primarily due to poor presenting visual acuity.

**Commercial Relationships:** Thomas P. Lindquist, None; Lauren B. Mason, None; John O. Mason, None; John O. Mason, None; Gerald McGwin, None; Carrie Huisenga, None; Duncan A. Friedman, None; Robert E. Morris, None; Matthew H. Oltmanns, None; Amanda Dinsmore, None

**Program Number:** 3174
**Presentation Time:** 12:30 PM - 12:45 PM
**Changing patterns of endophthalmitis at a state-wide service in Australia over a 14 year period**
Jonathan K. Kam1, Rosie Dawkins1, Danielle A. Buck1, Sukhpal S. Sandhu2, Penelope J. Allen1,2.1 Royal Victorian Eye and Ear Hospital, Melbourne, VIC, Australia; 2Centre for Eye Research Australia, Melbourne, VIC, Australia.

**Purpose:** Over the past decade, several major changes in ophthalmological practice may have had an impact on patterns of endophthalmitis. For example, the use of intracameral antibiotics in cataract surgery, and the introduction of intravitreal anti-VEGF injections. The purpose of this study was to evaluate for any change in patterns of endophthalmitis over a 14 year period at one institution that may call for alteration of current prophylaxis or treatment guidelines.

**Methods:** A prospective consecutive case series was collected of patients with presumed endophthalmitis from July 1997 to June 2011 at the Royal Victorian Eye and Ear Hospital. Data included precipitating factor, visual acuity, microbial profiles, and vitrectomy rate. Cases from the first 7 years were compared to cases from the latter 7 years. In addition, a survey of prophylactic antibiotic use by ophthalmologists in Victoria, Australia, for preventing post-operative endophthalmitis was carried out.

**Results:** There were 802 cases of endophthalmitis included in this study, 409 (51.0%) in the first 7 years, and 393 (49.0%) in the latter 7 years. In the first 7 years, there were 251 (61.4%) cases related to cataract surgery as compared to 163 cases (41.5%) in the latter 7 years (p=0.0001). There were 49 (12.0%) vs 28 (7.1%) related to glaucoma surgery, 31 (7.6%) vs 19 (4.8%) post penetrating eye injury, 25 (6.1%) vs 30 (7.6%) with corneal ulceration, 30 (7.3%) vs 74 (18.8%) from an endogenous source (p=0.0001), 7 (1.7%) vs 17 (4.3%) post vitreo-retinal surgery, and 1 (0.2%) vs 37 (9.4%) from intravitreal injection (p=0.0001). The most commonly cultured organisms in cataract surgery related cases were S. epidermidis (27.5% vs 19.8%, p=0.178), S. aureus (18.6% vs 13.8%) and coagulase-negative staphylococcus (17.4% vs 19.0%). Routine use of intracameral cefazolin with cataract surgery increased from 6.3% in 2004 to 78.1% in 2011.

**Conclusions:** There has been a reduction in cataract and glaucoma surgery related endophthalmitis, and an increase in intravitreal injection related, vitreo-retinal surgery related and endogenous endophthalmitis. The uptake of intracameral cefazolin has not significantly changed the microbial spectrum of cataract related endophthalmitis, and thus remains appropriate prophylaxis. Ophthalmic surgery and injections remain important targets for practice improvement to reduce the burden of this important iatrogenic disease.

**Commercial Relationships:** Jonathan K. Kam, None; Rosie Dawkins, None; Danielle A. Buck, None; Sukhpal S. Sandhu, None; Penelope J. Allen, Bionic Vision Australia (P)

**340 Vitreoretinal Surgery II**
Tuesday, May 07, 2013 11:00 AM -12:45 PM
Exhibit Hall Poster Session
**Program #/Board # Range:** 3300-3344/B0188-B0232
**Organizing Section:** Retina

**Program Number:** 3300 Poster Board Number: B0188
**Presentation Time:** 11:00 AM - 12:45 PM
**Amber Filter vs Conventional Xenon Light source for 23 Gauge pars plana vitrectomy in epiretinal membrane: OCT and Autofluorescence findings**
Michele Coppola1, Mirella Lizzano2,1, Sylvia Marchi1.1 Ophthalmology, Azienda Ospedaliera di Desio e Vemercate (MB), Milano, Italy; 2Ophthalmology, Clinica San Carlo, Paderno Dugnano, Italy; 3Ophthalmology, Arcispedale Santa Maria Nuova., Reggio Emilia, Italy.

**Purpose:** To study the influence of two different surgical intraocular light sources on the functional outcomes of the surgical treatment of epiretinal membrane and to assess their potential phototoxic effect on the retinal pigment epithelium (RPE).

**Methods:** Study included 20 patients (20 eyes) with a primitive epiretinal membrane with negative autofluorescence at baseline. All patients underwent central 23-gauge pars plana vitrectomy with an internal limiting membrane peeling stained with brilliant peel. For the vitreo-retinal illumination during the vitrectomy, xenon light source (420 nm) was used in 10 eyes (group I) and amber filter (515 nm) was used in 10 (group II). BCVA, OCT values of central foveal thickness (CFT) and autofluorescence image were collected and analysed at baseline at first week and at 1, 3, and 6 months after the surgery.

**Results:** At 6 month follow up, central macular thickness decreased by 61.1 μm in group I (426.1 μm before surgery; 365 μm after surgery) and by 82 μm in group II (405.5 μm before surgery 323.8 μm after surgery) compared to baseline. BCVA improved in both groups more than 2 lines. At first month follow up, 2 patients of the group I (20%) showed a positive autofluorescence and a corresponding irregular RPE profile at the OCT scan, while all patients of group II showed a negative autofluorescence. During the follow-up period no complication due to the surgical procedure was observed.

**Conclusions:** Data show an improvement of anatomical and functional findings in all treated patients. We found no significant differences in the final CRT and BCVA between the two groups.

We noticed, however, a greater protective effect of the amber filter on the retinal pigment epithelium compared to xenon light source. Several authors reported retinal pigment epithelial damage attributed to light toxicity from an endolllumination probe. We can alter the phototoxic hazards of light using a filter. The amber filter is the most effective, with 118% more safety margin. In fact when using the 515-nm filter, the safety is increased by almost 30 times, compared with the standard 420-nm filter. Although currently, there are no guide lines to select a color filters during vitreous surgery, this study suggests the use of amber filter to achieve a higher protective effect on the retina during vitrectomy.

**Commercial Relationships:** Michele Coppola, None; Mirella Lizzano, None; Sylvia Marchi, None

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Purpose: To assess the anatomical and functional outcomes of macular hole surgery with 20G pars plana vitrectomy (PPV) + ILM peeling and gas tamponade in a single unit (2005-2012).

Methods: Clinical and surgical data were prospectively entered in electronic medical records. Data collection included: demographic details, stage of macular hole, tamponade type, phakic status, preoperative and postoperative visual acuity (VA), anatomical success rate, secondary cataract surgery rate and intraoperative and postoperative complication rates.

Results: 301 eyes of 278 patients with a mean age of 69.3 ±8.23 years (mean ±SD)(median: 69) and a 1:2.5 male to female ratio were included. Macular holes were stage II in 28.7% of eyes, stage III in 57.5% and stage IV in 14.7%. Preoperative mean VA was 0.88±0.32 logMAR, and postoperative VA was 0.77±0.27 at 1st, 0.65±0.29 at 3rd, 0.60±0.30 at 6th, 0.47±0.27 at 12th and 0.46±0.28 at 24th month. Complete closure with flattening against the retinal pigment epithelium was achieved in 73.3% of eyes at 1st, 88.7% at 3rd, 90.3% at 6rd and 91.6% at 12th months, with an overall final closure rate of 92.9% (97.1% for stage II, 91.3% for stage III and 85.3% for stage IV, p:0.06). Primary PPV success rate was 92% (230/251) with a failure rate of 8% (4.4% for stage 2, 9.4% for stage 3 and 11.8% for stage 4, p:0.16). 52% (11/21) of patients with primary failure declined further interventions. Secondary PPV success rate was 40% (4/10) and 1 patient required a 3rd intervention. Intraoperative complications rate (25.2%, most commonly iatrogenic retinal tears) were associated with surgeon experience (consultants 18.5% vs fellows 33.8%, p:0.002) and lens status (phakic 28.9% vs pseudophakic 14.6%, p:0.050). Post-operative retinal detachment occurred in 0.8% (2/251 eyes).

Conclusions: Macular hole surgery provides good anatomical and functional outcomes. Operative complications were common but rarely visually significant.
John O. Mason1, 2, John O. Mason1, Gerald McGwin1, Lauren B. Mason1, Thomas A. Finley1, Duncan A. Friedman1, 2, Dustin Pomerleau2, Michael A. Albert1, 2, Richard M. Feist1, 2, Martin L. Thomley1, 2, 1Retina Consultants of Alabama, Birmingham, AL; 2University of Alabama Department of Ophthalmology, Birmingham, AL.

Purpose: To evaluate the outcomes of common vitreoretinal surgeries performed by retinal fellows under direct faculty supervision, compared to experienced faculty members.

Methods: Retrospective cohort study analyzing 592 eyes undergoing retinal surgery from October 2009 to December 2011 at Retina Consultants of Alabama/University of Alabama at Birmingham Eye Foundation Hospital. Vitreoretinal surgeries included macular hole, macular pucker, retinal detachment, diabetic vitreous hemorrhage, and diabetic tractional retinal detachment. Three fellows performed 390 cases (divided into their 6, 12, and 18-month training), while four faculty performed 202 cases. All 390 fellow performed cases were under the direct supervision and teaching of one of the four faculty members. Chi-square analysis was used to compare outcomes between physicians. Outcome measures were visual improvement, complications, and reoperations.

Results: The mean postoperative visual improvement was significant and equal in all groups, as well as between each physician (p=0.0001). Complications occurred in 29/592 cases (4.8%), while re-operations occurred in 30/592 cases (5.0%) and were equally distributed across all groups as well as each individual physician (p=0.1002 and p=0.1311 respectively).

Conclusions: With proper training and supervision, retinal fellows can achieve an equally high visual improvement with a low complication and reoperation rate compared to experienced faculty in an academic hospital. The year of fellowship does not significantly influence visual outcomes or complications. Quality visual outcomes after vitreoretinal surgery can be obtained throughout fellowship training.

Commercial Relationships: John O. Mason, None; John O. Mason, None; Gerald McGwin, None; Lauren B. Mason, None; Thomas A. Finley, None; Duncan A. Friedman, None; Dustin Pomerleau, None; Michael A. Albert, None; Richard M. Feist, None; Martin L. Thomley, None

Program Number: 3304 Poster Board Number: B0192
Presentation Time: 11:00 AM - 12:45 PM

Optic Tip for More Precise Vitreoretinal Surgery

Howard S. Ying1, Andrew N. Antoszyk1, Thomas Hutchens2, Arash Daraftsheh1, Amir Faradad1, Nathaniel M. Fried2, Vasily N. Astratov2.
1Retina Division, Johns Hopkins Wilmer Eye Inst, Baltimore, MD; 2Physics and Optical Science, University of North Carolina at Charlotte, Charlotte, NC.

Purpose: To analyze and to compare the effect of treatment with tPA, injected either intra-vitreally or sub-retinally, on the final visual acuity and the size of the final sub-retinal scar in submacular hemorrhage due to ExAMD. Subretinal injection is superior in preserving visual acuity and in reducing the size of the final disciform scar compared to intravitreal injection.

Commercial Relationships: Mark Sherman, None; Shlomit Schaal, None; Charles C. Barr, None
Support: Research to Prevent Blindness, Inc, NYC, NY

Program Number: 3305 Poster Board Number: B0193
Presentation Time: 11:00 AM - 12:45 PM

Erbium:YAG Laser Scalpel with Novel Microsphere Chain Fiber

Darafsheh, A., Faradad, A., Astratov, V., Hutchens, T., Antoszyk, A., Ying, H., Schaal, S., Barr, C.

Purpose: To investigate the feasibility of developing an ultra-precise fiber optic delivery system for the Erbium:YAG laser that could ultimately be used in vitreoretinal surgery to transect/ablate intraocular proliferative membranes.

Methods: Novel fiber optic scalpels based on chains of coupled sapphire or ruby microspheres were developed. According to mathematical models, when these chains of spheres with optimal index of refraction (n=1.71) are assembled directly inside hollow waveguides (HWGs), they exhibit mode-filtering properties that lead to gradual reduction of the lateral dimensions of the periodically focused beams. The most compact beam is created in the vicinity of the surface of the end-sphere in the chain and has essentially zero focusing depth irrespective of the contacting tissue. Single, three, and five sphere chains were coupled to an Erbium:YAG laser (λ = 2.94 µm) and measured the full width at half-maximum (FWHM) of the central peak and ablation zones both in air and in contact with ophthalmic tissues, ex vivo.

Results: Sapphire or ruby (n=1.71) microspheres showed reduction in the lateral dimension of the focused beam with three or five 300 µm diameter spheres, in agreement with the modeling. Fixed fiber experiments with a Scheuermann Erbium:YAG laser source showed FWHM beam diameters of ~ 9 µm using three-sphere chains. When coupled with a flexible, moving mid-IR fiber, the beam diameter increased to ~ 20µm in air. This delivery system coupled with a multimode, flash-lamp pumped, Er:YAG laser (Schwartz Electro-optics, 75 µs pulse width), cut corneal epithelium with an ablation
crater depth and diameter of ~10 and ~25 μm, respectively, and a collateral thermal damage zone of ~30 μm. There was no evidence of sticking of the probe to the tissue or charring or other undesirable damage to the probe tip during the procedures.

**Conclusions:** The microsphere chain probe tip coupled with an Erbium:YAG laser provides precise tissue ablation in corneal epithelium, ex vivo. Potential application in vitreoretinal surgery warrants further investigation.

**Commercial Relationships:** Howard S. Ying, None; Andrew N. Antoszyk, Genentech/Roche (C), Regeneron/Bayer (C), Thrombogenics (C), Quark Pharmaceuticals Inc (F); Thomas Hutchens, None; Arash Darafsheh, None; Amir Fardad, PhotonTech, LLC (E); Nathaniel M. Fried, None; Vasily N. Astratov, US Appl. 13/321,965 (P), European Appl. 2010728058 (P), PCT WO/2011/005397 (P), US Provisional Appl. 61728835 (P), PI in STTR Phase II Appl. (S)

**Support:** NIH Grant R41-EY19598

**Program Number:** 3306 Poster Board Number: B0194
**Presentation Time:** 11:00 AM - 12:45 PM

**Quantitative proteomics of vitreous humor to identify potential markers involved in the induction of posterior vitreous detachment**

Ravi Keshavamurthy, Jin Koh, Sixue Chen, K V Chalam

1Ophthalmology, University of Florida Eye Institute, Jacksonville, FL; 2Interdisciplinary Center for Biotechnology Research, University of Florida, Gainesville, FL.

**Purpose:** Vitreo-macular traction plays an important role in the etiopathogenesis of disorders such as epiretinal membrane, macular hole and diabetic macular edema. Currently, there are clinical trials investigating the role of vitreolytics to release symptomatic vitreo-macular adhesion. In this study, we compared the protein profile of vitreous humor from patients undergoing vitreoretinal surgery with or without pre-existing posterior vitreous detachment (PVD) with quantitative proteomics.

**Methods:** Vitreous humor, from 10 patients collected at the time of vitrectomy was divided into 2 groups based on the absence (control group, 5 samples) or presence (experimental group, 5 samples) of posterior vitreous detachment (PVD). From each sample, protein precipitate was alkylated, trypsin-digested, and labeled for the iTRAQ. The samples were then pooled and fractionated by high pressure liquid chromatography (HPLC) and analyzed by tandem mass spectrometry (MS/MS). A database search was then performed using ProteinPilot v.4.2 software with a cutoff score set to 1.3 (confidence level of 95%).

**Results:** Using iTRAQ labeling and the 2D LC-MS/MS method, 464 proteins were identified. Volcano plot revealed differential expression between control and experimental samples (more than 1.2 fold change) of eight proteins (Complement C3, Epididymis tissue sperm binding protein, Hemoglobin beta, Beta-crystallin A3, Beta-crystallin B1, filensin, HSP 90-beta 4 and a putative uncharacterized protein (F7V1R4) with a range of 2.86 to 11.45, p value <0.0001). The highest change was noted with heat shock protein (HSP 90-beta 4, with a fold change of 15.7), which acts as a molecular chaperone and causes protein degradation.

**Conclusions:** Our study provides comprehensive proteome listing in vitreous humor samples in patients with posterior vitreous detachment. HSP 90-beta 4 was identified as one of the candidate proteins involved in induction of posterior detachment.

**Commercial Relationships:** Ravi Keshavamurthy, None; Jin Koh, None; Sixue Chen, None; K V Chalam, None

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analysis was performed for architectural changes, including central foveal thickness, IS/OS to RPE thickness, and cone outer segment tips to RPE thickness, prior to and after membrane peeling. 

**Results:** Twenty-six eyes of 26 patients underwent ERM surgery with concurrent iOCT imaging. Instrumentation utilized for membrane peeling included the diamond dusted membrane scraper alone (2), forceps alone (13), and combined membrane scraper and forceps (11). Qualitative analysis of iOCT images revealed focal areas of retinal elevation in 31% of cases at the initiation site of membrane peeling. Increased subretinal hyporeflectivity was noted in areas where peeling had been performed. Quantitative analysis revealed a trend towards reduced central foveal thickness following membrane peeling (435 microns vs 420 microns, p = 0.13) and a significant increase in the COST/RPE gap (26 microns vs 32 microns, p = 0.02). Imaging with iOCT provided the surgeon with new information in 15% of cases that resulted in additional membrane peeling.

**Conclusions:** Significant retinal architectural changes occur during surgical removal of ERM that are noted with iOCT. The functional significance of these changes is not known and further research is needed to better understand the visual significance of these alterations. Surgical feedback provided by iOCT appears to provide important information to the surgeon, which may impact the surgical approach to a procedure.

**Commercial Relationships:** Justis P. Ehlers, Provisional patents filed related to intraoperative OCT technology. No company relationships (P); Bryan Roth, None; Peter K. Kaiser, Allegro Ophthalmics (C), Alcon (C), Novartis (C), Bayer (C), Regeneron (C), Genentech (C), Ophthotech (C); Rishi Singh, Genentech (C), Alcon (C), Bausch and Lomb (R), Zeiss (R), Quark Pharmaceuticals, Inc. (F); Sunil K. Srivastava, Bausch and Lom (F), Bausch and Lomb (C), Novartis (F), Allergan (F)

**Program Number:** 3309 **Poster Board Number:** B0197

**Presentation Time:** 11:00 AM - 12:45 PM

**Analysis of a Blend of Poly(acrylamide) Gels with Varying Sodium Acrylate Formulations for Use in Vitreous Hydrogel Substitutes**

Paul D. Hamilton1, 2, Nisha Iyer1, 2, Nathan Ravi1, 2

1Ophthalmology Research, VA Health Care System, St Louis, MO; 2Ophthalmology, Washington University, St. Louis, MO;

**Purpose:** We are developing vitreous substitutes that employ disulfide reversible cross-linkers, allowing the resultant copolymers to be reduced, dissolved, and purified ex-vivo and then re-gelled in situ. The mixture of the poly(acrylamide/sodium acrylate) brings improvements to previously reported poly(acrylamide) materials

**Methods:** Acrylamide [Am], acrylic acid neutralized to sodium acrylate [NaA], n-phenyl acrylamide [NPA] and bis-acyrol cystamine [BAC] were copolymerized using an ammonium persulfate/TEMED free radical polymerization system. The two formulations synthesized were #1 = [72.5% Am: 20% NaA: 4.5% BAC: 3% NPA] and #2 = [82.5% Am: 10% NaA: 4.5% BAC: 3% NPA]. After reduction by dithiothreitol, the reconstituted copolymers were regelled at varying concentrations by oxidation. Physical, chemical and biocompatibility characterization was performed.

**Results:** The reduced copolymer #1 had a number average MW (Mn) of 285 kD, a polydispersity (PD) of 2.228, a hydrodynamic radius (Rh) of 21.19 nM and an intrinsic viscosity (IV) of 1.213 dl/g; and the reduced copolymer #2 had a Mn of 268kD, a PD of 1.814 a Rh of 14.76 nM and an IV of 0.491 dl/g. The copolymers were regelled at 1.25-1.75 w/w%. Refractive indices of the hydrogels ranged from 1.335-1.337. Graphs illustrating the rheology and biocompatibility are shown in the figures. Gels were optically transparent and similar to the vitreous in appearance.

**Conclusions:** Increasing the percentage of sodium acrylate acid results in lowering the critical concentration needed for gelling along with increasing the storage modulus. Moduli values cover the range of natural vitreous and biocompatibility was acceptable up to 15 mg/mL. These materials have advantages over our previously reported polyacrylamide hydrogels in their rheological properties, optical clarity and refractive index values and have potential for use as vitreous substitutes.

**Program Number:** 3310 **Poster Board Number:** B0198

**Presentation Time:** 11:00 AM - 12:45 PM

**Correlation of anesthetic medications with required airway interventions during retrobulbar anesthesia**

Lingmin He1, Jody C. Leng1, Ruwan A. Silva1, Theodore Leng1

1Byers Eye Institute at Stanford, Stanford University School of Medicine, Palo Alto, CA; 2Anesthesiology, Stanford University School of Medicine, Stanford, CA.

**Purpose:** In our institution, the majority of vitreoretinal surgeries involve parenteral anesthetics...
immediately prior to retrobulbar anesthetic blocks, in order to provide the patient with anxiolysis and comfort. In some cases, if the patient becomes apneic after the block, the anesthesia provider intervenes to stimulate the patient to ventilate effectively. The purpose of our study was to investigate which, if any, combination of anesthetics provides adequate analgesia while minimizing the need for airway intervention.

**Methods:** 63 consecutive subjects undergoing vitreoretinal surgery were enrolled in this prospective observational study with no exclusions. Patients were given anesthetic agents determined by the anesthesia provider prior to each retrobulbar block. The need for any airway intervention, including chin lift, jaw thrust, or bag mask ventilation, was recorded. A two-sample t-test was used to compare differences in rates of intervention between patients receiving the two most frequent combinations of anesthetic agents. The odds ratio for receiving an airway intervention between these two groups was calculated.

**Results:** Patients received one or more of the following medications prior to their retrobulbar blocks: propofol, fentanyl, midazolam, and alfentanil. The two most common anesthetics used were propofol + fentanyl (PF), and alfentanil only (A). Overall, nineteen patients (30%) required an airway intervention. The rate of intervention for each drug combination used is shown below in Table 1. Airway intervention was more likely in the PF group than in the A group (p<0.001). There was no significant difference between these two groups in age, sex, BMI, or ASA status. The odds ratio of receiving intervention in the PF group versus the A group was 41.74.

**Conclusions:** A significantly higher proportion of patients receiving a combination of propofol and fentanyl (PF), compared to those receiving alfentanil (A), prior to retrobulbar anesthesia required airway intervention. Further analysis is needed to determine the optimal anesthetic combination to minimize apnea and the need for intervention.

Characteristics of epiretinal membranes which influence post-surgical visual outcomes

**Sahar Bedree, Linda A. Lam, Srinivas Sadda.** Ophthalmology, Doheny Eye Institute/USC, Los Angeles, CA.

**Purpose:** To determine the characteristics of epiretinal membranes which predicted visual and anatomic outcomes following vitrectomy and membrane peeling.

**Methods:** We retrospectively reviewed the clinical records and imaging data from 95 patients with epiretinal membranes (ERM) who underwent pars plana vitrectomy and membrane peeling. To be included in this analysis, subjects had to have an ERM involving the central macula that resulted in vision less than 20/30, and a complete clinical record and SD-OCT volume scan obtained preoperatively and 1 and 2 month postoperatively. Exclusion criteria include the presence of any other retinal or visually significant disease. In addition to patient demographic data and duration of disease, retinal thickness, OCT characteristics of the ERM (reflectivity, thickness, type of attachment), and best-corrected visual acuity (BCVA) were collected at baseline and the follow-up visits. Pearson correlation was used to assess the association between baseline characteristics and 1 and 2 month post-surgical visual outcomes.

**Results:** The average age of patients was 70 years and 73% were female. Average pre-operative BCVA was 20/47 (ratio 0.42 +/- 0.17). The mean pre-operative foveal central subfield (FCS) thickness as measured by SD-OCT was 425 um (SD +/- 64 um). The mean post-operative Month 2 BCVA was 20/38 (ratio 0.52 +/- 0.18) and the mean post-op Month 2 FCS thickness was 346 (SD +/- 0.44). Preoperative visual acuity and foveal thickness positively correlated with postoperative visual acuity and foveal thickness (r=0.18, 0.48, respectively). Additionally, we found the number of days between diagnosis and surgery demonstrated a weak negative correlation with post-operative visual acuity.

**Conclusions:** For patients with ERM, early membrane removal and higher preoperative visual acuity resulted in improved visual prognosis postoperatively. These findings support the notion that chronicity of ERM and delay to surgery can negatively impact the overall post-operative visual prognosis.

**Commercial Relationships:** Sahar Bedree, None; Linda A. Lam, None; Srinivas Sadda, Allergan (C), Genentech (C), Regeneron (C), Optos (C), Carl Zeiss Meditec (C), Optos (F), Carl Zeiss Meditec (F), Optovue (F)

**Support:** Research to Prevent Blindness

**Program Number:** 3312 Poster Board Number: B0200

**Presentation Time:** 11:00 AM - 12:45 PM

**Blue Perfluoro-n-Octane and Blue Perfluorodecaline Stability and Residue Testing**

**Fabio M. Trindade1,3, Jose Garcia-Arumi1,2, 1Universitat Autonoma de Barcelona, Barcelona, Spain; 2Hospital Vall D’Hebron, Barcelona, Spain; 3Hospital Dr. Nélido Mendonça, Funchal, Portugal.

**Purpose:** Complications have been reported with perfluorocarbon liquids (PFCLs), which can be attributed to the transparent nature of these compounds. The use of colored PFCLs would help in a more complete and safe removal of these substances. Our objectives were to test (1) stability, (2) residue formation inside the vial and (3) evaluation of residual pigment inside the eye of blue perfluoro-n-octane (PFnO) and blue perfluorodecaline (PFD).

**Methods:** A total of 15 enucleated pig eyes, 10 vials of blue PFnO and 10 vials of blue PFD were used:

1. Stability: 2 groups (blue PFnO and blue PFD), 23G pars plana vitrectomy (PPV), colored PFCL introduction and endophotocoagulation during 15 minutes were performed. After the colored PFCL was aspirated to a syringe and MALDI-TOF
EXPLORER 70107 analysis performed.
(2) Residue formation inside the vial: 2 groups (blue PFnO and blue PFD). The vials were stored at 20°C at 4°C for 7 and 14 days. Residue formation was evaluated at day 7 and day 14. Freshly prepared samples served as control.
(3) Evaluation of residual pigment inside the pig eye: 3 groups (blue PFnO, blue PFD and blue powder used to color the PFCL). 23G PPV, colored PFCL/powder introduction and air exchange were performed. After the eye was fixed in 10% formaldehyde solution and residual pigment analysis performed.

Results: (1) Stability: MALDI-TOF EXPLORER 70107 analysis did not show alteration of both colored PFCLs analyzed when comparing previous composition of those substances to the composition of the same substance after laser stress test.
(2) Residue formation inside the vial: (a) Blue PFD: no crystals were seen except when solutions were stored at 4°C for 7 days. (b) Blue PFnO: crystals were seen in all situations.
(3) Evaluation of residual pigment inside the pig eye: (a) Blue PFD: discrete amounts of vitreous residues were observed. (b) Blue PFnO: small blue particles homogeneously localized on whole retinal surface and also on the vitreous. (c) Blue powder: particles not homogeneously distributed on the retinal surface and large blue particles/agglomerates detected in the vitreous samples.

Conclusions: In a phakic enucleated pig eye extraction of all PFCL residues was not possible. Although blue PFnO was as stable as blue PFD, it showed more residue formation and residual pigment than PFD. Only blue PFD presents the correct characteristics to proceed to the phase I clinical trial on human subjects.

Commercial Relationships: Fabio M. Trindade, None; Jose Garcia-Arundi, None

Program Number: 3313 Poster Board Number: B0201
Presentation Time: 11:00 AM - 12:45 PM
Relation between retinal vessel printings and visual acuity in patients with macular epiretinal membranes
Roberto dell’Omo, Francesco Cifariello, Mariuccia Cassetta, Di Salvatore Angela, Antonio De Lena, Mariaelena Filippelli, Ermanno dell’Omo, Ciro Costagliola. Medicine and Health Sciences, University of Molise, Campobasso, Italy.

Purpose: To compare visual acuity (VA) and metamorphopsia scores in patients affected by idiopathic macular epiretinal membranes (ERM) respectively associated or not to retinal vessel printings (RVPs) on fundus autofluorescence (FAF) imaging.

RVPs are hyperautofluorescent lines parallel to retinal vessel and are a sign of retinal translocation.

Methods: Cross-sectional study. The enrolled patients were divided in two groups on the basis of the presence/absence on FAF imaging of RVPs.

LogMAR best-corrected VA measured using ETDRS charts, spectral-domain optical coherence tomography (sd-OCT) and FAF using the Spectralis HRA+OCT (Heidelberg Engineering, Heidelberg, Germany) were recorded in each case. The eyes showing irregularity or disruption of the hyperreflective outer retinal lines at the fovea by OCT were excluded. Metamorphopsia scores were evaluated using M-charts (Inami Co., Tokyo, Japan).

Central foveal thickness (CFT) and average foveal thickness (AFT) [1-mm area centered on the umbo] were automatically calculated using the integrated software of the machine. The Mann-Withney U-test was used to compare the data. P<0.05 was considered statistically significant.

Results: Fifteen patients were recruited for each group. CFT, AFT and horizontal and vertical metamorphopsia scores did not differ between the two groups (P=1.0, 0.7, 0.5 and 0.7 respectively).

Median best-corrected VA was 0.4 [95% confidence interval 0.2-0.5] and 0.15 [95% confidence interval 0.1-0.3] in the group with and without RVPs respectively and such difference was statistically significant (P=0.007).

Conclusions: FAF is an elegant and non-invasive tool to evaluate tangential retinal contraction in patients affected by ERMs. The reason why only some eyes with ERM and evidence of associated retinal contraction show RVPs has to be elucidated.

In this study similar CFT, AFT and metamorphopsia scores were found in the group with and in the group without RVPs.

However, eyes with RVPs resulted to have lower VAs in comparison to eyes without RVPs.

The lower VA recorded in the eyes with RVPs might be secondary to the more rapid development of retinal contraction caused by the ERM in comparison to eyes showing no RVPs.

Commercial Relationships: Roberto dell’Omo, None; Francesco Cifariello, None; Mariuccia Cassetta, None; Di Salvatore Angela, None; Antonio De Lena, None; Mariaelena Filippelli, None; Ermanno dell’Omo, None; Ciro Costagliola, None

Program Number: 3314 Poster Board Number: B0202
Presentation Time: 11:00 AM - 12:45 PM
Two-year Results of AcrySof Toric Intraocular Lens Implantation in Patients with Combined Microincision Vitrectomy Surgery and Phacoemulsification
Dong Ho Park, Jin Young Lee, Jae Pil Shin, In Taek Kim. Ophthalmology, Kyungpook National Univ Hospital, Daegu, Republic of Korea.

Purpose: To evaluate the effects and stability of AcrySof toric intraocular lens (IOL) implantation in patients who had combined microincision vitrectomy surgery (MIVS) and phacoemulsification for vitreoretinal diseases and cataract with corneal astigmatism.

Methods: A retrospective comparative study with 20 patients (20 eyes) who had combined 23-gauge MIVS and phacoemulsification with regular corneal astigmatism (>1.00 diopters) was done. Ten eyes had toric IOL and 10 eyes had non-toric IOL implantation. Main outcome measures were uncorrected visual acuity (UCVA), refractive cylinder, and toric IOL axis rotation at postoperative periods 1, 6, 12, 18, and 24.

Results: The mean UCVA of toric IOL was better than non-toric IOL at each postoperative period (p=0.019, 0.001, 0.007, 0.004, and 0.001, respectively). The mean absolute residual refractive cylinder of toric IOL was less than non-toric IOL at each postoperative period (p=0.001, <0.001, <0.001, <0.001 and <0.001, respectively). At month 24, the mean toric IOL axis rotation was 3.3±2.1°, which was within 5° in 80% and within 10° in 100%.

Conclusions: Toric IOL implantation could be an effective method of correcting corneal astigmatism in patients who have vitreoretinal diseases and cataract. The toric IOL showed good rotational stability, even in vitrectomized eyes for 24 months.

Commercial Relationships: Dong Ho Park, None; Jin Young Lee, None; Jae Pil Shin, None; In Taek Kim, None

Program Number: 3315 Poster Board Number: B0203
Presentation Time: 11:00 AM - 12:45 PM
Retinal Unfolding after Vitrectomy for Idiopathic Macular Pucker
Mads Kofod, Morten D. de La Cour. University of Copenhagen, Glostrup, Denmark.

Purpose: To quantify retinal vessel movement following vitrectomy for idiopathic macular pucker. By measuring retinal vessel movement following removal of macular pucker we can describe how much and

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How fast the retina unfolds after vitrectomy.

Methods: Quantification of retinal vessel movement was measured by identification of retinal vessel branch points or features in aligned Spectralis OCT scanner infrared fundus images. The location of the same retinal vessel feature was analyzed before surgery, one month, three months, six months and 12 months following surgery. Patients included in this study were participating in a randomized clinical trial on early surgery of macular pucker. Retinal vessel movement in nine macular subfields was summed to an estimate of total retinal vessel movement called retinal tangential movement. Retinal thickness was measured by 20x20 degree OCT scans at each visit. Data is presented as mean and 95% confidence intervals.

Results: The images of thirteen patients were analyzed in this study. Mean best corrected visual acuity measured on ETDRS charts was 76.2 (70.3-82.1) ETDRS letters before surgery. Following surgery it initially fell to 71 (63.8-78.2) ETDRS letters at one month post-surgery but increased to 76.4 (70.6-82.2) ETDRS at three months, 82.5 (78.7-86.4) ETDRS letters at six months and 81.3 (78.1-84.5) ETDRS letters at 12 months. Retinal tangential movement was 680 (495-865) µm after one month and increased to 734 (454-1014)µm after three months, 782 (529-1035)µm at six months and 885 (651-1119)µm after 12 months. These retinal tangential movements increased over time but no statistically significant correlation was shown. Retinal thickness reduction statistically significantly with time (p=0.010).

Conclusions: The study, despite its small size, found two common patterns following vitrectomy. One subgroup show fast unfolding of the retinal vessels within the first month following surgery. In these patients no significant retinal unfolding occurs after the first month. A second subset of patients showed slow unfolding with continued increased retinal tangential movement following surgery. A larger study is needed to successfully describe the difference between these groups and better estimate when the process of retinal unfolding is complete.

Commercial Relationships: Mads Kofod, None; Morten D. de La Cour, Alcon (C), Novartis (C)

Clinical Trial: NCT00902629

Program Number: 3316 Poster Board Number: B0204

Presentation Time: 11:00 AM - 12:45 PM

Clouding of intraocular silicone oil in the absence of emulsification

Martin S. Spitzer1, Jan Willem de Vries2, Andreas Herrmann2, Karl-Ulrich Bartz-Schmidt1, Sascha Dammeier1,1, Ophthalmology, Tuebingen University Eye Center, Tuebingen, Germany; 2University of Groningen, Zernike Institute for Advanced Materials Department of Polymer Chemistry, Groningen, Netherlands.

Purpose: Intraocular silicone oil impurities may cause intraocular inflammation, retinal toxicity and emulsification resulting in opacification of the optical media. However, clouding or color changing of silicone oil in the absence of emulsification have not been described before.

Methods: Twelve patients who received 5000cs medical grade silicone oil developed opacification of the intraocular silicone oil tamponade without emulsification within few weeks after surgery. The medical charts and surgical notes of the respective patients were investigated in order to find out whether a common cause for the opaque oil could be determined. Moreover, a variety of physicochemical analyses were performed in order to reveal molecular differences in between different production lots of silicone oil.

Results: Chart review revealed that all patients that presented with "dirty" intraocular silicone oil had received silicone oil from the same production lot from a single manufacturer. All other patients that also had silicone oil instillation from the same production lot were traced, informed and scheduled for silicone oil removal. No obvious retinal toxicity due to the impure oil could be observed. Unused vials from the respective lot and samples obtained from patients during silicone oil removal were analyzed by matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI TOF), gel permeation chromatography (GPC), high performance liquid chromatography (HPLC) and thermogravimetric analysis (TGA). The first three methods all show the presence of what presumably is a small molecular weight compound in the reference silicone oil, but that is absent in the opaque lot. Surprisingly, TGA revealed that the opaque lot is more temperature stable than the reference oil that did not show opacification. As such it is hypothesized that the reference lot contains a stabilizing agent against coloration, but that has a negative influence on the thermal stability of the product.

Conclusions: Opacification of intraocular silicone oil could be traced down to a specific production batch of one manufacturer.

Commercial Relationships: Martin S. Spitzer, None; Jan Willem de Vries, None; Andreas Herrmann, None; Karl-Ulrich Bartz-Schmidt, Retina Implant (P); Sascha Dammeier, None

Program Number: 3317 Poster Board Number: B0205

Presentation Time: 11:00 AM - 12:45 PM

25-gauge Vitrectomy For Macular Holes With And Without Retinal Detachment In Highly Myopic Eyes

Francesco Boscia, Nicola Recchimurzo, Luigi Sborgia, Ermete Giancipoli, Claudio Furino. Ophthalmology, University of Bari, Bari, Italy.

Purpose: To evaluate the surgical outcome of 25-gauge pars plana vitrectomy (PPV) for macular holes (MH) in highly myopic eyes, with and without retinal detachment (RD).

Methods: Fourteen consecutive highly myopic eyes with MH, with and without RD, were retrospectively studied. Outcome measures were visual acuity (VA), closure of MH, anatomical retinal reattachment, SD-OCT findings, and complications. Mean patients’ age was 59.2 years (range 40-77). Mean preoperative VA was 0.45±0.68 log MAR. Mean refraction error was -13.15 (range -6 to -22.0 diopters). Mean axial length was 29.4±2.9 mm. In all cases 25-gauge PPV (Constellation, Alcon) was performed with triamcinolone visualization. Premacular membrane peeling and ICG-assisted ILM peeling were carried out. Tamponading agents were in 4 cases SF6 24%, in 5 cases air, and in the others silicone oil 1000 cs.

Results: After a follow-up of 6.14±1 months (range 4-9), VA was preserved (pre-op 0.45±0.68 log MAR, post-op 0.3±0.43 log MAR, p=0.15). Anatomical flattening of the macular hole, confirmed by SD-OCT, and successful retinal reattachment were achieved in all eyes. In 3 eyes the MH remained open. IOP was stable during the whole follow-up (pre-op 14.55±3.17 mmHg, post-op 16±2.72 mmHg, p=0.55). Patients with photoreceptor layer disruption had significantly worse final best-corrected VA (P = 0.035, 0.005). None of the patients had hypotony (≤5 mmHg), choroidal detachment or endophthalmitis.

Conclusions: Twenty-five-gauge transconjunctival sutureless PPV showed favorable results for the management of myopic macular hole with or without retinal detachment. Photoreceptor layer defects on SD-OCT persist despite surgery, limiting visual outcome

Commercial Relationships: Francesco Boscia, None; Nicola Recchimurzo, None; Luigi Sborgia, None; Ermete Giancipoli, None; Claudio Furino, None

Program Number: 3318 Poster Board Number: B0206

Presentation Time: 11:00 AM - 12:45 PM

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Robot-assisted vitrectomy

Mathias M. Maier1, M. Ali Nasseri2, Daniel M. Zapp1, Martin Eder2, Karin Kobuch1, Chris P. Lohmann1, Alois Knoll2. Ophthalmology, Klinikum rechts der Isar, Technische Universität München, Munich, Germany; 1Robotics and Embedded Systems, Technische Universität München, Munich, Germany.

Purpose: To find a way performing current ophthalmonic operations with more precision and getting future possibilities for new treatment options. Retinal Vein Occlusion (RVO) is an example of such a disease with currently no generally approved surgical treatment. One promising treatment concept of RVO is injecting clot-dissolving drugs like tissue Plasminogen Activator (tPA) directly into the blocked vessel. The procedure of placing a needle and specifically holding the needle tip perfectly still during the injection is practically impossible for human surgeons. This work investigates the design and development of a surgical assistance robot which overcomes the current limitations and moreover provides new surgical abilities.

Methods: Based on 23G pars-plana vitrectomy equipment, an additional interface tool was designed to dock to the patients eye and stabilize the instrument. The robot itself consists of 6 piezo motors (5 prismatic, 1 rotational) with sub-nanometer precision but the encoders used have micrometer precision. Therefore the final linear precision of the device is around 5μm and the angular precision of the robot is 5.88×10^-5 rad which should be largely sufficient for all ophthalmonic applications. The working volume of the robot resembles a box of 50X50X50 mm with 360 degrees of free tool rotation while the maximum linear velocity of the tool motion in different directions is 40mm/s and the maximum linear velocity of the robot is 1.11 rad/s. The robot was designed with an adjustable RCM (remote center of motion) point that allows it to be configured to manipulate the tool pivoting around the insertion point.

Results: A compact 6DOF robot smaller than a human hand and with the weight of 312gr was developed. This robot is mounted on the patients head and is able to use conventional surgical tools. The surgeon controls the robot using a master console located close to the head of the patient. The compatibility in an ophthalmic operation environment was evaluated. This evaluation approved that the robot won’t conflict other surgical devices such as the microscope and assured that the surgical area remains accessible for the surgeon. The entire setup was already tested successfully in pig eyes.

Conclusions: This abstract introduced the developed robot to assist the surgeons during vitrectomical surgery. Although vein cannulation is the main objective of this project, it enables other retinal micro manipulation procedures as well.

Commercial Relationships: Mathias M. Maier, None; M. Ali Nasseri, P729210111 (P); Daniel M. Zapp, None; Martin Eder, None; Karin Kobuch, None; Chris P. Lohmann, None; Alois Knoll, None

Program Number: 3319 Poster Board Number: B0207
Presentation Time: 11:00 AM - 12:45 PM

Macular hole formation after vitrectomy: Preventable?

Rebecca Kim, Yu Cheol Kim, Kwang-Soo Kim. Department of Ophthalmology, Dongsan Medical Center, Keimyung University, Daegu, Republic of Korea.

Purpose: To evaluate the secondary macular hole formation after vitrectomy and to know the preventability.

Methods: A retrospective review of 27 patients (28 eyes) who had secondary macular hole formation after vitrectomy. Age, sex, best-corrected visual acuity (BCVA) before and after primary vitrectomy, operation methods, duration between the vitrectomy and the secondary macular hole surgery, the causes of the primary vitreectomy, preoperative and postoperative macular findings with optical coherence tomography (OCT) and fundus examination, and BCVA before and after macular hole surgery were recorded.

Results: Of 28 eyes which had undergone vitrectomy, 12 eyes had proliferative diabetic retinopathy, 6 eyes had rhegmatogenous retinal detachment, 2 eyes had branch retinal vein occlusion, 3 eyes had age-related macular degeneration, and 5 eyes had trauma such as eyeball rupture or intraocular foreign body. Mean duration between primary vitrectomy and macular hole formation was 20.4 months (4 days-115 months). The estimated causes of macular hole formation included cystoid macular edema (CME) (n=13), thinning of macula (n=6), thickening of internal limiting membrane (ILM) and/or recurrence of preretinal membrane (PRM) (n=7), recurrence of subretinal hemorrhage (n=1) and macular damage during primary vitrectomy (n=2). Macular holes were closed successfully with additional surgical procedures except 1 eye with CME after primary vitrectomy. Final BCVA after macular hole surgery decreased when compared with BCVA before macular hole formation except 7 eyes (25%) and macular hole related with CME showed the worst visual prognosis.

Conclusions: Secondary macular hole formations may be occurred from sustained CME, macular thinning and tangential traction due to thickening of ILM and/or recurrence of PRM after primary vitrectomy. Secondary macular holes had poor visual outcome in comparing to idiopathic macular holes. Therefore close observation of vulnerable macula and additional surgical maneuver in proper time after primary vitrectomy are necessary for preventing secondary macular hole formation. In addition, we have to take effort to avoid excessive tractional force to macula not to makeiatrogenic damage during removal of PRM.

Commercial Relationships: Rebecca Kim, None; Yu Cheol Kim, None; Kwang-Soo Kim, None

Program Number: 3320 Poster Board Number: B0208
Presentation Time: 11:00 AM - 12:45 PM

Surgical outcomes of idiopathic epiretinal membrane with good visual acuity

Sung Il Kim1, Seung ho Cho2, Sung Who Park2, Ik Soo Byon1, Jaeho Jung1, Ji-Eun Lee2, Ji Eun E. Lee1. 1Ophthalmology, Pusan National University Hospital, Busan, Republic of Korea; 2Ophthalmology, Yangsan Pusan National University Hospital, Yangsan, Republic of Korea.

Purpose: Surgical treatment is recommended for idiopathic epiretinal membrane (ERM) with visual acuity of 20/40 or worse traditionally. Recent developments of surgical instruments and technique have been expanded indications for vitrectomy. The surgical outcomes for ERM with good visual acuity were investigated to evaluate rationale for early intervention for ERM.

Methods: Twenty four eyes which had been diagnosed as idiopathic ERM with best corrected visual acuity (BCVA) better than 20/40 and were followed up for 12 months or more after vitrectomy and membrane removal, were investigated retrospectively. BCVA, metamorphopsia, central foveal thickness, foveal shape, and status of photoreceptor inner/outer segment (IS/OS) junction were assessed based on the medical records and optical coherence tomography (OCT) images.

Results: The mean follow-up period was 25.7 ± 13.3 months. The mean BCVA was not significantly changed from 0.26 ± 0.06 at baseline to 0.26 ± 0.22 at 6 months, and 0.27 ± 0.29 at 12 months after surgery. BCVA improved more than 2 lines in six eyes, and decreased more than 2 lines in 6 eyes. Four eyes had metamorphopsia, which persisted in all of them at 12 months. Central foveal thickness decreased significantly from 417 ± 86 μm at baseline to 335 ± 46 μm at 6 months (p<0.01), and 331 ± 42 μm at 1 year (p<0.01). Of 17 eyes without foveal depression at baseline, 11 eyes...
had foveal depression after 6.6 months in average. IS/OS signal was intact in 19 eyes, attenuated in three eyes, and disrupted in two eyes at baseline. It was recovered to be intact in 21 eyes, attenuated in two eyes, and disrupted in one eye at 12 months.

**Conclusions:** Vitrectomy for ERM with good visual acuity resulted in anatomical improvement, but not functional improvement. Worsening of visual acuity was not rare, and would be related with surgical trauma. Decision for surgery in idiopathic epiretinal membrane with good visual acuity should be made cautiously, and the surgeon should attempt to minimize surgical trauma in the operation.

**Commercial Relationships:** Sung Il Kim, None; Seung ho Cho, None; Sung Who Park, None; Ik Soo Byon, None; Jaeho Jung, None; Ji-Eun Lee, None; Ji Eun E. Lee, None

**Program Number:** 3321 Poster Board Number: B0209  
**Presentation Time:** 11:00 AM - 12:45 PM  
**Mechanical Properties of Vitreous Humor in Eye Pairs**  

**Purpose:** To investigate the possibility of bilateral symmetry in the viscoelastic properties of the porcine vitreous humor.

**Methods:** Bilateral porcine eyes were obtained from Sierra for Medical Science (Whittier, CA) within 10 hours post mortem (four animals, n=8). For each sample a 2 mm cross sclerotomy was made in the sclera 3 mm posterior to the limbus. A 1.7 mm diameter cylindrical probe attached to an AR2000 rheometer was subsequently inserted 7 mm into the vitreous cavity via the sclerotomy. The creep compliance of the vitreous samples was obtained by setting the rheometer to apply a constant 1 μN·m torque for 300 seconds and record the rotational displacement of the rod.

**Results:** Creep compliance is the quotient of the strain of a material and the constant stress applied. Figure 1 shows the creep compliance of four porcine eye pairs as a function of time under stress.

The plateau compliance (i.e. the value at which the plot begins to flatten) is characteristic of the inverse of the elasticity or stiffness of the vitreous humor. By inspection, the plateau compliance as well as the general trends of the compliance plots are very similar for the paired eyes of individual animals. There exists, however, distinct differences between those values of the different animals. In fact, there was only a 0.01 ± 0.004 1/Pa average difference in plateau compliance within the pairs but a 0.178 ± 0.043 1/Pa average difference between the pairs.

**Conclusions:** We found a clear similarity between the viscoelastic responses of the vitreous humor in the right and left eye of a pair. This similarity may have some clinical correlation with bilateral vitreoretinal pathologies.

**Commercial Relationships:** Pirouz Kavehpour, None; Ryan Freeman, None; Rommina Vedadghavami, None; Sanket U. Shah, None; Rouzbeh Amini, None; Jean-Pierre Hubschman, None

**Program Number:** 3322 Poster Board Number: B0210  
**Presentation Time:** 11:00 AM - 12:45 PM  
**The impact of hospital admission on systemic adverse outcomes after pediatric vitreoretinal surgery**  

**Purpose:** The intent of this study was to investigate the indications for hospital admission, rate of systemic complications, and rate of urgent return visits after vitreoretinal surgery in the pediatric population (6 months to 16 years).

**Methods:** Medical charts of 2307 patients who underwent vitreoretinal surgery from January 2002 through November 2011 at the Vanderbilt Eye Institute in Nashville, Tennessee, were reviewed. Of these, 151 charts were identified as patients between 6 months and 16 years of age undergoing outpatient vitreoretinal surgery and analyzed for baseline demographic information, indication for surgery, hospital admission, systemic complications, and urgent return visits within 30 days of surgery. Logistic regression and chi square analysis were performed to correlate hospital admission with indications for surgery and urgent return visits.

**Results:** All 151 patients underwent general anesthesia. Indications for surgery were retinal detachment (39%), trauma (31%), glaucoma (16%), cataract (5%), uveitis (5%), epiretinal membrane (1%), persistent fetal vasculature (1%), and vitreous hemorrhage (1%).

There were no documented systemic complications during or within 30 days of surgery. Thirty (20%) patients were admitted for one of the following surgical indications: retinal detachment (43%), glaucoma (37%), trauma (13%), retinoschisis (3%) and uveitis (3%). The mean age of admitted patients was 8.2 ± 5.0 years versus 8.8 ± 4.5 years for those not admitted (P=0.5). Surgical indication of glaucoma was significantly associated with hospital admission (P =0.001) while trauma was inversely associated (P = 0.02). There were 11 patients (7%) who had urgent return visits but there was no significant correlation (p=0.5) with patients who had been admitted (10%) and those who had not (7%) been admitted.

**Conclusions:** The most common indications for pediatric vitreoretinal surgery in this series were retinal detachment, trauma and glaucoma. Despite all surgeries being performed under general anesthesia, there were no documented systemic complications in this specific population. Surgery for glaucoma was significantly associated with hospital admission while in contrast trauma was associated with post-operative discharge. Hospital admission did not impact rates of systemic complications or urgent return visits.

**Commercial Relationships:** Richard Y. Hwang, None; Ajay Shalwala, None; Ariana K. Tabing, None; Stephen J. Kim, None
were included. Outcome measures included visual acuity and anatomic success rates with a minimum follow-up of 3 months. Results: Sixty-three eyes of 49 patients were included in the study. All eyes underwent 25-gauge PPV for repair of diabetic tractional retinal detachment. Mean age at the time of surgery was 47.7 years. Mean follow-up was 454.3 days. Forty-six eyes (73.0%) had vitreous hemorrhage present pre-operatively. Forty-two eyes (66.7%) had a rhegmatogenous component to their detachment. The type of tamponade used was as follows: 20 eyes (31.7%) with balanced salt solution, 19 eyes (30.2%) with SF6 gas, 21 eyes (33.3%) with C3F8 gas, and 3 eyes (4.8%) with silicone oil. The average visual acuity improved from pre-operative logarithm of the minimum angle of resolution (logMAR) of 1.58 to a post-operative logMAR of 0.56 (p < 0.0001); six eyes could not be evaluated for change in visual acuity as their pre- or post-operative visual acuity was light perception or worse, thus, could not be converted to logMAR visual acuity). Primary reattachment was achieved in 58 eyes (92.1%). Five eyes (7.9%) reattached; of these, 4 were reattached with a total of 5 surgeries. Attachment at the final visit was achieved in 62 eyes (98.4%). Complications included recurrent vitreous hemorrhage in 14 eyes (22.2%), recurrent vitreous hemorrhage requiring repeat PPV in 6 eyes (9.5%), and epiretinal membrane requiring repeat PPV in 1 eye (1.6%). Three eyes (4.8%) had no light perception vision at their final visit but were attached anatomically.

Conclusions: Twenty-five gauge PPV for tractional retinal detachment secondary to proliferative diabetic retinopathy is an effective procedure for this complex disease. Complication rates are low and comparable to those reported in 20- and 23-gauge vitrectomy.

Commercial Relationships: Kevin Patel, None; Mark S. Dikopf, None; Vikram Setlur, None; Jennifer I. Lim, QLT (F), Genentech (R), Regeneron (R)

Program Number: 3324 Poster Board Number: B0212
Presentation Time: 11:00 AM - 12:45 PM

Visual Acuity Outcomes in Patients Undergoing Epiretinal Membrane (ERM) and Internal Limiting Membrane (ILM) Peel With and Without Intraoperative Intraocular Triamcinolone Shawn Agee, Robert Wang, Richard Winslow. Ophthalmology, University of Texas Southwestern Medical Center, Dallas, TX.

Purpose: To determine if those who underwent vitrectomy for idiopathic ERM with peeling ILM along with administration of intraocular triamcinolone resulted in improved final visual acuity outcomes compared to those not receiving intraocular triamcinolone at the end of the case.

Methods: A retrospective review of medical records for those who underwent vitrectomy with ERM and ILM peeling. Patients included had an idiopathic ERM, vision worse than or equal to 20/60, and returned for at least 12 months of follow up postoperatively. Patients with visual acuity better than 20/60, insufficient follow up, previous vitrectomy, or secondary ERM were excluded from the study. The injection group received intraocular injections of 0.1cc triamcinolone (Kenalog-40; Bristol Myers Squibb, Princeton, NJ) with the suprarnatant removed at the end of the case for biologic purposes, where as the control group did not receive any intraocular steroids. Statistical analysis was performed using independent sample T-tests as well as Mann-Whitney U-tests using MedCalc Software 12.2.1.0 (Mariakerke, Belgium). P values of less than 0.05 were considered statistically significant.

Results: Fifty-eight eyes of 58 patients met the inclusion criteria. The injection group contained 27 eyes and the control group had 31 eyes. There were no statistically significant differences among the preoperative demographics between the two groups. The preoperative average visual acuity in the injection group was 0.66 logMAR, 0.56 logMAR at 1 month, 0.53 logMAR at 3 months, 0.49 logMAR at 6 months, and 0.38 logMAR at 12 months. The baseline/preoperative average visual acuity in the control group was 0.64 logMAR, 0.56 logMAR at 1 month, 0.49 logMAR at 3 months, 0.44 logMAR at 6 months, and 0.40 logMAR at 12 months. Analysis of the data shows that there was no statistically significant difference in the visual acuity at the 12 month endpoint. P=0.8.

Conclusions: Surgery for epiretinal membrane has been the treatment of choice since the 1980's, but new techniques and medical adjuvants have allowed for better outcomes, both anatomically and functionally. Further studies looking at higher intraocular steroid concentrations or perhaps sustained release inserts of steroids may provide better final visual acuity outcomes in those undergoing epiretinal membrane removal.

![Table 1. Visual Acuity](image)

<table>
<thead>
<tr>
<th>Injection Group</th>
<th>logMAR</th>
<th>Snellen Equivalent</th>
<th>Snellen Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>0.66</td>
<td>20/91</td>
<td>20/60-20/200</td>
</tr>
<tr>
<td>1 Month</td>
<td>0.56</td>
<td>20/73</td>
<td>20/30-20/400</td>
</tr>
<tr>
<td>3 Months</td>
<td>0.53</td>
<td>20/68</td>
<td>20/20-20/200</td>
</tr>
<tr>
<td>6 Months</td>
<td>0.49</td>
<td>20/62</td>
<td>20/20-20/200</td>
</tr>
<tr>
<td>12 Months</td>
<td>0.38</td>
<td>20/48</td>
<td>20/20-20/200</td>
</tr>
<tr>
<td>Control Group</td>
<td>0.64</td>
<td>20/87</td>
<td>20/60-20/400</td>
</tr>
<tr>
<td>1 Month</td>
<td>0.56</td>
<td>20/73</td>
<td>20/30-20/400</td>
</tr>
<tr>
<td>3 Months</td>
<td>0.49</td>
<td>20/62</td>
<td>20/20-20/200</td>
</tr>
<tr>
<td>6 Months</td>
<td>0.44</td>
<td>20/55</td>
<td>20/20-20/200</td>
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<tr>
<td>12 Months</td>
<td>0.4</td>
<td>20/50</td>
<td>20/20-20/400</td>
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</table>

Commercial Relationships: Shawn Agee, None; Robert Wang, None; Richard Winslow, None

Program Number: 3325 Poster Board Number: B0213
Presentation Time: 11:00 AM - 12:45 PM

Complications in Heavy Silicone Oil Surgery Hendrik Schwarzer, Babac A. Mazinani, Niklas Plange, Peter Walter, Gernot Roessler. Ophthalmology, RWTH Aachen University, Aachen, Germany.

Purpose: To demonstrate development and complications in heavy silicone oil (HSO) surgery in 100 eyes following primary vitreoretinal surgery.

Methods: 100 eyes were included in this retrospective study in which two different types of heavy silicone oil (HSO) were used, Oxane®HD (Bausch & Lomb, n=27) and Densiron®68 (FLUORON, n=73) respectively. Indication diagnoses were retinal detachments (n=74), complicated macular holes (MH) (n=21) and open globe injuries (n=5). HSO removal was performed after a mean period of 20.2±19.04 weeks. Mean follow-up time was 35.9±51.78 weeks. In 36 eyes silicone oil surgery was combined with cataract extraction, either combined with HSO insertion or removal. Before and after surgery routine examinations included testing of the best corrected visual acuity (BCVA), slit lamp examination, indirect funduscopy, intraocular pressure (IOP) measuring using Goldmann applanation tonometry.

Results: The mean IOP before HSO surgery was 13.3±5.9mmHg and raised to an average maximum of 23.3±8.53mmHg.
postoperatively (p <0.001) with a range between 4 and 50 mmHg. The mean IOP before HSO removal was 15.8 ± 7.15 mmHg and after removal 13.1 ± 4.46 mmHg (p=0.001). The difference of IOP before HSO surgery and after HSO removal was statistically not significant (p=0.86). Secondary IOP raise due to emulsification of the silicone oil endotamponade was seen in 29 eyes after a mean time of 7.8 ± 4.53 weeks. Other complications being observed with HSO installed were persistent corneal erosion (n=3) and prolonged anterior chamber inflammation (n=29) out of which the majority was recurrent after HSO removal. In n=3 eyes recurrent retinal detachment occurred with HSO installed while there were 10 recurrent retinal detachments after HSO removal. In 18 eyes with poor functional prognosis the silicone oil remained permanently for stabilisation. In all other eyes HSO surgery led to satisfactory functional and anatomical results.

Conclusions: According to our analysis HSO surgery might deliver satisfying results in complicated cases of ophthalmological surgery. After HSO removal a prior secondary elevated IOP could be normalised. In most eyes the retinal situation remained stable after HSO removal. However, some severe complications that might occur in the course of time need special attention and treatment and should always be taken into account when making the decision to use HSO in complicated retinal surgery.

Commercial Relationships: Hendrik Schwarzner, None; Babac A. Mazinani, None; Niklas Plange, Implantable Ophthalmic Products (F); Peter Walter, Novartis (R), Bayer (R), Second Sight (R), Bayer (F), Novartis (F); Gernot Roessler, None

Program Number: 3326 Poster Board Number: B0214
Presentation Time: 11:00 AM - 12:45 PM

Purpose: To assess how cannula size and cannula bevel angle effect silicone oil aspiration rates.

Methods: In vitro aspiration rates of silicone oil 1000 and silicone oil 5000 using 20, 23, and 25 gauge cannulas, 23 and 25 gauge cannula adapters, and 20 gauge angiocaths cut beveled and unbeveled were measured. Aspiration rates were determined by timing fixed vacuum suction of silicone oil, then weighing the silicone oil with a precision analytical scale. Three timed trials were performed for each aspiration condition. The results were averaged and aspiration rates normalized to grams aspirated per minute.

Results: Normalized aspiration rates (grams/minute) of silicone oil 1000 (fastest to slowest) were: 20 G beveled angiocath (5.96), 23 G trocar with adaptor (3.78), 20 G unbeveled angiocath (3.56), 23 G short tip cannula (2.96), 25 G trocar with adaptor (1.8), 25 G short tip cannula (1.22). Normalized aspiration rates for silicone oil 5000 (fastest to slowest) were: 20 G beveled angiocath (1.16), 23 G trocar with adaptor (0.77), 20 G unbeveled angiocath (0.66), 23 G short tip cannula (0.59), 25 G trocar with adaptor (0.35), 25 G short tip cannula (0.27).

Conclusions: Aspiration rates of silicone oil are affected by silicone oil viscosity and cannula gauge. Beveling the 20 gauge angiocath tip nearly doubled the silicone oil aspiration rates. Among 23 and 25 gauge trocar systems, the trocar with adaptor demonstrated faster aspiration than short cannula systems.

Commercial Relationships: David Cupp, Alcon (F); Colin A. McCannel, Alcon (S), Thromboogenics (C)

Program Number: 3327 Poster Board Number: B0215
Presentation Time: 11:00 AM - 12:45 PM

The influence of vitreotomy fluidics on the rate of iatrogenic retinal breaks in primary small-gauge vitrectomies

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findings of intraretinal schisis, with or without foveal detachment or macular hole. In the current study of surgical outcomes, patients were required to have at least 6 months of post-operative follow-up.

**Results:** A total of 41 eyes of 38 patients were identified. The average age at the time of surgery was 61.2 years. Macular hole was present in 11 eyes and foveal retinal detachment present in 16 eyes. Internal limiting membrane peeling was performed in 35 eyes. Mean visual acuity at presentation was 20/130, (range 20/30-4/200). At 6 months, mean visual acuity was 20/70, (range 20/20-count fingers). Visual acuity improved in 29/41 (70.7%) patients and was stable in 4 patients. In 14/41 (34.1%) patients, visual acuity was 20/40 or better following surgery. In 12 patients vision was 20/200 or worse following surgery.

Central foveal thickness as measured by OCT was available for 34 patients at baseline, with mean 558 micrometers (range 227-848). Central foveal thickness for 20 patients was available at 6 months with mean 265 micrometers (range 138-459). Re-operation was performed in 11 eyes. Indications for re-operation included foveal retinal detachment, macular hole, rhegmatogenous retinal detachment, elevated intraocular pressure, vitreous hemorrhage and cataract.

**Conclusions:** Visual acuity and anatomic outcomes were generally improved or stabilized for myopic macular retinoschisis.

**Commercial Relationships:** Jonathan S. Chang, None; Anita R. Shane, None; Michael Engelbert, Genentech (C), BMS (C); William E. Smiddy, None; Stanley Chang, Alcon Laboratories (C), Alimera Sciences (C); Harry W. Flynn, None

**Program Number:** 3329 Poster Board Number: B0217

**Presentation Time:** 11:00 AM - 12:45 PM

**Comparison of fundus-viewing quality using wide-field observation system through various intraocular lenses**

Haruhiko Yamada. Ophthalmology, Kansai Medical University, Hirakata, Japan; Yamada Eye Clinic, Sakai, Japan.

**Purpose:** Many kinds of intraocular lenses (IOLs) are available, but the quality of vision during vitrectomy with IOL implantation has not been well documented. In this study, we aimed to clarify differences of fundus-viewing quality using a wide-field observation system by quantifying fundus images taken through various IOLs.

**Methods:** We used an artificial model eye (Eyetechn Co, USA) with a 100 dot/cm2 grid pattern at the fundus. An IOL was properly engaged and was exchangeable. A Leica 841 surgical microscope with a wide field attachment (Leica Microsystems GMBH, Germany) and a CCD camera were used to capture fundus images through the IOLs. The IOLs tested were: X-70, X-60 (Santen), AR40e, ZA9003 (Abbott), SA60AT, SN60WF (Alcon), VA60BBR, VA65BB, PY60R, PY60AD, and VA70AD (HOYA). The ZA9003, SN60WF, PY60AD, and VA70AD lenses were aspherical (Asph) and all other IOLs were spherical (Sph). X-70 and VA70AD had a 7.0 mm optic diameter (OD), VA65BB had a 6.5 mm OD and the others had a 6.0 mm OD. All images were processed using Photoshop 4.0 software (Adobe Co, USA). The images were evaluated as follows: 1) the number of dots visible through the lens, 2) the area of the dots visible through the lens, and 3) the average area of the dots visible through the lens. ANOVA was used for statistical analysis.

**Results:** 1) X-70 and X-60 had the highest number of dots. 2) The visible dot area was largest in X70 (p=0.0002-0.026). 3) The average area of the dots was bigger in X-70 and VA65 IOLs, but this did not reach statistical significance. There were no statistical differences between Asph IOLs and Sph IOLs, or between IOLs with larger optics and smaller optics except the average area of the dots was greater in larger IOLs.

**Conclusions:** Compared to a similar study we previously performed in which we analyzed the observation quality through various IOLs using a direct observation system, the differences of the quality parameters between IOLs in a wide-field viewing system are thought to be very small. We hypothesized that the difference of the viewing quality between the direct and wide-field systems may be due to the direction of the reflecting light, which is crossed through the IOL in the wide-field system.

**Commercial Relationships:** Haruhiko Yamada, None

**Program Number:** 3330 Poster Board Number: B0218

**Presentation Time:** 11:00 AM - 12:45 PM

**A new 25G back flush needle**

Shumpei Ohata1, Kenji Someya2, Masashi Kakinoki1, Masahito Ohji1.

1Ophthalmology, Shiga University of Medical Science, Otsu, Japan; 2HOYA CORPORATION, Tokyo, Japan.

**Purpose:** A straight type back-flush needle is usually used in vitreous surgery, however contact of the back flush needle with the wide-angle viewing system may limit the working range. We developed a new 25G back-flush needle that can provide wider working range in the fundus than the regular straight type back flush needle. The purpose is to show the usefulness of the new back-flush needle through a simulation and actual vitrectomy.

**Methods:** The new back flush needle is shown in the figure. We simulated the working range in the eye and compared the working range with that with the regular straight back-flush needle under three types of wide-angle viewing system including Peyman-Wessels-Landerds (PWL), Resight and BIOM. We defined the visual axis as 0 degree, insertion side as minus degree and the opposite side as plus degree.

**Results:** In simulations of the regular straight-back-flush needle, the working range was limited up to +29 degrees in PWL, +8 degrees in Resight and +2 degrees in BIOM. It was expanded up to -27 degrees, -20 degrees and -27 degrees, respectively. Thus, the hummingbird back-flush needle provides wider working range than the strait type back-flush needle. The wider working range in the hummingbird back-flush needle was confirmed in vitrectomy.

**Conclusions:** The new 25G hummingbird back-flush needle provides wider working range than straight type back flush needle under the wide-angle viewing system. It may be useful in vitrectomy under wide-angle viewing system.

**Commercial Relationships:** Shumpei Ohata, None; Kenji Someya, HOYA CORPORATION (E); Masashi Kakinoki, None; Masahito Ohji, Alcon (F), Novaris (F), Novarits (C), Pfizer (C), Santen (F), Santen (C), Shionogi (C), Carl Zeiss (C), Bayer (C), Senju (C)

**Support:** None in the Support

**Program Number:** 3331 Poster Board Number: B0219

**Presentation Time:** 11:00 AM - 12:45 PM

**Ex Vivo Evaluation of Thermosensitive Hydrogels as Vitreous Substitutes**

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**Purpose:** Currently used vitreous substitutes such as gases or perfluorocarbon liquids are not compatible to stay intraocular for a longer time and silicone oils can lead to numerous complications. For this reasons recurrence rates of retinal detachment are still high. Therefore, it was envisioned to use injectable thermosensitive hydrogels as substitutes of the vitreous body, which gelate upon heating to body temperature. For this purpose, blends of hyaluronic acid and Poly(ethylene glycol-b-propylene glycol-b-ethylene glycol) (PEPE) were used in concentrations of 20 wt.% eq. solutions.

**Methods:** During the development phase of the hydrogels, tests on the operative handling had been conducted to examine thermosensitivity, its reversibility and injectivity through cannulas of different size. According to ISO 10993-5 tests for in vitro toxicity have been done to evaluate cell proliferation and cytotoxicity of mouse fibroblast cells L929 both qualitatively, by bringing cells and gel into direct contact, and quantitatively, through a test with dilutions of the hydrogels. To investigate gel effects on the retina in an organotypical model of the eye, perfusion tissue culture has been performed followed by a histological evaluation.

**Results:** Tests showed repeatedly reversible gelation of the at room temperature liquid gel after 2 minutes at 37°C, no spontaneous miscibility with an aqueous phase, but after 3 days with an aqueous phase at 37°C the gel became liquid through water absorption and lost its gelation ability. The hydrogel is injectable trough cannulas of 27g without losing its characteristics. In cell culture no migration of cells into the gel could be observed but cytotoxicity of the tested substances was found. Histological findings after perfusion tissue culture showed that the gel layer was adjacent to the retina but there were some toxic reactions of the retina, in terms of a disintegration of the internal layers, in those areas where there was direct contact between the hydrogel and the retina.

**Conclusions:** The hydrogels' physical properties suggest them as promising candidates for future eye surgery, but the biocompatibility has to be improved. One key point is to keep osmolarity and pH constant and close to physiological values.

**Commercial Relationships:** Sabrina M. Bohnacker, None; Nadine Hagedorn, Fluoron GmbH (E), alamedics GmbH& Co. KG (E); Stefan Kamlage, None; Wilfried Kugler, Fluoron GmbH (E); Andreas Lendlein, None; Mathias M. Maier, None; Axel T. Neffe, None; Arthur Messner, Dr. Schmidt Intraocularlinsen GmbH (E); Christine Korb, None; Karin Kohbich, None

**Support:** BMBF AZ13N0326

**Program Number:** 3333 Poster Board Number: B0220
**Presentation Time:** 11:00 AM - 12:45 PM

**Serum protein analysis of patients with different vitreoretinal diseases by means of antibody microarrays**

**Methods:** Serum samples were collected from 63 patients with macular pucker (n=19), idiopathic macular hole (n=16), proliferative diabetic retinopathy (DR, n=10), rhegmatogenous (n=6) or tractional (n=9) retinal detachment and neovascular age-related macular degeneration (AMD, n=3). As control group, serum samples from 27 healthy subjects were used. Protein expression levels were estimated using customized antibody microarrays. The 29 spotted antibodies represented families of proteins known to be involved in a variety of important biological pathways, including heat shock proteins (HSPs), proteins of the complement pathway and cytokines. Emitted fluorescence signals were digitized and spot intensities were compared to estimate changes in protein expression.

**Results:** Complex patterns of proteins could be detected in all clinical groups. Furthermore, differences in mean protein intensity could be detected in all diseases in comparison to the control cohort. Mean intensities of some proteins, e.g. Interleukin 2, HSP 27, and Protein S100A8 were lower in serum in all clinical groups compared controls. Some of the detected protein levels were about 3 fold higher in only some clinical groups , for example PEDF: > 3.6 change in AMD or II-1-beta: > 2.8 in DR.

With respect to the control subjects with no ocular disease, protein abundance of complement protein C9, HSP 90 and HSP 70 was lower in serum especially in the group of patients with neovascular age-related macular degeneration (protein expression in patients compared to controls is decreased about 50%).

**Conclusions:** Our study provides a proteomic analysis of the serum proteome and reveals protein alterations in the included clinical groups compared to the group of healthy subjects. Each vitreoretinal disease altered a unique set of proteins. These potential biomarkers could lead to new insights in underlying pathomechanisms of the analyzed diseases.

**Commercial Relationships:** Christina A. Korb, None; Sabine Beck, None; Katrin Lorenz, Sensimed AG (F), Sensimed AG (R), MSD (F), Ivantis Inc (F), BAYER (R); Alireza Mirshahi, None; Bernhard Stoffels, None; Norbert Pfeffer, Sensimed AG (F), Sensimed AG (R), MSD (F), MSD (R), Alcon (F), Allergan (F), Novartis (F), Novartis (R), Bayer (F), Boehringer Ingelheim (F), Carl Zeiss Meditec (F), Chibret (F), Nidek (F), Pfizer (F), Santen (F), Santen (R), Topcon (F), Ivantis Inc (F), Ivantis Inc (R); Franz H. Grus, None

**Support:** travel grant from Novartis

**Program Number:** 3333 Poster Board Number: B0221
**Presentation Time:** 11:00 AM - 12:45 PM

**Outcomes of Idiopathic Macular Hole Surgery**

**Purpose:** The present study was performed to investigate the surgical findings and outcomes after vitrectomy for full-thickness macular hole.

**Methods:** Case records of 19 patients (19 eyes) who underwent vitrectomy for visually symptomatic macular hole in a 2 year period up to July 2012 were reviewed. All patients underwent vitrectomy and internal limiting membrane (ILM) peeling with staining by indocyanine green (ICG) dye. Intraoperative and postoperative complications were documented, and preoperative and final postoperative best-corrected visual acuities (BCVA) were recorded at periods of 1-4, 5-8, 9-12, and 13-24 months postoperatively. When necessary for the statistical analysis, data were transformed to logMAR format. Postoperative OCT to evaluate for macular hole
closure was performed in the majority of patients and compared with preoperative findings.

**Results:** Surgery was performed on 19 eyes of 19 patients. Patient follow-up ranged from 2 weeks to 24 months, with a mean duration of 9 months. Visual acuity improved postoperatively in 17 of 19 (89%) patients, with a mean improvement of ≥ 3 Snellen lines which was statistically significant at periods of four and twelve months postoperatively (p= 0.034 and 0.029 respectively by the single factor ANOVA test). Preoperative and postoperative OCT images were obtained in 18 of 19 eyes (95%) and were judged to have improved or normalized in 16 of 18 (89%) of these patients.

**Conclusions:** In our series of 19 patients, vitrectomy in general was found to be beneficial with regard to both visual acuity and anatomic (OCT) foveal appearance in the majority of patients. The few patients that did not show visual or anatomic improvement after surgery had chronic macular holes and proliferative vitreoretinopathy, factors that are recognized as important predictors of anatomical and visual success in macular hole surgery.

**Commercial Relationships:** Janet Manalac, None; John Frisbee, None; D Anthony Mazzulla, None

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**Program Number:** 3334
**Poster Board Number:** B0222
**Presentation Time:** 11:00 AM - 12:45 PM
**Name:** Inner Retinal Dimples Occur Following Inner Limiting Membrane Peeling Without Staining
**Abstract:** Franck Amouyal, Carolyn K. Pan, Steven D. Schwartz, Jean-Pierre Hubschman. Jules Stein Eye Institute, Los Angeles, CA.

**Purpose:** To report and analyze the appearance and evolution of inner retinal defects, often referred to as dimples, after inner limiting membrane (ILM) peeling for full thickness macular hole (FTMH) with spectral-domain optical coherence tomography (SD-OCT).

**Methods:** Retrospective observational case series. Patients with the diagnosis of FTMH, who underwent 23-gauge pars plana vitrectomy with ILM peeling without adjunctive ILM staining were included. All surgeries were performed by a single surgeon (J-PH). The inner retina was evaluated pre-operatively and post-operatively with both standard SD-OCT and en face OCT. Inner retinal defects were detected, measured and analyzed 1, 3, 6 and 12 months after surgery. Snellen visual acuity (VA) was also assessed for functional evaluation pre-operatively and post-operatively.

**Results:** A total of 50 patients were identified. No inner retinal dimples were observed preoperatively. Of the 50 patients, inner retinal dimples involving the nerve fiber layer (NFL) were observed in 39 patients (78%) in the first post-operative month. These appear to enlarge with time. Average pre-operative and post-operative VA were 20/125 and 20/50, respectively; no difference were found between patients with dimples and patients without dimples.

**Conclusions:** Inner retinal dimples are commonly observed following ILM peeling, emerging weeks after the surgery. These lesions appear to evolve in the post-operative period. No staining agents were used in this study, which negates the prior hypothesis that these defects were consequences of dyes commonly used in membrane peeling. Other hypotheses include injury to or loss of Müller cells that are necessary to maintain adhesion of NFLbundles or trauma incurred with the « pinch » to initiate peeling. The etiology of these dimples is still unclear and further studies with more patients and longer follow-up are indicated.

**Commercial Relationships:** Franck Amouyal, None; Carolyn K. Pan, None; Steven D. Schwartz, None; Jean-Pierre Hubschman, None

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**Program Number:** 3335
**Poster Board Number:** B0223
**Presentation Time:** 11:00 AM - 12:45 PM
**Name:** 23-Gauge Transconjunctival Sutureless Pars Plana Vitrectomy In Different Posterior Segment Diseases. Complications, Visual Outcomes And Results: An Update

**Abstract:** Marcelo Zas 1, Carina P. Rinaudo, Lucas Adamo, Gaston Gomez Caride, Pablo Chiaradia 2. Ophthalmology, Hosp de Clinicas, Univ of Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina; 2Centro de Ojos Quilmes, Buenos Aires, Argentina.

**Purpose:** To assess the effectiveness, visual outcomes and results of the transconjunctival sutureless pars plana vitrectomy for several posterior segment diseases in our Retina Section.

**Methods:** A retrospective chart review of 125 consecutive 23-gauge vitrectomy cases done by the vitreoretinal surgeons of our staff. All surgeries were performed using the two-step 23-gauge system. The indications for surgical intervention were proliferative diabetic retinopathy (PDR) (n=46), rhegmatogenous retinal detachment (RRD) (n=28, 20 pseudophakic and 8 phakic), traumatic retinal detachment and PVR (n=13), macular epiretinal membrane (MEM) (n=17), macular hole (MH) (n=7), endophthalmitis (n=3), and vitreous hemorrhage secondary to branch retinal vein occlusion (BRVO) (n=11). All patients had at least a 6-month follow-up. Main outcome measures included visual acuity (VA), intraocular pressure (IOP), OCT pre and post-op, and operative complications.

**Results:** Mean overall VA was counting fingers (range light perception to 0.2) preoperatively and 0.3 (range 0.1 to 0.7) postoperatively (p=0.001). Statistically significant VA improvement was observed in eyes with PDR, RRD, MEM, MH endophthalmitis, BRVO and PVR cases. Mean IOP was 16 mmHg (range 10-26 mmHg) preoperatively and 16.4 mmHg (range 10-21 mmHg) at 2 months postoperatively. Worrising complications were 5 cases of hypotony occurring on day 1, 1 case of endophthalmitis and 4 cases of pseudophakic retinal detachment that recurred.

**Conclusions:** In this updated series we have found that 23-gauge transconjunctival sutureless vitrectomy is an effective and safe surgical technique in the management of vitreoretinal diseases. This minimally invasive and completely sutureless technique appears to decrease the operating time and improve patient comfort. A comparison with 25 and 27-gauge technique is needed.

**Commercial Relationships:** Marcelo Zas, None; Carina P. Rinaudo, None; Lucas Adamo, None; Gaston Gomez Caride, None; Pablo Chiaradia, None

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**Program Number:** 3336
**Poster Board Number:** B0224
**Presentation Time:** 11:00 AM - 12:45 PM
**Name:** Effects of Ozurdex on Persistent Macular Edema After Vitrectomy with Membrane Peeling

**Abstract:** John Khadem,1,2, Shayan Khorsandzadeh3, Jane Pan2, Cristina Pieroni1,2,1Ophthalmology, New York University, New York, NY; 2Ophthalmology, New York Eye and Ear infirmary, New York, NY; 3Metropolitan State University of Denver, Denver, CO.

**Purpose:** The purpose of this study was to evaluate the effect of Ozurdex, FDA approved sustained release dexamethasone intravitreal implant, on macular thickness post epiretinal membrane removal surgery. Macular thickening and edema are often associated with epiretinal membranes and thought to contribute to symptoms of decreased visual acuity and metamorphopsia. Although vitrectomy with membrane peeling can often result in an improvement of both the retinal morphology and patient symptomatology in this condition, macular edema often persists after successful surgery with or without ILM removal and often leads to persistence of some symptoms

**Methods:** Methods: IRB approval was obtained for this study. A prospective randomized six months clinical trial was performed with Ozurdex 0.7mg injections at various times (Early and late intervention) and stages of macular edema after ERM surgery in...
contrast to other current standard care such as Avastin 1.25mg, Lucentis 0.5mg, Triamcinolone (4mg), and topical steroids.

Results: Thirty-three patients were followed monthly for six months. ETDRS visual acuity and ocular coherence tomography (OCT) imaging were obtained at each monthly visit. Analysis of the six months OCT data shows a trend with reduction in thickness, an average of 29µm change, 10 weeks following the injection of Ozurdex on the group treated at least 3 months after the peeling procedure. The control group, which received an average of one steroid injection during the six months trial, showed no improvement in thickness reduction or visual acuity. An average improvement of one line gain in visual acuity was recorded from the group that received late intervention (six months post surgery) with Ozurdex in the first two months following the injection. Early intervention with Ozurdex mostly stabilized the visual acuity, whereas late intervention resulted in an improvement.

Conclusions: Conclusions: Results of this study suggest a role for Ozurdex in ERM-associated macular edema inhibition; however, further study with larger sample size is required to confer statistical significance.

Commercial Relationships: John Khadem, Allergan, Inc (F); Shayan Khorsandzadeh, None; Jane Pan, None; Cristina Pieroni, Allergan (F)

Support: Allergan, Inc

Clinical Trial: 3433-001

Program Number: 3337 Poster Board Number: B0225

Presentation Time: 11:00 AM - 12:45 PM

Macular function in patients with macular pucker treated with 23 gauge vitrectomy

Giancarlo Dell’Avversana Orabona, Angelo Rampone, Luigi Di Perna, Francesco Testa, Settimio Rossi, Michele Della Corte, Francesca Simonelli. Second University of Naples, Napoli, Italy.

Purpose: The aim of this study is to investigate the effect of via pars plana 23 gauge vitrectomy in patients with macular pucker.

Methods: We followed up 7 patients with macular pucker (4 females and 3 males; age ranged from 67 to 86 years mean 75.9 ± 5.9 SD). The following examinations were performed before and after surgery: ophtalmoslooscopic exam, best corrected visual acuity (BCVA), optical coherence tomography (OCT), microperimetry (MP-1) and multifocal electroretinography (mfERG). In particular, we studied the P1 wave in the six macular concentric rings as already described in literature. The surgical treatment was a via pars plana 23 gauge vitrectomy with ILM peeling and water tamponade.

Results: The pre-operative BCVA ranged from 0.2 to 0.5 (mean 0.33 ± 0.14) and from 0.3 to 1 (mean 0.73 ± 0.28) post-operative. The OCT exam had shown a pre-operative central macular thickness ranged from 366 to 605 µm (mean 458 ± 82.25 µm) and from 358 to 480 µm (mean 420 ± 122 µm) post-operative. MP-1 had shown a preoperative sensitivity from 9.6 to 14.5 dB (mean 11.9 ± 1.7 dB) and a postoperative sensitivity from 7.8 to 18.0 dB (mean 13.4 ± 10.2 dB). In all patients the improvement of BCVA, OCT macular thickness and MP-1 macular sensitivity was not statistically significant.

Instead, as regards mfERG responses, after surgery, namely the number of recordable P1 waves in the second ring increased significantly (Fisher test, p: 0.029) and the P1 wave amplitude in the third ring decreased significantly after surgery (Wilcoxon Signed Rank Test, p: 0.04). Moreover, we observed a significant correlation between the central macular thickness and the Inner/Outer Segment junction photoreceptor layer (Spearman rho=−0.79; p: 0.03).

Conclusions: This study revealed that surgical treatment of macular pucker with the MLI peeling induced a reappearance of electrical activity in the central macular region (in the second ring) probably due to the resolution of the macular traction, but, at same time, P-wave amplitude in peri-central macular region (third ring) was reduced, probably, for the removal of generative electrical stimulus cells during the surgery. The surgical treatment also resulted in an improvement of BCVA, OCT macular thickness and MP-1 macular sensitivity, even if no statistically significant differences were observed.

Commercial Relationships: Giancarlo Dell’Avversana Orabona, None; Angelo Rampone, None; Luigi Di Perna, None; Francesco Testa, None; Settimio Rossi, None; Michele Della Corte, None; Francesca Simonelli, None

Program Number: 3338 Poster Board Number: B0226

Presentation Time: 11:00 AM - 12:45 PM

Association of Retinal Sensitivity and Morphology in epiretinal membranes before and after vitrectomy

Patricia Udaondo, Ana Hervás Ontiveros, Salvador García-Delpech, David Salom, Sebastian Martinez-Castillo, Manuel Diaz-Llopis. Ophthalmology, La Fe University Hospital, Valencia, Spain.

Purpose: Epiretinal membranes (ERM) could lead to significant metamorphopsia and vision loss, that is why a concise evaluation of the macular function in ERM is needed. The assessment of central retinal thickness by OCT predominantly supplies information of the anatomical rather than the functional outcome. The use of microperimetry, that measures the retinal sensitivity, has greatly improved the psychophysical testing role in the evaluation of any maculopathy including ERM. Vitrectomy with internal limiting membrane (ILM) peeling is used to treat eyes with ERM. The purpose of this study is to analyze the correlation of visual function with macular morphological and volumetric changes of the retinal layers before and after the idiopathic ERM surgery.

Methods: 10 patients with ERM underwent a vitrectomy with ILM peeling. A complete standardized evaluation was performed including best corrected visual acuity (BCVA). A macular integrity assessment device named MAIA (Topcon Medical Systems, Inc.) was used to measure visual sensitivity and fixation stability and the Optical Coherence Tomography 3D OCT-1000 (Topcon Medical Systems, Inc.) to study the anatomical profile and central macular thickness (CMT) in all cases before and after the surgery.

Results: In all cases the complete ERM was removed without complication and was confirmed by OCT but regarding BCVA only 6 patients improved a mean of 2 lines of visual acuity; 3 maintained the same vision and 1 lost one line. We analyzed the correlation between the morphological changes and the visual function before and after surgery to better understand the visual results after surgery.

Conclusions: Microperimetry can provide useful information of retinal function and analyze the progression of the functional loss or improvement after surgical treatments. Functional (central visual acuity and visual field) and morphologic parameters (retinal thickness) are significantly related.

Commercial Relationships: Patricia Udaondo, None; Ana Hervás Ontiveros, None; Salvador García-Delpech, None; David Salom, None; Sebastian Martinez-Castillo, None; Manuel Diaz-Llopis, None

Program Number: 3339 Poster Board Number: B0227

Presentation Time: 11:00 AM - 12:45 PM

Vitrectomy with Intentional Bulbous Retinal Detachment to Mobilize and Move Recent Subfoveal Hemorrhage in Age-related Macular Degeneration

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Deepthi Reddy, Matthew H. Oltmanns, Mathew R. Sapp, Robert E. Morris. Ophthalmology, University of Alabama-Birmingham, Birmingham, AL; Retina Specialists of Alabama, Birmingham, AL.

**Purpose:** To describe a novel “Mobilize and Move” (M&M) approach and determine the ability of extensive subretinal recombinant tissue plasminogen activator (rtPA) irrigation during vitrectomy with gas tamponade to rapidly mobilize and move recent subfoveal hemorrhage in Age-Related Macular Degeneration (ARMD) to an extra-foveal location.

**Methods:** This is a retrospective consecutive case series of patients (N=6) with ARMD and recent subfoveal hemorrhage that underwent the M&M technique. A standard 3-port 25 gauge pars plana vitrectomy is performed. Next, using a 32 gauge Lambert needle, rtPA, 25µG/0.1mL, is injected into the subretinal space in the area of the clot, loosening the clot from its adherences to the retina and RPE (“Mobilize”). Additional rtPA is injected into the subretinal space contiguous with the area of hemorrhage but outside the infero-temporal arcade, in an area of normal retina. A total of 0.5-0.7 cc is injected into the subretinal space. This step creates an area that the loosened clot can move into via subsequent pneumatic displacement (“Move”). Fifty percent of fluid is removed from the vitreous cavity (air-fluid exchange), followed by an exchange of air for 15% sulfur hexafluoride. Patients are then positioned 4 hours supine followed by face down positioning for 12-14 hours, to facilitate pneumatic displacement.

**Results:** Snellen acuity improved from 20/1074 pre-op to 20/135 3-6 weeks post-op (P=0.03). Visual acuity past 6 months post op (mean 9.33 months) was 20/148 (P=0.07). All 6 eyes had total clearing of subfoveal blood on post-op week 1.

**Conclusions:** After a recent submacular hemorrhage, the rapid resolution of blood is the primary controllable variable in pursuing optimal return of visual acuity/central visual field. Such resolution is most certainly achieved by mobilizing and moving the hemorrhage as here described, rather than by awaiting spontaneous resolution, or employing lesser measures. In large hemorrhages, consideration can be given to M&M vitrectomy, simply to resolve the submacular component, as an alternative to high risk “giant retinotomy” with be given to M&M vitrectomy, simply to resolve the submacular component, as an alternative to high risk “giant retinotomy” with

**Commercial Relationships:** Deepthi Reddy, None; Matthew H. Oltmanns, None; Mathew R. Sapp, None; Robert E. Morris, None

Program Number: 3340 Poster Board Number: B0228Presentation Time: 11:00 AM - 12:45 PM

**Morphological Change of Inner Retinal Layer on Spectral Domain Optical Coherence Tomography following Macular Hole Surgery**

Hyung-Woo Kwak, Kook Young Kim, Taegi Kim, Kyung Hoon Seo, Seung-Young Yu. Ophthalmology, Kyung Hee University Hospital, Seoul, Republic of Korea.

**Purpose:** To investigate the morphological changes of the inner retinal layer by spectral-domain optical coherence tomography (SD-OCT) after idiopathic full thickness macular hole surgery.

**Methods:** This retrospective study examined 52 eyes of 49 patients with macular holes closed surgically following vitrectomy. All patients were followed postoperatively for more than 6 months. Cross-sectional and retinal surface images were obtained using SD-OCT (Cirrus HD-OCT; Carl Zeiss Meditec, Dublin, CA) before and after surgery. In 40 of the 52 eyes, macular ganglion cell-inner plexiform layer (GCIPL) thickness was assessed by SD-OCT. In 24 of the 52 eyes, fundus autofluorescence (FAF) was analyzed.

**Results:** The incidence of dissociated optic nerve fiber layer (DONFL) increased gradually over time after surgery: 22 eyes (42.3%, 1 month), 41 eyes (78.8%, 3 months), and 46 eyes (88.5%, 6 months) by cross-sectional imaging; 23 eyes (44.2%, 1 month), 39 eyes (75.0%, 3 months), and 43 eyes (82.7%, 6 months) by retinal surface imaging; and 15 eyes (28.8%, 1 month), 33 eyes (63.5%, 3 months), and 36 eyes (69.2%, 6 months) by color fundus photography. 57.7% had defects of only the retinal nerve fiber layer (RNFL) and 30.8% had defects in the inner plexiform layer at 6 months after surgery. The GCIPL thickness of all subfields were significantly decreased (p<0.05), and the temporal GCIPL thickness decreased more than nasal GCIPL (p<0.001). Postoperative BCVA did not differ significantly based on the depth of the DONFL (p = 0.299). There were no changes in FAf in the area with DONFL.

**Conclusions:** The incidence of DONFL increased to 80% at 6 months after surgery. The healing process after vitrectomy for MH is not limited to the RNFL affecting deeper structural changes. Further investigations are required to evaluate the pathophysiologic mechanism of inner retinal change after MH surgery.

**Commercial Relationships:** Hyung-Woo Kwak, None; Kook Young Kim, None; Taegi Kim, None; Kyung Hoon Seo, None; Seung-Young Yu, None

Program Number: 3341 Poster Board Number: B0229Presentation Time: 11:00 AM - 12:45 PM

**Triamcinolone Acetonide (TA) Assisted Removal of Internal Limiting Membrane (ILM)**

Homayoun Tabandeh, David S. Boyer, David Liao. Retina Vitreous Assoc Med Group, Los Angeles, CA.

**Purpose:** Staining of ILM may be associated with toxicity, increased cost, and increased surgical time. Recently, there have been reports of infectious endophthalmitis associated with the use of some of these staining agents. Specckling of ILM by TA assists in visualization and removal of ILM. The purpose of the current study was to evaluate the status of the perifoveal ILM after TA-assisted stripping of ILM.

**Methods:** Interventional, non-comparative, clinical case series. Participants included patients undergoing removal of ILM as part of macular hole or ERM surgery. The ILM was visualized by TA and removed with intraocular ILM forceps. Indocyanine green (ICG) was used to visualize the status of the remaining ILM. Quality of intraoperative visualization of retina was graded as good, fair, or poor. The extent of ILM removal was graded as: 1) Complete removal of perifoveal ILM, 2) >90% removal of Perifoveal ILM, 3) 75-90% removal of perifoveal ILM, 4) 50-75% removal of perifoveal ILM, 5) < 50% removal of ILM, and 6) ILM removal with TA visualization was aborted and ILM peeling was completed by staining with ICG.

**Results:** 21 eyes of 21 patients were included in the study. Intraoperative visualization of retina was graded as good in 18 eyes, fair in 6 eyes, and poor in 2 eyes. Complete removal of perifoveal ILM (grade 1) was achieved in 21 (81%) eyes. ILM removal was grade 2 in 2 eye (8%), grade 3 in 1 eye, and grade 5 in 1 eye. In one eye ICG had to be used for visualization and subsequent removal of the ILM (grade 6).

**Conclusions:** TA is a useful adjunct for intraoperative visualization of ILM. In most cases ILM can be removed without a need for staining of ILM, reducing risk of toxicity, infection, and cost. Staining of ILM with dyes such as ICG may be reserved for selected cases with suboptimal visualization. Techniques for ILM removal will be further discussed.

**Commercial Relationships:** Homayoun Tabandeh, Alcon (C), Allergan (C); David S. Boyer, Alcon (C), Allegro (C), Allergan (C), Alcon (C), Allegro (C), Allergan (C), Alcon (C), Allegro (C), Allergan (C)}
Bayer (C), Genentech (C), Glaukos (C), GSK (C), Neurotech (C), Optos (C), Regeneron (C); David Liao, None

Program Number: 3342 Poster Board Number: B0230
Presentation Time: 11:00 AM - 12:45 PM

Vitrectomy outcomes for diabetic vitreous hemorrhage
Gaston Gomez Caride1, Leonardo Ferlini1, Luciano Perrone1, Gerardo Valvecchia1, Marcelo Zas2, \textsuperscript{1}retina, centro de ojos quilmes, quilmes, Argentina; \textsuperscript{2}retina, hospital de clinicas, buenos aires, Argentina.

Purpose: To evaluate the efficacy and safety of 23-gauge transconjunctival sutureless vitrectomy (23-G TSV) in the management of diabetic vitreous hemorrhage in our series.

Methods: Single-center, retrospective, noncomparative series of 33 eyes (33 patients) with diabetic vitreous hemorrhage. All patients underwent pars plana 23-gauge vitrectomy, endolaser panphotocoagulation and perfluoropropane gas (C3F8) was used in all cases, peeling was performed in three cases. All patients had at least 6-month follow-up. Main outcome measures included visual acuity (VA), intraocular pressure (IOP), and intraoperative and postoperative complications.

Results: Mean overall VA was 0.062 Decimal (0.001 to 0.4) preoperatively and 0.229 Decimal (range 0.001 to 0.8) postoperatively. Mean IOP was 15 (range 10-23 mmHg) preoperatively and 15.7 mmHg (range 5-26 mmHg) at 6 months postoperatively. Concerning complications, rhegmatogenous retinal detachment occurred in two eyes and one patient presented hipotony (5 mmhg) one month after surgery.

Conclusions: 23-gauge transconjunctival sutureless vitrectomy offers a safe surgical technique and with fewer intraoperative complications been feasible for the treatment for diabetic vitreous hemorrhage.

Commercial Relationships: Gaston Gomez Caride, None; Leonardo Ferlini, None; Luciano Perrone, None; Gerardo Valvecchia, None; Marcelo Zas, None

Program Number: 3344 Poster Board Number: B0232
Presentation Time: 11:00 AM - 12:45 PM
12 Month Follow-up of Epiretinal Membranectomy

Purpose: To assess the long-term effectiveness of an epiretinal membraneectomy (ERM) surgery and analyze how differences in surgical protocol and demographics affect visual acuity and center point thickness outcomes.

Methods: A retrospective chart review of cases indicating epiretinal membraneectomy surgery with a follow-up of at least 12 months. Differences in surgical protocol that were recorded include the use of gas, type and concentration of gas if used, and size of needle used for the surgery. Other factors collected include length of follow-up, gender, age of patient, history of smoking, history of diabetes, history of hypertension and indication of cataract surgery. Center Point Thickness was measured by Optical Coherence Tomography and visual acuity was measured by the Snellen chart. Clinical assessments were made by 8 retina doctors within a multi-center retina practice.

Results: In total, 282/538 (52.4%) surgeries were eligible for

Commercial Relationships: Narcisa Ianopol, None

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inclusion, which excludes eyes needing re-operation for post-operative complications, eyes with other ocular diseases, or lack of follow-up, with an average follow-up of 9.21 months. 56/282 eyes (19.9%) did not receive cataract surgery pre-operatively, during the 12-month follow-up or up to the date at the time the last data collection was made. There was an average gain of 1.45 lines with an average pre-operative visual acuity of 20/62, 79/282 eyes (28%) gained >3 lines, 19/282 (6.7%) lost >3 lines and 263/282 (93.3%) maintained vision or lost <3 lines of vision. There was an average loss of 104 microns over the course of follow-up from the pre-operation average of 436 microns, 50/282 (17.7%) received gas (SF6, air, or C3F8) during surgery and gained an average of 2.52 lines with an average pre-operative visual acuity of 20/93. The remaining 232/282 (82.3%) did not receive gas with surgery and gained 1.22 lines with an average pre-operation visual acuity of 20/58. 18 patients that were tobacco users at the time of surgery required surgery on average 9 years earlier than non-tobacco users.

**Conclusions:** As opposed to visual acuity and retinal thickness pre-operation, ERM surgery seems to have an effective response in most patients and use of gas may have an added benefit. It was observed that pre-operation visual acuity and center point thickness have an effect on the final outcome. In addition, use of tobacco may cause an earlier need of an ERM but further study may be required.

**Commercial Relationships:** David S. Dyer, None; William Anderson, None; Michael P. Ellis, None

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363 AMD: Morphology and Novel Risk Factors

Tuesday, May 07, 2013 2:45 PM-4:30 PM  
6E Paper Session  
Program #/Board # Range: 3658-3664  
Organizing Section: Retina

**Program Number:** 3658  
**Presentation Time:** 2:45 PM - 3:00 PM  
**Geographic atrophy risk factors in participants of the Comparison of Age-related Macular Degeneration Treatments Trials (CATT)**

Juan E. Grunwald1, Ebenezer Daniel2, Gui-Shuang Ying1, Jiayan Huang1, Glenn J. Jaffe3, Cynthia A. Toth4, Stephanie A. Haystrom5, Stuart L. Fine6, Daniel F. Martin7, Maureen G. Maguire8, 1Ophtalmic-Scheie Eye Inst, Univ of Pennsylvania, Perelman Sch of Med, Philadelphia, PA; 2Ophthalmology, Duke University, Durham, NC; 3Ophthalmology, Cole Eye Institute, Cleveland Clinic, Cleveland, OH; 4Ophtalmology, University of Colorado, Denver, CO.  
**Purpose:** To describe baseline risk factors for geographic atrophy (GA) during anti-VEGF therapy of choroidal neovascularization (CNV) in the Comparison of Age-related Macular Degeneration Treatments Trials (CATT).  
**Methods:** Participants included 1020 CATT participants with no GA visible on digital color photographs (CP) or fluorescein angiograms (FA) at enrollment. Participants were randomly assigned to ranibizumab (0.5mg) or bevacizumab (1.25mg) treatment and to a 2-year monthly or PRN injection dosing regimen, or monthly injections for 1 year and PRN injections the following year. Demographic, baseline ocular characteristics, and baseline lesion features of CP/FA and OCT were evaluated as risk factors for development of GA within 2 years using univariate and multivariate time-dependent Cox proportional hazard models. Adjusted hazard ratios (aHR) and associated 95% confidence intervals (CIs) were estimated. Among 770 participants in the CATT genetic study, the associations between AMD-associated SNPs (CFH, ARMS2, HTRA1, and C3) and risk of GA were evaluated using linear trend p-value, with adjustment for age, gender and smoking status.

**Results:** GA developed in 187 (18.3%) of 1020 participants by 2 years. In multivariate analysis, poor baseline visual acuity, presence of retinal angiomatous proliferation (RAP), absence of blocked fluorescence on FA, presence of GA in the fellow eye, ranimizumab treatment and monthly treatment regimen (Table 1), thinner subretinal fluid, decreased sub-RPE height, and foveal center intra-retinal fluid (Table 2), were independently associated with increased risk of GA. ARMS2 (rs10490924) (aHR=1.7, 95% CI (1.1, 2.7)) and HTRA1 (rs11200638) (aHR=1.8 (1.2, 3.0)) risk alleles were associated with increased incidence of GA, but no association was observed for CFI (rs1061170) (p=0.57) or C3 (rs2230199) (p=0.50).  
**Conclusions:** Approximately one-fifth of CATT participants developed GA within 2 years. Independent baseline risk factors included poor visual acuity, RAP, intra-retinal fluid, monthly dosing, and ranibizumab treatment. ARMS2 and HTRA1 risk genotypes were also associated with incident GA. Anti-VEGF therapy may have a role in the development of GA.

---

**Table 1: Multivariate analysis of baseline risk factors for geographic atrophy (GA) incidence**

<table>
<thead>
<tr>
<th># of Subjects (No. of eyes)</th>
<th>% with GA in 2 years (n)</th>
<th>Adjusted Hazard Ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-retinal fluid (mm2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;0</td>
<td>626</td>
<td>1.54 (2.49)</td>
<td>0.0007</td>
</tr>
<tr>
<td>&lt;0.5 to &lt;=0.95</td>
<td>75</td>
<td>1.33 (0.69, 2.56)</td>
<td>0.34</td>
</tr>
<tr>
<td>&gt;0.5 to &lt;=1.0</td>
<td>277</td>
<td>5.22 (1.98, 13.31)</td>
<td>0.0001</td>
</tr>
<tr>
<td>&gt;1.0 to &lt;=2.0</td>
<td>239</td>
<td>5.21 (0.37, 81.9)</td>
<td>0.26</td>
</tr>
<tr>
<td>&gt;2.0</td>
<td>256</td>
<td>5.22 (2.54, 10.72)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Sub-RPE Height (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;0.5 to &lt;=7</td>
<td>227</td>
<td>5.22 (1.98, 13.31)</td>
<td>0.0001</td>
</tr>
<tr>
<td>&gt;7 to &lt;=15</td>
<td>53</td>
<td>5.21 (0.37, 81.9)</td>
<td>0.26</td>
</tr>
<tr>
<td>&gt;15 to &lt;=25</td>
<td>233</td>
<td>5.24 (0.39, 70.4)</td>
<td>0.0004</td>
</tr>
<tr>
<td>&gt;25</td>
<td>236</td>
<td>5.22 (2.54, 10.72)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Intra-retinal fluid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No fluid</td>
<td>254</td>
<td>20.29 (1.29, 329.3)</td>
<td>0.0017</td>
</tr>
<tr>
<td>Fluid in inner center</td>
<td>249</td>
<td>44 (2.77, 135.1)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Fluid in inner center</td>
<td>442</td>
<td>138 (4.89, 403.1)</td>
<td>0.0004</td>
</tr>
</tbody>
</table>

**Table 2: Multivariate analysis of baseline risk factors for geographic atrophy (GA) incidence**

**Commercial Relationships:** Juan E. Grunwald, None; Ebenezer Daniel, None; Gui-Shuang Ying, None; Jiayan Huang, None; Glenn J. Jaffe, Heidelberg Engineering (C), Regeneron Pharmaceuticals (F), Neurotech USA (C), Abbott (C), Psvida (F), Pfizer (C), Bayer (C), Cynthia A. Toth, Genentech (F), Biopigen (F), Physical Sciences Inc. (F), Unlicensed (P); Stephanie A.
Sustained Severe Visual Acuity Loss in the Comparison of AMD Treatments Trials (CATT)

Gui-Shuang Ying1, Benjamin J. Kim1, Maureen G. Maguire1, Jiayan Huang1, Ebenezer Daniel1, Glenn J. Jaffe2, Daniel F. Martin2, Juan E. Grunwald2. 1Ophthalmology, Scheie Eye Institute, Philadelphia, PA; 2Ophthalmology, Duke University Medical Center, Durham, NC; 2Cole Eye Institute, Cleveland Clinic, Cleveland, OH.

Purpose: To determine the incidence, characteristics, causes and baseline predictors of sustained severe visual acuity (VA) loss during 2-years of anti-VEGF treatment in the Comparison of AMD Treatments Trials (CATT).

Methods: Participants were randomly assigned to treatment with ranibizumab or bevacizumab and to monthly injections for 2 years, PRN injections for 2 years, or monthly injections for 1 year and PRN injections the following year. Masked readers evaluated baseline and follow-up morphology in color fundus photographs (CFP), fluorescein angiograms (FA), and optical coherence tomography (OCT). Sustained severe VA loss was defined as a loss of 15 letters or more from baseline at both weeks 104 and 88. Morphology features at baseline and 2 years were compared between eyes with and without sustained VA loss. A retina specialist reviewed image morphology to determine the likely cause of sustained VA loss.

Results: Among 1030 patients who completed 2 years of follow-up, 61 (6%) developed sustained VA loss of ≥3-lines, including 38 (4%) with sustained VA loss of ≥6-lines. At 2 years, eyes with sustained VA loss had more scarring and geographic atrophy (GA) on CFP and FA especially in the foveal center, and lesions were approximately twice as large (Table 1). On OCT at 2 years, the proportions with intraretinal fluid, subretinal fluid, retinal thinning/thickening, or subretinal hyper reflective material were higher, and retinal thickness or sub-RPE thickness were greater (Table 1). The cause of sustained VA loss included foveal scarring (41%), GA (12%), RPE tear (5%). Most of the remainder (28%) had non-elevated pigmentary abnormalities, some with retinal thinning (15%), and some with retinal thickening (7%). Independent baseline risk factors for sustained VA loss were the presence of GA, larger area of CNV, and bevacizumab treatment (Table 2).

Conclusions: Among CATT participants, sustained VA loss of ≥3-lines occurred in 6% of patients. The development of scar or GA in the fovea center contributed to the majority of the sustained VA loss after 2 years of treatment with ranibizumab or bevacizumab. Treatment targeting the prevention of scar or GA may improve the VA outcomes of anti-VEGF treatment.

Table 1: Comparison of morphology features at 2 Years between patients with and without sustained ≥3-lines VA loss

<table>
<thead>
<tr>
<th>Morphology Features</th>
<th>With Sustained ≥3 Lines VA Loss (%)</th>
<th>Without Sustained ≥3 Lines VA Loss (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFP</td>
<td>61 (6%)</td>
<td>939 (94%)</td>
<td>0.0006</td>
</tr>
<tr>
<td>Baseline geographic atrophy Non-sustained Present 6965 51 (5.3%) 1.0 2.94 (1.6, 6.1)</td>
<td>70 10 (14.3%) 1.0 2.94 (1.6, 6.1)</td>
<td>0.0006</td>
<td></td>
</tr>
<tr>
<td>Baseline area of CNV (DD) &gt;11 mm 417 14 (4.9%) 1.0 0.0076</td>
<td>200 10 (9%) 1.0 0.0076</td>
<td>0.0076</td>
<td></td>
</tr>
<tr>
<td>Drug Group</td>
<td>Ranibizumab 528 24 (4.6%) 1.0 0.03</td>
<td>Bevacizumab 501 37 (7.4%) 1.0 0.183</td>
<td>1.8 (1.3, 3.3)</td>
</tr>
</tbody>
</table>
Purpose: To quantify the ability of retinal features on colour photographs and optical coherence tomography (OCT) line scans to diagnose active neovascular age-related macular degeneration (nAMD) classified by fluorescein angiography (FA).

Methods: Image sets collected as part of the IVAN study were graded prospectively in the Network of Reading Centres UK for presence/absence of haemorrhage and intraretinal fluid cysts (IRF), neuroretinal foveal thickness (NFT) and height of subretinal fluid (SRF) at the foveal centre. FA were graded for presence/absence of leakage (reference standard for activity). Feature discrimination between presence/absence of activity was quantified by receiver operating characteristic curve (ROC) areas. The relative increase/decrease in odds of activity for each parameter was described using positive/negative likelihood ratios (LR+/LR-) and the effect of combining data using logistic regression and ROC statistics.

Results: The prevalence of activity in FAs at baseline (92%) precluded cross-sectional analysis. Data available at 12 and 24 months were: 12 months: 478 colours, 513 OCT, 449 FA; 24 months: 442 colours, 436 OCT, 436 FA. Activity was present in 41% (183/449) and 38% (168/436) of FA at 12 and 24 months. Haemorrhages and IRF were present in 53% (11%) and 186% (36%) at 12 and 35% (8%) and 159% (35%) at 24 months. Median NFT heights (mm) were 0.15 (inter-quartile range (IQR), 0.12 - 0.19) at 12 months, and 0.14 (IQR, 0.11 to 0.18) at 24 months. 14% and 15% of OCTs showed any SRF at 12 and 24 months: median SRF heights where present were 0.07 (0.05 to 0.10) at both times. LR+ and LR- were: haemorrhage 4.38 and 0.84 (12 months), 5.51 and 0.87 (24 months); IRF were 1.72 and 0.72 (12 months), 1.25 and 0.88 (24 months); any SRF 5.47 and 0.76 (12 months), 0.10 and 0.71 (24 months). ROC areas for NFT and SRF, or combinations of features, were consistently ≤0.7 with no cut-off providing useful additional discrimination.

Conclusions: None of the features, separately or in combination, ‘diagnosed’ FA-classified active disease well. Haemorrhage and any SRF have high specificity, so help to ‘rule in’ the presence of activity; however, the majority of FAs classified with active disease did not have these features. The routine adoption of OCT-guided treatment for nAMD needs to be carefully considered.

Commercial Relationships: Simon P. Harding, Novartis (F), Novartis (R); Barnaby C. Reeves, None; Alyson Muldrew, None; David G. Parry, None; Chris Rogers, Novartis (R); Jayashree Sahni, Novartis (R), Allergan (R), Alimera (R); Tunde Peto, None; Usha Chakravarthy, Bayer (C), Novartis (F), Neovista (C), Oraya (F).

Support: National Institute for Health Research Health Technology Assessment programme (project number 07/36/01)

Clinical Trial: ISRCTN92166560

Program Number: 3661

Presentation Time: 3:30 PM - 3:45 PM

Risk Factors for Scarring in the Comparison of Age-related Macular Degeneration Treatments Trials (CATT)

Ebenezer Daniel1, 2, Cynthia A. Toth3, 4, Juan E. Grunwald1, 2, Daniel F. Martin4, Gui-Shuang Ying1, 1, Jiayan Huang4, Glenn J. Jaife3, 5, Stuart L. Fine1, Maureen G. Maguire1, 7. "Department of Ophthalmology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA; 3: Scheie Ophthalmology Reading Center, University of Pennsylvania, Philadelphia, PA; 4: Center for Preventive Ophthalmology and Biostatistics, University of Pennsylvania, Philadelphia, PA; 5: Department of Biomedical Engineering, Duke University, Durham, NC; 6: Duke Reading Center, Duke University Eye Center, Durham, NC; 7: Department of Ophthalmology, Duke University, Durham, NC; 8: Cole Eye Institute, Cleveland Clinic Foundation, Cleveland, OH; 9: Department of Ophthalmology, University of Colorado-Denver, Aurora, CO.

Purpose: To describe risk factors for scarring of neovascularization during anti-VEGF therapy for age-related macular degeneration (AMD).

Methods: Participants with neovascularization were randomly assigned to treatment with ranibizumab (0.5mg) or bevacizumab (1.25mg) and to a dosing regimen of monthly injections for 2 years, PRN injections for 2 years, or monthly injections for 1 year and PRN injections the following year. Demographic, baseline ocular characteristics, and baseline lesion features of color photography, fluorescein angiography, and optical coherence tomography (OCT) were evaluated as risk factors for development of scarring within 2 years using univariate and multivariate time-dependent Cox proportional hazard models. Adjusted hazard ratios (aHR) and associated 95% confidence intervals (CIs) were estimated.

Results: Among 1053 eyes with no scarring at baseline and known scar status, scarring developed in 339 (32%) in the first year and 141 (13%) in the second year. Multivariate analysis (Table) showed increased risk of scarring with classic choroidal neovascularization and blocked fluorescein on angiography at baseline. OCT characteristics at baseline including greater retinal thickness, greater sub-RPE thickness, sub-retinal fluid in the fovea and sub-retinal hyper reflective material were associated with higher risk of scarring while RPE elevation was associated with lower risk. Treatment drug and regimen, and SNPs associated with AMD (CFH, HTRA1, ARMS2, C3) were not associated with incident scar.

Conclusions: Approximately half of the CATT participants developed scarring in two years of anti-VEGF treatment. Scar development did not differ with treatment drug and regimen. A number of baseline fluorescein angiographic and OCT features predict scar development. These risk factors for scarring, which is associated with poor visual outcome, may guide the development of treatments that decrease scarring of neovascular lesions.

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Commercial Relationships: Ebenezer Daniel, None; Cynthia A. Toth, Genentech (F), Biogen (F), Physical Sciences Inc. (F), Unlicensed (P); Juan E. Grunwald, None; Daniel F. Martin, None; Gui-Shuang Ying, None; Jiayan Huang, None; Glenn J. Jaffe, Heidelberg Engineering (C), Regeneron Pharmaceuticals (F), Neurotech USA (C), Abbott (C), Psivida (F), Pfizer (C), Bayer (C); Stuart L. Fine, None; Maureen G. Maguire, Inspire Pharmaceuticals (F), Amakem (F), Idx LLC (F), Merck (C)

Support: U10 EY017823, U10 EY017825, U10 EY017826, U10 EY017828

Clinical Trial: NCT00593450

Program Number: 3662
Presentation Time: 3:45 PM - 4:00 PM

Metabolomic analysis in patients with age related macular degeneration

Sreekumari R. Pushpooth1, 2, Martin A. Fitzpatrick2, Stephen Young2, Yit C. Yang1, James S. Talks1, Graham R. Wallace1. 1Ophthalmology, Royal Victoria Infirmary, Newcastle upon tyne, United Kingdom; 2Translational Inflammation Research, University of Birmingham, Birmingham, United Kingdom; 2Ophthalmology, The Royal Wolverhampton Hospitals NHS Trust, Wolverhampton, United Kingdom.

Purpose: Age related macular degeneration is a complex disease where multiple factors show associations but do not explain the full nature of the disease. We hypothesized that a systems approach based on metabolomic analysis would be able to segregate diseases types and provide insights into the pathology. Metabolomics assesses the broad range of low molecular weight metabolites in biofluids and, since these are influenced by important AMD-related factors including diet, age and smoking, this approach may provide a useful novel window into the AMD-disease process.

Methods: Serum and urine samples were collected from 8 patients with dry and 35 with wet macular degeneration. Serum samples were centrifuged to remove cells, and 0.5ml aliquots stored at -80 degree C. After thawing, serum was filtered through 3kD MW cutoff filter to remove proteins. The filtrate was made with 10% in D2O, 100mM phosphate 0.5mM TMS and pH 7.00. One-dimensional 1H spectra were acquired using a standard spin-echo pulse sequence on a Bruker DRX 600MHz NMR spectrometer equipped with a 1.7mm cryoprobe. 2D JRes spectra were also acquired to aid metabolite identification. Spectra were be segmented into 0.005-ppm (2.5 Hz) chemical shift ‘bins’ between 0.2 and 10.0 ppm, and the spectral area within each bin integrated. Principal component analysis (PCA) and partial least squares discriminant analysis (PLS-DA) of the processed data was conducted using PLS Toolbox (Eigenvector Research) within MATLAB.

Results: The samples from dry AMD patients cluster together reasonably well based on their metabolomics profile. With regards to samples from patients with wet AMD the clustering is far more complex. Several samples from wet AMD locate within the dry AMD cluster. Samples from patients with dry AMD show an increase in arginine, and decreased glucose, lactate, glutamine and reduced glutathione

Conclusions: Metabolomic analysis showed clear separation between body fluid samples from patients with wet and dry AMD. Investigation of the profiles produced identified arginine which may indicate increased nitric oxide production and a decrease in metabolites involved in the oxidative pathway that would support previous findings in AMD. That several samples from patients with wet AMD cluster with samples from dry AMD strongly indicates that common pathways are involved in both types of disease and that dry AMD can develop into the wet form.

Commercial Relationships: Sreekumari R. Pushpooth, None; Martin A. Fitzpatrick, None; Stephen Young, None; Yit C. Yang, Novartis (R); James S. Talks, None; Graham R. Wallace, None

Clinical Trial: 11/ NE0162

Program Number: 3663
Presentation Time: 4:00 PM - 4:15 PM
Circling Mesenchymal Progenitor Cells in Patients with Neovascular Age-Related Macular Degeneration

Scott W. Cousins1, 2, Priyatham S. Mettu1, 2, Tiffany Pridgen1, Sara Crowell1, M. Grazia Spiga1, 2Duke Eye Center/Ophthalmology, Duke University School of Medicine, Durham, NC; 3Immunology, Duke University School of Medicine, Durham, NC.

Purpose: To characterize circulating vascular progenitor cells (VPCs) from the blood of subjects with neovascular age-related macular degeneration (NVAMD). Previously our group has shown that bone marrow-derived mesenchymal progenitor cells (MPCs) regulate the severity and vascular maturation of laser-induced choroidal neovascularization (CNV) in mice.

Methods: Peripheral blood mononuclear cells were isolated from subjects with NVAMD (n=40) and from young, healthy subjects (n=20) and were cultured on a fibronectin/Matrigel substrate supplemented with specific mesenchymal growth factors, using EGM2-MV growth medium. Late-outgrowth colonies appearing after day 7 were characterized until day 30 (passage zero or P0) by number of colonies, morphologic appearance, and population doubling time. Endothelial progenitor cell (EPC) and MPC markers were analyzed in P0, P3, and P5 samples via quantitative RT-PCR and immunofluorescence. In vitro angiogenesis tube assay was used with VPCs co-cultured with HUVEC on Matrigel to assess the functional contribution of VPCs in tube formation and stability for up to 7 days. In NVAMD subjects, VPC culture markers were correlated with CNV morphologic subtypes determined by indocyanine green angiography.

Results: Late-outgrowth colonies were successfully isolated from 35 of 40 NVAMD subjects and from 16 of 20 young, healthy subjects. P0 cultures demonstrated a mixed population of cells in a 90:10 MPC:EPC distribution. P0 MPCs were characterized as CD34+, PDGFR-β+, NG2+, and SMA+ (low), while EPCs were characterized as CD34+ and vWF+. Multiple passages of VPCs beyond P0 demonstrated changing patterns of gene and marker expression with each subsequent passage, especially change in MPC and EPC marker distribution, suggesting culture-induced artifact. Co-culture of VPCs with HUVECs in the tube assay extended the duration of tube stability as compared to HUVECs alone (7 vs. 2 days). P0 VPCs isolated from NVAMD patients with CNV manifesting mature branching arterioles appeared to demonstrate greater proportion of NG2+ (pericyte-like) MPCs as compared to patients with immature vessels or young, healthy controls.

Conclusions: Circulating MPCs can be isolated from the peripheral blood of patients with NVAMD. Isolation of P0 cells with high proportion of NG2 positivity may identify a subset of subjects prone to develop mature CNV with feeder vessels and branching arterioles.

Commercial Relationships: Scott W. Cousins, Alcon (F), Alcon (C), Heidelberg Engineering (C), Narrow River (C), Nordic Biotech (C), PanOptica (C), Pfizer (C), Salutaris Medical Devices (C), Sanofi-Fovea (C), Valeant Ophthalmics (C), Imageon Biotech (I); Priyatham S. Mettu, Salutaris Medical Devices (R); Tiffany Pridgen, None; Sara Crowell, None; M. Grazia Spiga, None

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Subclassification of clinically-indistinguishable AMD patients based on metabolic characteristics

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Purpose: To determine if clinically-indistinguishable AMD patients can be subclassified based on metabolic characteristics.

Methods: We performed metabolicomic analysis using C18 liquid chromatography-Fourier-transform mass spectrometry on frozen plasma samples from 44 AMD patients and 29 controls. Data were collected by a Thermo LTQ-Fourier-transform mass spectrometer from mass/charge ratio (m/z) 85 to 850 over 20 minutes, and peak extraction and quantification of ion intensities were performed by adaptive processing software. Benjamini and Hochberg False Discovery Rate (FDR) correction was employed to account for multiple testing. Principal component analysis (PCA) was performed to identify metabolic features that distinguish AMD patients from controls. Hierarchical Clustering Analysis (HCA) was used to depict the relationship between participants and the metabolites that differentiated AMD patients and controls.

Results: Metabolicomic analysis yielded a total of 2708 m/z features after quality control. Following quantile normalization, replicate averaging, and log2 transformation, m/z features exhibiting greater or less than 0.4-fold change were selected for analysis. With FDR q=0.1, 16 m/z features were significantly different in AMD and controls. HCA using Pearson correlations was applied to the 16 m/z features and the participants; certain m/z features clustered and subsets of individuals clustered as well. The analysis generated 14 clusters of individuals distributed into two major groupings: Group A, made up of 58% controls, and Group B, consisting of 78% AMD patients. Cluster 13 from Group B and Cluster 14 from Group A both consisted entirely of AMD patients but showed complete separation by PCA. FDR analysis of the 2708 m/z features for the individuals in these clusters showed that 715 features significantly differed at q = 0.05 and 335 differed at q = 0.01.

Conclusions: These results show that high-resolution metabolomics can be useful for subclassification of AMD. Metabolic phenotyping may reveal previously unknown pathophysiologic mechanisms of AMD and may help reveal the differences among AMD patients that account for variable disease progression or treatment response.

Commercial Relationships: Milam A. Brantley, None; Youngja Park, None; Megan B. Parks, None; L. Goodwin Burgess, None; Karan Uppal, None; Paul Sternberg, None; Dean P. Jones, None

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Effect of Aldehyde Dehydrogenase 2 on Intravitreal Ranibizumab Treatment for Polypoidal Choroidal Vasculopathy in Japanese Patients

Eiichi Sato, Hiroyuki Kagokawa, Akira Takamiya, Daiki Kameyama, Shinji Ono, Akitoshi Yoshida. Ophthalmology, Asahikawa Medical University, Asahikawa, Japan.

Purpose: Aldehyde dehydrogenase 2 (ALDH2) has a well-established function in the detoxification of reactive aldehyde, in particular ethanol-derived acetaldehyde. ALDH2 also protects against oxidative stress, which has been hypothesized to contribute to the development of age-related macular degeneration. The purpose of this study was to investigate the effect of ALDH2 on ranibizumab...
treatment for polypoidal choroidal vasculopathy (PCV) in Japanese patients.

**Methods:** Twenty-four Japanese patients with PCV (18 men, 6 women; mean age, 73 years) underwent ethanol patch testing (EPT). Each patch was a 15x10x1 mm lint pad stuck to adhesive tape. Just before application, several drops of ethanol (70% v/v) were dripped on the lint pad. The patch was attached to the inner surface of the upper arm of a patient for 7 minutes and then removed. The presence of erythema 10 minutes after removal of the patch was considered positive (deficient levels of ALDH2); the absence of erythema (where ALDH2 was present) was considered positive. The macular thickness (MT) was measured using Fourier-domain optical coherence tomography (RTVue-OCT) before and 1 month after intravitreal ranibizumab (IVR) treatment.

**Results:** We found that 45.9% (11/24) of patients had no erythema on EPT (presence of ALDH2; active-ALDH2 group), and 54.1% (13/24) had erythema (no ALDH2; inactive-ALDH2 group). The MT in the active-ALDH2 group was 465.5 ± 161.5 (mean ± standard deviation) μm before IVR and 353.2 ± 132.5 μm 1 month after IVR, a difference that reached significance (p=0.033). The MT in the inactive-ALDH2 group was 464.8 ± 172.2 μm before IVR and 390.9 ± 255.0 μm 1 month after IVR, a difference that did not reach significance (p=0.084).

**Conclusions:** The MT significantly decreased 1 month after IVR in patients with PCV with active ALDH2. In patients with PCV treated with ranibizumab, ALDH2 may be effective.

**Commercial Relationships:** Ugo Introini, None; Giacinto Triolo, None; Giuseppe Casalino, None; Francesco Bandello, ALLERGAN Inc. (S), NOVARTIS PHARMACEUTICALS CORPORATION (S), FARMILIA-THEA (S), BAYER SCHERING PHARMA (S), PFIZER Inc. (S), ALCON Inc. (S), BAVSCH AND LOMB (S), GENENTECH Inc. (S), ALIMERA SCIENCES Inc. (S), SANOFI AVENTIS (S), THROMBOGENICS (S)

**Support:** Oraya Therapeutics CLH006

**Clinical Trial:** NCT01516294

**Program Number:** 3787 Poster Board Number: B0097

**Presentation Time:** 2:45 PM - 4:30 PM

**Novel Minimally-Invasive Episcleral Brachytherapy for the Treatment of Neovascular Age-Related Macular Degeneration (nAMD): Results of a Twelve Month Prospective Phase I Safety and Tolerability Evaluation**

**Kamaljit S. Balaggra**,1, Leonard Joffe2, Praveen J. Patel1, Baldassare Stea2, Adnan Tufail3, Laurence Marsteller2

1Department of Genetics, Institute of Ophthalmology, London, United Kingdom; 2Medical Retina Service, Moorfields Eye Hospital, London, United Kingdom; 3Vitreoretinal Service, Moorfields Eye Hospital, London, United Kingdom; 4SalutarisMD, Tucson, AZ; 5Ophthalmology, University of Arizona, Tucson, AZ; 6Radiation Oncology, University of Arizona, Tucson, AZ.

**Purpose:** To evaluate the safety and feasibility of a novel episcleral brachytherapy device (SMD-1) for nAMD. Although anti-VEGF treatments have revolutionised the management of nAMD, they fail to significantly improve vision in the majority of patients, with some patients demonstrating no response to treatment. As neovascular regression is not achieved, many patients will likely require lifelong and often frequent invasive intravitreal injections. Radiation has multiple angiostatic properties which could address these issues, and has recently been evaluated using both vitrectomy and stereotactic external beam delivery methods. These approaches, however, are either invasive with predictable adverse effects or necessitate large complex expensive devices. A locally-delivered non-penetrating brachytherapy approach could overcome these limitations.

**Methods:** Six patients received 24Gy radiation over 5.5 minutes directly to the macular CNV by positioning the SMD-1 brachytherapy probe adjacent to the macular sclera via a subtenon retrobulbar approach. The probe was then removed. Patients also received concomitant anti-VEGF injections with further readministration as-needed. Adverse effects and changes in BCVA and macular thickness were evaluated monthly.

**Results:** The procedure was readily performed and was well tolerated with no serious adverse effects. At 3 months, all patients experienced increases in BCVA (mean ±19 ETDRS letters). By 12 months, 3 patients continued to demonstrate improved or stabilised BCVA (mean ±7 letters), 2 of whom required no further anti-VEGF injections during follow-up. All patients demonstrated reduced macular thickness compared with baseline. Three patients demonstrated reductions in BCVA.

**Conclusions:** This prospective study supports the safety and tolerability of this novel device, and its further evaluation in planned larger phase II/III trials.

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The SMD-1 Episceral Brachytherapy for nAMD Device

**Commercial Relationships:** Kamaljit S. Balaggan, None; Reid Schindler, SalutarisMD (F), SalutarisMD (I), SalutarisMD (C), SalutarisMD (S); Leonard Joffe, SalutarisMD (F), SalutarisMD (I), SalutarisMD (S); Praveen J. Patel, Allergan (R), Bayer (C), Novartis UK (C), Heidelberg UK (R), Topcon UK (R), Thrombogenics (C); Baldassare Stea, SalutarisMD (C); Adnan Tufail, Allergan (C), Bayer (C), GSK (C), Oculogics (C), Pfizer (C), Thrombogenics (C), Amakem (C), Heidelberg Engineering (R), Novartis/Alcon (C), Sanofi/Genzyme (C); Laurence Marsteller, SalutarisMD (I), SalutarisMD (P)

**Program Number:** 3788 Poster Board Number: B0098
**Presentation Time:** 2:45 PM - 4:30 PM

**Prospective Study of Pegaptanib in the Treatment of Serous Pigment Epithel Detachments Complicating Age-related Macular Degeneration**

Andras I. Seres1, Huba Kiss2, 1Budapest Retina Associates, Budapest, Hungary; 2Ophthalmology, Semmelweis University, Budapest, Hungary.

**Purpose:** To evaluate the efficacy and safety of pegaptanib in the treatment of serous retinal pigment epithel detachment (PED) in age-related macular (AMD) degeneration and to assess the rate of PED rips associated with this treatment modality.

**Methods:** The study included 30 eyes of 30 patients diagnosed with previously untreated early lesions of PED secondary to AMD. Patients with visual acuity better than 20/100 and PED size less than 6 disc area were enrolled. All patients received pegaptanib intravitreal injections every 6 weeks for one year (9 injections). Best corrected visual acuity, colour and autofluorescence fundus photography and optical coherence tomography were performed each visit, together with fluorescein angiography at baseline and at one year. Primary endpoint was proportion of patients losing 15 or more ETDRS letters at one year. Rates of eyes losing 30 or more letters, rate of gainers, together with the rate of PED rips were calculated.

**Results:** 25 females and 5 males were recruited, the mean age at enrollment was 74 years. Eleven of the 30 patients (37%) lost more than 15 letters, 3 of these had severe visual loss of more than 30 letters. At least 5 letter gain was observed in 3 (10%) cases. Mean change of BCVA was -11 letters. Flattening of the PED was observed in 11 cases, however, mean BCVA loss was still 12 letters in this group mainly due to scarring or persistence of retinal edema. Intra- and subretinal fluid disappeared in 8 eyes. Rupture of the RPE occurred in 2 cases, one further case of RPE rip was observed 19 months after the end of the study, that patient received no treatment in that period. One other rip occurred in an untreated fellow eye.

**Conclusions:** Use of pegaptanib failed to protect our patients from visual loss and RPE rips. No important new safety concerns were found using the drug. The hope that the use of pegaptanib instead of more potent anti-VEGF agents like ranibizumab or bevacizumab might help to avoid RPE rips was not supported by our data.

**Commercial Relationships:** Andras I. Seres, None; Huba Kiss, None

**Support:** Pfizer IIR grant: # GA9000J2

**Clinical Trial:** 2006-006312-30

**Program Number:** 3789 Poster Board Number: B0099
**Presentation Time:** 2:45 PM - 4:30 PM

**Photodynamic therapy, anti-vascular endothelial growth factor therapy, and combination therapy for polypoidal choroidal vasculopathy**

Hae Min Kang, Naeun Lee, Hyoung Jun Koh. Department of Ophthalmology, Yonsei Univ College of Medicine, Seoul, Republic of Korea.

**Purpose:** To compare treatment outcomes of photodynamic therapy (PDT), anti-vascular endothelial growth factor (VEGF) therapy, and combination therapy (PDT with the anti-VEGF therapy ranibizumab) for polypoidal choroidal vasculopathy (PCV).

**Methods:** Among 62 eyes (62 patients) retrospectively reviewed, 19 eyes received PDT only (PDT group), 23 received intravitreal ranibizumab injections only (anti-VEGF group), and 20 received combined PDT with anti-VEGF therapy (combination group). Best-corrected visual acuity (BCVA, logarithm of minimum angle resolution [logMAR]) and recurrence after treatment were compared at baseline and 1, 3, 6, 12, and 24 months.

**Results:** Mean baseline BCVA was 0.68±0.36 logMAR (20/95 Snellen equivalent) in PDT group, 0.67±0.43 logMAR (20/93 Snellen equivalent) in anti-VEGF group, and 0.64±0.35 logMAR (20/87 Snellen equivalent; P=0.723) in combination group. Both PDT and combination groups maintained improvement throughout 24 months, compared with baseline. The mean visual improvement at 24 months was 0.25 logMAR (P=0.013) in the combination group and 0.08 logMAR (P=0.183) in the PDT group, respectively. The anti-VEGF group maintained improvement until 12 months, then had a mean BCVA that was worse than baseline (P=0.673) at 24 months. Combination group mean BCVA was better than those of the PDT group and the anti-VEGF group at each follow-up. During 24-month follow-up, nine PDT group eyes (47.4%), 15 anti-VEGF group eyes (64.9%), and 10 combination group eyes (50.0%) showed at least one recurrence.

**Conclusions:** Visual outcomes but not recurrence rates were better with combination therapy compared to PDT and anti-VEGF monotherapy for 24-month follow-up.

**Commercial Relationships:** Hae Min Kang, None; Naeun Lee, None; Hyoung Jun Koh, None

**Support:** No financial/funding support

**Program Number:** 3790 Poster Board Number: B0100
**Presentation Time:** 2:45 PM - 4:30 PM

**AURORE STUDY: a french multicenter retrospective study in wet AMD patients treated with Verteporfin PDT plus Ranibizumab in routine clinical practice**

Franck Rumen1, Elisabeth Latour2, 1Visteopole, Lagord, France; 2Novartis Pharma, Rueil-Malmaison, France.

**Purpose:** AURORE is a multicenter retrospective observational study that aims to describe the treatment patterns with verteporfin plus ranibizumab in patients with subfoveal wet AMD over 12 months of treatment. The main objective of the study was to assess...
the average number of Ranibizumab intravitreal injections (IVT).

Methods: 132 consecutive wet AMD patients were included by 12 centers. Eyes had to be treatment naïve at inclusion and only be treated with verteporfin plus ranibizumab over the 12-month period following treatment initiation. Ranibizumab treatment had to be initiated with 3 monthly consecutive IVT injections. Verteporfin could be administered from 8 days before up to 12 months after ranibizumab treatment initiation. Mean ETDRS VA change at 12 months vs baseline, average number of verteporfin treatments and average number of monitoring visits over the 12-month period were part of the secondary evaluation criteria. The sample size calculation was performed to provide a minimal absolute precision of ± 0.33 IVT for the main criteria with an SD estimate of 2.1 IVT.

Results: Most included patients were female (66.7%), more than 75 years old (79.5%) at baseline. Mean VA was 50.4 ± 18.5 ETDRS letters and bilateral wAMD was present in 29.8% of the patients at inclusion. Mean lesion size was 1892.4 ± 932.6 µm. Mean follow-up was 11.4 ± 0.7 months. The average number of ranibizumab IVT injections over the follow-up period was 5.4 ± 2.1 (CI 95% [5.1; 5.8]) and the average number of verteporfin treatments was 1.5 ± 0.8 (CI 95% [1.3; 1.6]). Most patients (70.5%) received only one verteporfin treatment. Reduced fluence (RF; ca. 300 mW/cm², 25 J/cm², 83 s) was used. Mean VA change at the end of the follow-up period was 7.4 ± 11.9 letters (CI95% [5.4; 9.5]). The mean number of monitoring visits was 6.4 ± 1.8 (CI95% [6.1; 6.7]) over the follow-up period. 96.2% of eyes lost fewer than 15 letters and 27.3% of eyes gained 15 or more letters.

Conclusions: Ranibizumab combined with reduced fluence verteporfin PDT markedly improved mean VA despite a relatively low number of monitoring visits and of treatments.

Commercial Relationships: Franck Rumen, Novartis (F); Elisabeth Latour, NOVARTIS PHARMA SAS (E)

Program Number: 3791 Poster Board Number: B0101
Presentation Time: 2:45 PM - 4:30 PM

INTRAVITREAL ANTI-VEGF FOLLOWED BY PHOTODYNAMIC THERAPY VERSUS ANTI-VEGF MONOTHERAPY FOR RETINAL ANGIOMATOUS PROLIFERATION

Pietro Monaco1, Ezio Cappello2, Michele Del Borrello1, Antonio Frattolillo1, Luigina Tollot1, Marco Vaccaro2, Francesco Serti2, Mario V. Cigada3, 4. Ophthalmology, San Martino Hospital, Belluno, Italy; 2Ophthalmology, San Bassiano Hospital, Bassiano del Grappa, Italy; 3Eye Clinic, Luigi Sacco Hospital, Milano, Italy.

Purpose: To compare the efficacy of intravitreal anti-vascular endothelial growth factor (VEGF) plus photodynamic therapy (PDT) vs anti-VEGF monotherapy in retinal angiomatosus proliferation (RAP).

Methods: 54 eyes of 48 consecutive patients with newly diagnosed RAP were enrolled in this retrospective interventional study. Group 1 (27 eyes) received combo therapy, group 2 (27 eyes) received anti-VEGF monotherapy. Patients received ranibizumab (0.5 mg/0.05 ml) or bevacizumab injections (1.25 mg/0.05 ml) depending on visual acuity (Italian Healthcare Policy provide ranibizumab if best corrected visual acuity ≥ 0.2). A course of combination therapy (Group 1) consisted of one anti-VEGF injection and single session of standard verteporfin PDT within 10 days. Spot size was minimized to RAP lesion visible in indocyanine green angiography (ICGA). Group 2 received 3 monthly injections of anti-VEGF monotherapy. Best corrected visual acuity (BCVA) with ETDRS charts, complete eye examination including digital dynamic fluorescein and indocyanine green angiography (Heidelberg Engineering) and mean foveal thickness (MFT) using optical coherence tomography (OCT) (Stratus III OCT; Zeiss) were performed at baseline and after 3, 6, 9 and 12 months. Retreatment criteria, with the same therapeutic scheme in each group, were worsening of BCVA and/or deterioration of angiographic or OCT findings.

Results: Mean BCVA improved in Group 1 and worsened at the 12-month in Group 2 (+0.177 LogMar) (P<0.0002, ANOVA). The MFT decreased significantly in both groups (mean change -68 µm in Group 1, -140 µm in Group 2) (P<0.0001, ANOVA).

Conclusions: RAP is a distinct form of exudative AMD with a very poor natural course without an established treatment. In our study combination therapy is more effective than anti-VEGF monotherapy. These findings also suggest a possible benefit of combination therapy in the rate of intravitreal re-injections.

Commercial Relationships: Pietro Monaco, None; Ezio Cappello, None; Michele Del Borrello, None; Antonio Frattolillo, None; Luigina Tollot, None; Marco Vaccaro, None; Francesco Serti, None; Mario V. Cigada, None

Program Number: 3792 Poster Board Number: B0102
Presentation Time: 2:45 PM - 4:30 PM

Long-term Results of Combination Therapy with Half-time Reduced Fluence Photodynamic Therapy and Intravitreal Ranibizumab for Retinal Angiomatous Proliferation

Hirotaka Yokouchi, Masayasu Kitahashi, Madoka Sakurai, Mariko Kubota-Tanai, Takayuki Baba, Shuichi Yamamoto. Ophthalmology, Chiba Univ Graduate School of Med, Chiba, Japan.

Purpose: To determine the efficacy of half-time reduced fluence photodynamic therapy (RF-PDT) combined with intravitreal ranibizumab (IVR) for retinal angiomatosus proliferation (RAP).

Methods: Ten eyes of 10 patients with RAP were studied; there were 2 eyes with RAP stage II A, 3 eyes with stage II B, and 5 eyes with stage III. One course of combination therapy consisted of three injections of IVR at monthly intervals and a single half-time RF-PDT with verteporfin about 1-3 days after the first IVR. The dose and fluence of the half-time RF-PDT were administered according to the standard protocol for age-related macular degeneration (AMD). The laser was applied for 42 seconds guided by the indocyanine green angiographic images. The best-corrected visual acuity (BCVA) in logMAR units and central foveal thickness (CFT) measured on the optical coherence tomographic (OCT) images were examined before and 12 months after treatment.

Results: The BCVA significantly improved from 0.76±0.11 to 0.60±0.10 logMAR units 12 months after the treatment (P<0.01). The BCVA improved by ≥0.15 logMAR units in 6 eyes (60%), remained stable in 3 eyes (30%), and worsened in 1 eye (10%). The CFT was significantly reduced from 613.0±91.8 µm to 217.6±39.1 µm (P=0.001) at 12 months. The CFT decreased by ≥30% in 8 eyes (80%), remained stable in 2 eyes (20%), and worsened in no eye. No additional treatment was required in 6 eyes (60%), but additional IVR was required in 4 eyes. A complete occlusion of the retina-retinal anastomosis (RRA) was achieved and central macular edema (CME) disappeared in 9 eyes at 12 months. The mean number of PDT treatments and mean number of IVR injections during 12 months, including that of the initial regimen, was 1 and 3.6, respectively. No complications such as severe vision loss, endophthalmitis, occlusion of the choriocapillaris, or systemic events developed.

Conclusions: Combined IVR and half-time RF-PDT for RAP effectively maintained or improved visual acuity and reduced the exudation for at least 12 months. Although further evaluations with a larger number of patients and a longer follow-up are required, our results suggest a beneficial effect of the combination therapy for RAP.

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Commercial Relationships: Hirotaka Yokuchi, None; Masayasu Kitahashi, None; Madoka Sakurai, None; Mariko Kubota-Tanai, None; Takayuki Baba, None; Shuichi Yamamoto, None

Program Number: 3793 Poster Board Number: B0103
Presentation Time: 2:45 PM - 4:30 PM

Analysis of 24 month data from the HARBOR study indicates that anti-therapeutic antibodies status had no significant impact on the treatment response to ranibizumab
Gary Sternberg, Kha Le, Eric Wakshull, Jeriza Rusit, Jennifer Visich, Jeffrey A. Nau. Genentech, Inc., South San Francisco, CA.

Purpose: To study the relationship between treatment response and presence of anti-therapeutic antibody (ATA) at Month 12 and 24 following repeated intravitreal (IVT) ranibizumab (RBZ) administration in patients with neovascular age-related macular degeneration (AMD) in the HARBOR study.

Methods: This sub-analysis included patients with wet AMD (n=1095) randomized 1:1:1:1 to receive IVT injections of RBZ 0.5 mg or 2.0 mg monthly or pro-re-nata (PRN) dosing following 3 monthly loading doses. Serum samples to measure RBZ concentrations were collected at screening, days 3, 7, 14, 30, and months 12 and 24. Serum samples for the evaluation of immunoreactivity to RBZ were collected at screening and at months 6, 12, and 24. Treatment response was assessed using best-corrected visual acuity (BCVA) and optical coherence tomography (OCT) imaging at days 7, 30 and at monthly intervals afterwards. Serum RBZ concentrations were determined using a ligand-capture method. Serum ATA to RBZ was detected using a bridging ELISA.

Results: The percentages of patients treated monthly that were ATA positive were 12.4% (2mg) vs. 7.5% (0.5mg) at month 12 and 16.2% (2mg) vs. 9.4% (0.5mg) at month 24. Among PRN patients the percentages were 12% (2mg) vs. 8% (0.5mg) at month 12 and 14.2% (2mg) vs. 8.4% (0.5mg) at month 24. Positive ATA status did not correlate with a change in serum RBZ concentrations, change in BCVA or change in central foveal thickness (CFT) in any treatment groups. Furthermore, there were no differences in the relationship between RBZ serum concentration and CFT and VA in ATA-positive versus ATA negative patients. The percent of patients that were ATA positive at month 24 was slightly higher than at month 12 (increase < 4%). However, patients with positive ATA at month 12 did not have increased antibody titers, nor worsening treatment response at month 24.

Conclusions: This is the most comprehensive analysis of the relationship between ATA status, pharmacokinetics and pharmacodynamics (VA and CFT) in a large group of AMD patients receiving RBZ 0.5 mg or 2.0 mg as monthly or PRN regimen for 12 or 24 months. Following repeated IVT administration for up to 2 years, the ATA status did not appear to alter pharmacokinetics, pharmacodynamics, or treatment efficacy of ranibizumab in AMD.

Commercial Relationships: Alessandra Acquistapace, None; Alba Xhepa, None; Roberta Secondi, None; Sara Bochicchio, None; Mario V. Cigada, None; Andrea Giani, Bayer (C), Novartis (R), Allergan (R); Giovanni Staurenghi, Ocular Instruments (P), GSK (C), Novartis (C), Alcon (C), Allergan (C), Bayer (C), Roche (C), Heidelberg Engineering (C), OD-OS (C), QLT (C), Optos (C)

Program Number: 3795 Poster Board Number: B0105
Presentation Time: 2:45 PM - 4:30 PM

Visual acuity loss at a two-year follow-up in patients with exudative age-related macular degeneration treated with ranibizumab and as needed retreatment basis
Takeyka Kohno1, Manabu Yamamoto1, tasuka yoneda1, Yusaku Yoshida1, Hiashi iwami1, Mayumi Kaida1, Michiko Hirabayashi2, Kumihiro Shiraiki3. 1Ophthalmology & Visual Science, Osaka City Univ Grad Sch of Med, Osaka, Japan; 2Ophthalmology, Shironiwa Hospital, Ikoma, Japan.

Purpose: To evaluate the characteristics of eyes with visual acuity (VA) loss at a two-year follow-up in patients with exudative age-related macular degeneration (AMD) initially treated with intravitreal injections of ranibizumab (IVR) and retreated as needed.

Methods: This is a retrospective case series study of a two-year follow-up. Among 66 eyes started with three monthly IVR, 25 eyes with the VA less than 0.7 had been scheduled to have a combined therapy with half-fluence photodynamic therapy, but patients preferred IVR monotherapy. The rest of the 41 eyes with the initial VA better than or equal to 0.7 had IVR monotherapy as scheduled. The 66 eyes consisted of 32 eyes with typical AMD, 31 eyes with polypoidal choroidal vasculopathy (PCV), 3 eyes with choroidal neovascularization (CNV) with chorioretinal anastomosis (type 3 CNV). Retreatment was done as needed. A change of 0.3 or more in the logMAR VA units was considered significant.

Results: The number of patients with decreased VA was 3 eyes out of 66 eyes at month 3 (3M), 1 eyes at 6M, 4 eyes at 12M and 8 eyes at 24M. The mean VA of the 8 eyes was 0.21 at pre-treatment, 0.28 at 3M (p=0.273), 0.31 at 6M (p=0.068), 0.49 at 12M (P=0.028) and 0.79 at 24M (P=0.012). The mean central foveal thickness (CFT) decreased from 322.9 µm at pre-treatment to 253.5 µm at 3M (p=0.263), then back to 329.3 µm at 24M (p=0.484). The mean total Eye Clinic Department of Biomedical and Clinical Science “Luigi Sacco”, Luigi Sacco Hospital, Milan, Italy.

Purpose: To evaluate changes in visual acuity and drug costs of anti-vascular endothelial growth factor (VEGF) therapy in patients with age related macular degeneration (ARMD).

Methods: Retrospective analysis of 261 consecutive patients (304 eyes) with choroidal neovascularization in ARM treated with ranibizumab and bevacizumab. The visual acuity at baseline and during follow-up visits, the total number of injections and the type of anti-VEGF agent employed were evaluated.

Results: The total eyes considered in this study were 178 for ranibizumab, 55 for bevacizumab and 71 for both. The mean follow-up time was 988 days (range 54-2394). The mean number of visits for each patient was 27.4. A total of 1713 ranibizumab and 646 bevacizumab were injected in this sample. The mean change of visual acuity was -2.6 letters for ranibizumab and -11.9 letters for bevacizumab. The total charges for each treated eye was 7,996 EURO for ranibizumab and 49 EURO for bevacizumab.

Conclusions: This is a retrospective chart review of patients treated with anti-VEGF therapy in exudative ARMD, and therefore the two groups are not comparable. However data suggests that the employment of ranibizumab may be able to stabilize visual acuity, even though it has significantly higher costs.

Commercial Relationships: Alessandra Acquistapace. None; Alba Xhepa. None; Roberta Secondi. None; Sara Bochicchio. None; Mario V. Cigada. None; Andrea Giani. Bayer (C), Novartis (R), Allergan (R); Giovanni Staurenghi. Ocular Instruments (P), GSK (C), Novartis (C), Alcon (C), Allergan (C), Bayer (C), Roche (C), Heidelberg Engineering (C), OD-OS (C), QLT (C), Optos (C)

Program Number: 3794 Poster Board Number: B0104
Presentation Time: 2:45 PM - 4:30 PM

Visual acuity outcomes and drug costs for different antiangiogenic agents in the therapy of exudative age-related macular degeneration in a clinical setting
Alessandra Acquistapace, Alba Xhepa, Roberta Secondi, Sara Bochicchio, Mario V. Cigada, Andrea Giani, Giovanni Staurenghi.

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IRV was 12.5. Cystoid lesions were found in 7 eyes of the macula. In the remaining 58 eyes, the mean VA was 0.18 at pre-treatment, 0.12 at 3M (P<0.001), and remained up to 24M (0.10, p<0.001). The mean CFT was decreased from 301.1 µm at pre-treatment to 192.1 µm at 3M (P<0.001) and 200.6 µm at 24M (P<0.001). The mean total IRV was 7.9. Cystoid lesions were found in 19 eyes. Significant difference was found between these two groups in age (p=0.033), in AMD type (PCV (p = 0.037) and type 3 CNV (p = 0.003)), in VA at 12M (p = 0.002) up to 24M (P<0.001), in CFT at 3M (p = 0.045) up to 24M (P<0.001), in the total IRV number (P<0.001) and in the presence of cystoid lesions (p = 0.003).

**Conclusions:** The number of patients losing VA increased, especially after 12M. The CFT at 3M and the cystoid lesions may be associated with the long-term visual loss.

**Commercial Relationships:** Takeya Kohno, None; Manabu Yamamoto, None; tasuku yoneda, None; Yusaku Yoshida, None; Hisashi Iwami, None; Mayumi Kaida, None; Michiko Hirabayashi, None; Kunihiko Shiraki, None

**Program Number:** 3796 **Poster Board Number:** B0106 **Presentation Time:** 2:45 PM - 4:30 PM **Short-term vision changes after switch to aflibercept therapy for age-related macular degeneration previously treated with other antiVEGF agents**

Irene A. Barbazetto$^1,2$, Roberto Gallego-Pinazo$^1$, Michael Engelbert$^{1,2}$.


**Purpose:** A subset of patients previously stabilized on antiVEGF therapy and switched to aflibercept (Eylea™, Regeneron, USA) experience a decrease in visual acuity after the initial injection. The purpose of this study is to characterize these patients and to evaluate their long-term outcomes.

**Methods:** This is a retrospective chart review of 80 patients/eyes (age 82.7 years; STDEV 7.15) switched from anti-VEGF therapy with ranibizumab (Lucentis™, Genentech Inc., USA) and or bevacizumab (Avastin™, Genentech Inc., USA) to aflibercept. Best corrected visual acuity (VA), clinical and imaging findings, including spectral-domain optical coherence tomography (OCT) and fundus autofluorescence were evaluated before and after switch of therapy.

**Results:** Twelve of 80 patients/eyes (15%) experienced visual decline of an average LogMar 0.18 one month after the first aflibercept injection. The average baseline visual acuity changed from LogMar 0.41 (STDEV 0.16) to LogMar 0.57 (STDEV 0.18). During follow-up 5/12 patients continued to worsen, 7/12 returned to baseline vision or improved eye further. The mean follow-up time was 5.3 months (range 3 - 8 months). The average number of injections in this group was 5.1 (range 2 - 7). Patients with persistent worsening after switch to aflibercept were more likely to have a lower CMT at baseline when compared to patients, who improved or returned to baseline VA at the last follow-up (246.8µm vs. 317.5µm, p = 0.050). No difference was found with regard to presence or absence of subretinal fluid, cystic changes or presence of a pigment epithelial detachment on OCT.

**Conclusions:** Aflibercept therapy is generally well tolerated. Switching patients to aflibercept therapy after treatment with other antiVEGF agents may lead to transient decrease of vision in a small subset of patients, most of whom recover and improve with further treatment. These events maybe different from those in patients experiencing loss of vision during long-term antiVEGF therapy and warrant further investigation.

**Commercial Relationships:** Irene A. Barbazetto, None; Roberto Gallego-Pinazo, Bayer (R), Novartis (R), Novartis (C), Carl Zeiss Meditec (R); Michael Engelbert, Genentech (C), BMS (C)

**Support:** Macula Foundation

**Program Number:** 3797 **Poster Board Number:** B0107 **Presentation Time:** 2:45 PM - 4:30 PM **Macular Morphology Changes Following Intravitreal Aflibercept for Treatment-Resistant Exudative AMD**

Geoffrey Broadhead$^1,2$, Haitao Li$^1$, Meidong Zhu$^1,2$, Jamie Chew$^1,2$, Wijeyanthi Wijeyakumar$^1$, Andrew A. Chang$^1,2$.

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**Purpose:** To evaluate the effectiveness of aflibercept in eliminating intraretinal and subretinal fluid (SRF and IRF) in patients with persistent macular fluid secondary to exudative age-related macular degeneration (AMD).

**Methods:** Method: Central macular thickness (CMT) measured with spectral domain optical coherence tomography (SD-OCT) from an open label, prospective intravitreal aflibercept clinical trial ((Australia-New Zealand Clinical Trials Registry, ACTRN1261200666820, registered 21/06/12, commenced 15/7/2012) was analysed. All patients had persisting macular fluid despite at least 4 anti-vascular endothelial growth factor (anti-VEGF) injections in the preceding 6 months prior to baseline aflibercept administration. Presence of SRF and IRF were defined by the location of retinal fluid by SD-OCT. Intravitreal aflibercept was administered at baseline and week 4.

**Results:** Results: 42 eyes of 42 patients were included for analysis. Average age of patients was 77.7±7.9 years and 38% of participants were male. At baseline, mean CMT was 439.5 ± 144.7 µm. 5 (10%) patients presented with IRF only, 16 (32%) presented with SRF alone and 21 (42%) had both IRF and SRF. Mean CMT reduction was 80.5 µm, 93.8 µm and 113.4 µm at weeks 1, 4 and 8 post aflibercept injection respectively compared to the baseline (p<0.001 at all time points). 14 patients (33%) were fluid-free at month 1 and 25 patients (60%) showed dry macular at month 2. There was a trend toward greater likelihood of fluid free status in those with SRF only at all time points (19% of SRF patients fluid-free at week 1, 50% at week 4 and 69% at week 8, respectively), followed by those with the type of IRF and SRF combination (10% week 1, 24% week 4 and 52% week 8, respectively). The group with both SRF and IRF showed a significant reduction in CMT at month 2 compared to the SRF only group (p=0.013).

**Conclusions:** Conclusions: Intravitreal aflibercept results in remarkable reduction in IRF and SRF in patients with persistent macular fluid secondary to AMD. Aflibercept eliminated macular fluid in a substantial number of patients with all subtypes of persistent exudation. Patients with combined SRF and IRF had the greatest mean reduction in CMT at month 2.

**Clinical Relationships:** Geoffrey Broadhead, None; Haitao Li, None; Meidong Zhu, None; Jamie Chew, None; Wijeyanthi Wijeyakumar, None; Andrew A. Chang, Alcon (C), Bayer (C), Novartis (C), Alcon (R), Bayer (R), Novartis (R), Bayer (F)

**Support:** Unrestricted Bayer Support Grant

**Clinical Trial:** ACTRN1261200666820
Cordoba, Argentina; Ophthalmology, Clinica Universitaria Reina Fabiola, Cordoba, Argentina.

**Purpose:** To evaluate different accessibilities to NV-AMD treatment in clinical practice and estimate their impact on therapeutic effects and visual outcome.

**Methods:** A retrospective chart review of 22 patients (96 eyes) with previously untreated exudative AMD, who were treated with ranibizumab (RNB) or bevacizumab (BVZ) between January 2009 and December 2011, was conducted. The main outcomes measured included time delay and change in mean best-corrected visual acuity (BCVA) between diagnosis and treatment, annual mean number of injections and follow-up examinations and the major clinical outcomes (mean BCVA change and proportion of patient who lost <15 letters and proportion of patients who gained > 15 letters) at 1 year of follow-up.

**Results:** Both studied groups showed a statistically significant reduction in BCVA (p < 0.01) over the delay time between diagnostic and treatment. This delay time and the decrease in visual acuity in this period were significantly higher for patients treated with Ranibizumab than those one treated with Bevacizumab (153.8 vs. 36.06 days, p<0.0001), (-13.01 vs. -5.46 letters, p<0.01).

After initial loading phase, there was a significant improvement in visual acuity for both groups with a non-significant difference in favor of BVZ (+10.06 vs. +6.27 letters p=0.097). Throughout the year of treatment, BVZ-group received significantly more injections than RNB-group (4.71 vs 2.98 p <0.0001) and also had better clinical outcomes (+0.11 vs -8.87 letters p<0.04).

**Conclusions:** The access to treatment, conditioned by bureaucratic aspects, can be a key factor for success of therapy. In this sense, using off-label BVZ was the option to get best results. However it is not the drug itself which is the most important factors, its accessibility when a dose is required.

**Commercial Relationships:** Jose D. Luna Pinto, None; Juan P. Real, None; Julio A. Urrets-Zavalia, None; Claudio P. Juarez, None; Santiago D. Palma, None; Gladys E. Granero, None

**Program Number:** 3799 Poster Board Number: B0109

**Presentation Time:** 2:45 PM - 4:30 PM

**The efficacy of aflibercept in the treatment of neovascular age-related macular degeneration previously treated with bevacizumab or ranibizumab**

Laura B. Hall, Nazlee Zebardast, Ron A. Adelman, Ophthalmology and Visual Science, Yale University School of Medicine, New Haven, CT.

**Purpose:** To study the visual outcomes and change in central macular thickness (CMT) in patients with neovascular age-related macular degeneration (AMD) previously treated with ranibizumab and/or bevacizumab who were subsequently switched to aflibercept (VEGF Trap-Eye, Eylea®). Aflibercept was approved based on randomized clinical trial data which studied patients with untreated AMD. This study aims to determine the utility of aflibercept in patients who received previous anti-VEGF treatment.

**Methods:** A retrospective chart review of 22 patients who met the inclusion criteria: 1) previous anti-VEGF treatment for AMD, 2) at least 6-month follow-up and 3) available medical record. The main outcome measures were best-corrected Snellen visual acuity (BCVA) logMAR and central macular thickness (CMT) as measured by optical coherence tomography (OCT). These values were recorded at the initial baseline visit prior to the first aflibercept injection and at subsequent 1-month, 3-month, and 6-month follow-up clinic visits and/or injections.

Results: The study population included 4 men and 18 women aged 78.0±3.20 years (mean±SEM) who received 5.36±0.38 aflibercept injections. Thirty patients previously received only bevacizumab (9.00±2.26 injections), one received only ranibizumab (11 injections) and 8 received both anti-VEGF agents (mean 21.4 injections). BCVA logMAR at the initial baseline visit was 0.50±0.07 (mean±SEM) (mean VA 20/64), 1-month 0.52±0.07 (20/66), 3-month 0.41±0.07 (20/52), and 6-month 0.43±0.10 (20/54) (p-value 0.14, two-tailed paired t-test comparing initial and 6-month follow-up). CMT results for initial baseline visit were 301±30.8 μm, 1 month 238±13.5, 3-month 236±11.1, and 6-month 247±10.7 (p-value 0.07, two-tailed paired t-test comparing initial and 6-month follow-up).

**Conclusions:** These findings demonstrate a trend towards improvement from baseline to 6-month follow-up in both BCVA and CMT in AMD patients previously treated with the mainstay agents ranibizumab and/or bevacizumab who were switched to aflibercept. Given the small sample size a larger study will be beneficial.

**Commercial Relationships:** Laura B. Hall, None; Nazlee Zebardast, None; Ron A. Adelman, None

**Support:** Richard K. Gershon Medical Student Research Fellowship (Yale University School of Medicine)

**Program Number:** 3800 Poster Board Number: B0110

**Presentation Time:** 2:45 PM - 4:30 PM

**Intravitreal Aflibercept for Recalcitrant Neovascular AMD**

Maria E. Maldonado, David M. Brown, Charles Wykoff, Retina Consultants of Houston, Houston, TX.

**Purpose:** Many eyes have recalcitrant age-related macular degeneration (AMD) with persistent activity despite monthly intravitreal 0.5 mg ranibizumab (RZB). The SAVE study demonstrated that these eyes improve anatomically and visually with a 2.0 mg/0.5 ml formulation of RZB (Ophthalmology 2012, PMID:23131717). As this experimental RZB formulation is no longer available, this study was designed to test whether commercially available 2.0 mg aflibercept could maintain the gains and/or improve anatomical and visual acuity outcomes in this well characterized cohort.

**Methods:** In this Phase IV controlled clinical trial, forty-five patients with recalcitrant neovascular AMD were treated with three mandatory monthly loading doses of 2.0 mg aflibercept followed by q6 week 2.0 mg aflibercept with PRN aflibercept given in the intervening months. Re-treatment was based on SD-OCT, clinical exam, and Early Treatment of Diabetic Retinopathy Study (ETDRS) four-meter refractions. To be included in the study, all patients must have received past 0.5 mg monthly RZB injections and subsequent 2.0 mg RZB injections through the SAVE trial.

**Results:** Forty-five patients were enrolled in the study. Patients had on average 18.6 prior injections of 0.5 mg RZB and 21.5 injections of 2.0 mg RZB (through the SAVE trial) prior to enrollment. Mean refracted VA was 73.9 ETDRS letters at baseline and mean central subfield was 343 μ. Anatomically, mean OCT central subfield thickness improvement from baseline was: -32.3 μ at day 7, -24.8 μ at month one, and -29.8 μ at month two. Mean visual acuity gain (ETDRS) over baseline was +0.59 letters at day 7, -0.04 letters at month 1, and +0.42 letters at month 2. For those patients who continued on through month 6, the mean central OCT improvement from baseline was -44.5 μ at month 3, -33.9 μ at month 4, -43.5 μ at month 5, and -32.8 μ at month 6. Visual acuity gains were +0.9 letters at month 3, 0.0 letters at month 4, +0.3 letters at month 5, and +0.8 letters at month 6. No serious adverse events, including ocular adverse events, have been observed in any subject.

**Conclusions:** 2.0 mg aflibercept intravitreal injections led to anatomic improvements even in patients with persistent fluid on a
regimen of 2.0 mg RZB. Visual acuity gains achieved with 2.0 mg RZB were overall maintained on the commercially available dose of aflibercept. 

Commercial Relationships: Maria E. Maldonado, None; David M. Brown, Regeneron Pharmaceuticals, Inc. (F), Regeneron Pharmaceuticals, Inc. (C), Regeneron Pharmaceuticals, Inc. (R), Bayer HealthCare (F), Bayer HealthCare (C), Bayer HealthCare (R), Genentech (C), Roche (C), Alimera (C), Alcon (C), Novartis (C), Thrombogenics (C), Genentech (F), Roche (F), Thrombogenics (F), GSK (F), Alimera (F), Alcon (F), Allergan (F), Eli Lilly (F); Charles Wykoff, Genentech (R), Regeneron (R), Bayer (C)

Clinical Trial: NCT01543568

Program Number: 3801 Poster Board Number: B0111
Presentation Time: 2:45 PM - 4:30 PM

Comparison of outcomes after switching treatment from intravitreal bevacizumab or ranibizumab to aflibercept in neovascular age-related macular degeneration


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Purpose: To compare outcomes in patients with neovascular age-related macular degeneration (AMD) after switching from previous intravitreal bevacizumab or ranibizumab to aflibercept. We hypothesize that aflibercept will provide an equivalent or improved therapeutic effect.

Methods: A retrospective comparative case series, comparing patients who were recalcitrant to treatment (persistent subretinal fluid seen on optical coherence tomography (OCT)) to patients who were dry (no subretinal fluid seen on OCT) at time of the switch to aflibercept treatment. All reviewed patients had at least 3 previous injections with bevacizumab or ranibizumab, and all had an injection within 45 days prior to switching to aflibercept. Each patient received 3 monthly injections of aflibercept. Main outcome measures included visual acuity (VA) and central retinal thickness (CRT).

Results: 86 eyes met the inclusion criteria for the study. There were 63 eyes (73.3%) in the recalcitrant group and 23 eyes (26.7%) in the dry group at the initiation of aflibercept treatment. VA did not change significantly within or between each group at any time point in either the recalcitrant group (0.57LogMar, SD 0.39 vs. 0.52LogMar SD 0.39; p=0.28) or the dry group (0.47LogMar, SD 0.36 vs. 0.54LogMar, SD 0.37; p=0.07). Among those in the recalcitrant group, CRT decreased significantly from visit 1 (mean 262.02, SD 85.6) to visit 2 (mean 245.98, SD 90.29; p=0.04) and from visit 1 to visit 3 (mean 237.91, SD 71.97; p=0.01). By visit 4 this decrease in CRT was no longer significant (mean 248.62, SD 77.86; p=0.07). Among those in the dry group, CRT did not change significantly over time. The CRT was not significantly different between groups at any time point.

Conclusions: In patients switched from bevacizumab or ranibizumab to aflibercept, there was a temporary decrease in CRT among patients who were in the recalcitrant group, however there were no apparent differences in visual acuity outcomes in either the dry or recalcitrant group. Aflibercept appears to provide a non-inferior therapeutic effect when compared to ranibizumab and bevacizumab. No visual benefit was seen by changing to aflibercept in either the dry or recalcitrant groups.

Commercial Relationships: Frank X. Venzara, None; John O. Mason, None; Jay Glover, None; Gerald McGwin, None; Carrie Huisingh, None; Duncan A. Friedman, None; Richard M. Feist, None; Martin L. Thomley, None; Michael A. Albert, None; Natalie Price, None

Program Number: 3802 Poster Board Number: B0112
Presentation Time: 2:45 PM - 4:30 PM

The effect of the reflux bleb of anti-VEGF injections on central macular thickness

Kaniska R. Mendis, Ana Galevska-Dimitrovska, Rhiana K. Thompson, Bruce Shadbolt.

Ophthalmology, The Canberra Hospital, Canberra, ACT, Australia.

Purpose: Purpose: To investigate the effect of the reflux bleb (RB) associated with intra vitreal anti-vascular endothelial growth factor (anti-VEGF) injections on central macular thickness (CMT- central sub-field of Cirrus spectral domain ocular coherence tomography- Cirrus SD OCT- Carl Zeiss Meditec, Dublin, CA)

Methods: Methods: Prospective, consecutive, observational, pilot study of patients administered anti-VEGF therapy (Bevacizumab and Ranibizumab- Genentech Inc, South San Francisco, CA) for wet age related macular degeneration, macular oedema secondary to branch and central vein occlusion, exudative diabetic maculopathy, myopic choroidal neovascular membrane and idiopathic polypoidal choroidal vasculopathy.

The bleb status following an anti-VEGF injection, the CMT1 and the CMT2 at the immediate next visit were recorded prospectively in all patients (fig. 1). Generalised linear models and logistic regression were used to evaluate the effect of bleb status on the difference between CMT1 and CMT2. The analyses adjusted for age, gender, time between injections, laterality, diagnosis and anti-VEGF agent. The statistical package used to run the analysis was SPSS v19.0.

Results: Results: The bleb status of 100 eyes was prospectively recorded. A post injection bleb was observed on 42% of eyes (42/100). There were an equal number of right and left eyes. There were 67 Bevacizumab injections and 33 Ranibizumab injections. The mean age of the patients was 73 years, and there were 53 females and 47 males.

Patients without a post injection bleb were 2.3 times more likely (95% CI = 0.9, 5.7) to have a reduction in CMT than those with a bleb (p=0.08).

Conclusions: Conclusion: This pilot project has provided some evidence that the development of a post injection bleb maybe associated with less of a reduction in CMT. The results indicate that a larger study is worth undertaking that includes a longer follow-up period.

Commercial Relationships: Kaniska R. Mendis, None; Ana Galevska-Dimitrovska, None; Rhiana K. Thompson, None; Bruce Shadbolt, None

Program Number: 3803 Poster Board Number: B0113
Presentation Time: 2:45 PM - 4:30 PM

Persistent Leakage During the Course of Anti-VEGF Monotherapy - Etiology and Treatment


Purpose: Determine the cause of persistent leakage in patients treated with anti-VEGF monotherapy

Methods: Retrospective evaluation of 64 treatment-naive patients with Exudative ARMD who comprised two treatment groups: Monthly (24 months of monthly ranibizumab) and Treat and Extend (12 months of monthly ranibizumab, followed by 12 months of a ‘treat and extend’ protocol. Pre-treatment evaluation of each patient included ICG/IVFA/OCT multimodality imaging. Post-treatment followup included monthly OCT and every three month ICG imaging.

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Results: 10% of patients from all groups were classified as Primary Anti-VEGF Failures (failed induction). 10% of patients in the Monthly group developed recurrent leakage, defined as a Secondary Anti-VEGF Failures. 20% of patients in the Treat and Extend group became Secondary Anti-VEGF Failures. All patients with recurrent leakage had ICG-identifiable lesions. All patients were treated with rescue protocols: increased ranibizumab frequency, aflibercept monotherapy, or ICG-Directed PDT Triple Therapy.

Conclusions: ICG multimodality imaging is critical to determine the etiology of the persistent leakage and to create a strategy for exudative and neovascular resolution.

Commercial Relationships: Mark H. Nelson, None

Program Number: 3804 Poster Board Number: B0114
Presentation Time: 2:45 PM - 4:30 PM
The efficacy of bimonthly injection of ranibizumab for age-related macular degeneration for six months

Purpose: To evaluate the efficacy of bimonthly intravitreal injection of ranibizumab for age-related macular degeneration (AMD) for six months.

Methods: Three bimonthly intravitreal injections of ranibizumab (0.5mg) were given to thirteen eyes with AMD and one eye with polypoidal choroidal vasculopathy. Twelve patients did not receive any previous treatment for AMD. Two patients received previous treatment for AMD three months before the initial injection of ranibizumab. The best-corrected visual acuity (BCVA) and the central retinal subfield thickness (CRST) were measured before and monthly after the initial injection for 6 months. As the rescued treatment, intravitreal injection of ranibizumab (0.05mg) could be added at month 1, month 3 or month 5 after the initial injection if either logMAR VA decreased more than 0.3, or the CRST increased more than 100 μm. BCVA was measured with Landolt C chart and converted logarithm of the minimum angle of resolution (logMAR) VA and analyzed. CRST was measured using spectral-domain OCT. The average retinal thickness in the central 1-mm area was analyzed. Friedman Repeated Measures Analysis of Variance on Ranks was used to compare the difference of BCVA and CRST before and after the intravitreal injection of ranibizumab.

Results: Twelve patients completed 3 injections while one patient denied the third injection and a rescue injection was given at month 5 in a patient because CRST increased. The mean BCVA in logMAR was 0.50 ± 0.41 at baseline, 0.46 ± 0.40 at month 1, 0.44 ± 0.38 at month 2, 0.39 ± 0.40 at month 3, 0.36 ± 0.43 at month 4, 0.37 ± 0.51 at month 5, 0.33 ± 0.44 at month 6. The BCVA improved significantly at month 4, at month 5 and at month 6 compared with baseline (all P <0.05). The mean CRST (μm) was 316 ± 60.6 at baseline, 239 ± 67.2 at month 1, 262 ± 103 at month 2, 242 ± 72.9 at month 3, 255 ± 71.9 at month 4, 256 ± 71.9 at month 5, 275 ± 91.0 at month 6. The CRST decreased significantly at month 1, at month 3 and at month 5 compared with baseline (all P <0.05). No drug or injection-related adverse event was reported.

Conclusions: The bimonthly injection of ranibizumab for AMD may be effective and could be an option.

Commercial Relationships: Tomoko Sawada, None; Masashi Kakinoki, None; Xiying Wang, None; Hajime Kawamura, None; Yoshitsugu Saishin, None; Masahito Ohji, Alcon (F), Novartis (F), Novartis (C), Pfizer (C), Santen (F), Santen (C), Shionogi (C), Carl Zeiss (C), Bayer (C), Senju (C)

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Clinical Trial: UMIN000005691

Program Number: 3805 Poster Board Number: B0115
Presentation Time: 2:45 PM - 4:30 PM
Response and dependence to ranibizumab therapy in AMD
Masako Kuroda1,2, Hiroshi Kojima1,2, Takenori Kameda1,2, Michiko Mandal1,3, Noriko Miyamoto1,2, Akihiko Nishida1,2, Yasuo Kurimoto1,2, 1Kobe City Medical Center General Hospital, Kobe, Japan; 2Institute of Biomedical Research and Innovation Hospital, Kobe, Japan; 3Laboratory for Retinal Regeneration, RIKEN Center for Developmental Biology, Kobe, Japan.

Purpose: Immediate practice of as-needed injection of ranibizumab is still a burden to some patients or facility. To estimate a situation of therapy requirement, we aim to evaluate the response and dependency to ranibizumab injection therapy and related factors in neovascular age-related macular degeneration (AMD).

Methods: Medical records of 81 treatment-naïve AMD eyes of 80 Japanese patients who received initial three monthly intravitreal ranibizumab induction therapy in our clinic from Jun 2009 to Dec 2011 were reviewed. One month after completion of induction therapy, all eyes were evaluated and classified into two groups: well responded group if they did not need additional ranibizumab injection according to the PrONTO study protocol (AO2009:148; 43-58), and insufficiently-responded group if they did.

If the exudative change in OCT worsened within three months after completion of induction therapy, the eye was defined as treatment dependent. We thereby defined each subgroup as follows: group A: well-responded and non-dependent, group B: well-responded but dependent, group C: insufficiently-responded and non-dependent, and group D: insufficiently-responded and dependent.

Results: Forty-eight eyes (59%) well responded to the induction therapy whereas 33 eyes (41%) had insufficient response. The eyes in insufficiently-responded group had had a higher rate of cystoid macular edema (CME) (P < 0.01) and larger great linear dimension (GLD) (P < 0.05) before induction therapy. They did not show a significant improvement in visual acuity after induction therapy. Twenty-three eyes were categorized as group A, 25 as B, 15 as C and 18 as D. Eyes in group A needed less additional injections than those in group B, and showed a better visual outcome. Eyes in group D needed more injections than those in group C.

Conclusions: Of all treatment-naïve AMD patients, 59% well responded to ranibizumab induction therapy. Half of these eyes were ranibizumab-dependent requiring repeated injections and showed poorer visual outcome. Insufficiently-responded eyes with CME or large GLD may require continuous re-injections or a combined therapy such as with photodynamic therapy.

Commercial Relationships: Masako Kuroda, None; Hiroshi Kojima, None; Takenori Kameda, None; Michiko Mandal, None; Noriko Miyamoto, None; Akihiko Nishida, None; Yasuo Kurimoto, HOYA (F), Santen (F), Senju (F), Abbott (F), Alcon (F)

Program Number: 3806 Poster Board Number: B0116
Presentation Time: 2:45 PM - 4:30 PM
Eylea Rescue Therapy in Eyes with Proven Non-Response to Other anti-VEGF Molecules
Benjamin Guidry, Ching J. Chen. University of Mississippi, Jackson, MS.

Purpose: In the treatment of wet AMD, nonresponsiveness to traditional anti-VEGF agents such as Lucentis(ranibizumab) or Avastin(bevacizumab) is an unfortunate reality for many patients.
This study's purpose is to investigate beginning Eylea (afiblerteo) treatment in patients with proven nonresponsiveness to Lucentis or Avastin.

**Methods:** Eyes included in the study must have active choroidal neovascular membranes secondary to macular degeneration that have required a minimum of 5 consecutive Avastin or Lucentis injections due to lack of CNV resolution. Eyes included in the study must have no other major pathology such as prior non-cataract surgery or other confounding variables. Included eyes then begin Eylea rescue therapy consisting of Eylea initiation treatment per package guidelines, specifically three consecutive monthly injections followed by assessments every two months following with as needed injections. Acuity is recorded for every office visit. Patients also receive a macular OCT, fundus exam, and intraocular pressure monitoring at each visit.

**Results:** A total of 52 patients and 60 eyes met inclusion criteria and were included in the study. Of these 60 eyes, 15 (25%) showed complete resolution of CNV activity at or within the initial three month treatment window. Subsequent follow-up shows only that a single additional eye showed resolution of CNV activity following the initial three month period. Therefore 26.7% of eyes showed complete resolution of CNV activity at some point during treatment. Also of note, in total 28 eyes (46.7%) displayed improved acuity following 3 Eylea rescue injections and 18 eyes (30%) showed decreased acuity following 3 injections. 14 eyes (23.3%) displayed no change in acuity following the 3 initial injections.

**Conclusions:** In the setting of nonresponsiveness to Avastin and or Lucentis, Eylea injections are a prudent alternative. In this retrospective case study, our data suggests that beginning Eylea rescue therapy can lead to CNV resolution in 25% of eyes previously nonresponsive to anti-VEGF therapy. Our data at this point suggests that CNV activity is unlikely to cease if it does not do so during the initial 3 rescue injections. Also of note, the majority (70%) of eyes undergoing rescue therapy maintained or gained acuity following the 3 rescue injections.

**Commercial Relationships:** Benjamin Guidry, None; Ching J. Chen, None

Program Number: 3807 Poster Board Number: B0117

**Presentation Time:** 2:45 PM - 4:30 PM

**Growth of Type 1 Neovascularization Following Cessation of Anti-Vascular Endothelial Growth Factor Therapy as a Possible Explanation for Treatment Resistance**

**Authors:** Roberto Gallego-Pinoza1, 2, Vinnie P. Shah3, K Bailey Freund2, 3

1Ophthalmology, Univ & Polytechnic Hosp La Fe, Valencia, Spain; 2Vitreous Retina Macula Consultants of New York, New York, NY; 3Ophthalmology, New York University School of Medicine, New York, NY.

**Purpose:** To demonstrate a possible mechanism of resistance to vascular endothelial growth factor (VEGF) inhibition in neovascular age-related macular degeneration (NVAMD) using serial eye-tracked spectral-domain optical coherence tomography (SD-OCT) imaging (Heidelberg Engineering, Heidelberg, Germany).

**Methods:** Retrospective review of the clinical histories and eye-tracked SD-OCT imaging findings in 2 eyes with NVAMD that developed recurrent and refractory subretinal fluid after cessation of anti-VEGF medication.

**Results:** Case 1 was an 86-year-old female who was treated with 4 monthly intravitreal injections of ranibizumab in her left eye for type 1 neovascularization secondary to NVAMD. Resolution of all fluid and reduction in lesion size were evidenced by SD-OCT, and thereafter the patient was switched to OCT-guided therapy with pro re nata dosing regimen. Eleven months after the last injection, subretinal fluid was noted to recur on SD-OCT. Case 2 was an 87-year-old male who was treated with 3 monthly intravitreal injections of ranibizumab in his left eye for type 1 neovascularization secondary to NVAMD, with resolution of a serous pigment epithelial detachment, consolidation of type 1 neovascular tissue and disappearance of all fluid on SD-OCT. The patient was then managed with a treat and extend dosing receiving 12 additional injections over the following 21 months. As there was no recurrent fluid noted during this period, the patient requested to be switched to an OCT-guided pro re nata dosing regimen. Twenty-seven months after the last injection, recurrent fluid was detected on SD-OCT. In both cases, serial eye-tracked SD-OCT imaging documented an increase in the type 1 neovascularization lesion size with following discontinuation of anti-VEGF therapy. When fluid recurred, reinstatement of monthly treatment with intravitreal ranibizumab followed by aflibercept was ineffective in resolving the exudation.

**Conclusions:** Serial eye-tracked SD-OCT imaging can detect slow growth of type 1 neovascularization in NVAMD following cessation of anti-VEGF therapy that may represent a possible mechanism for eyes becoming refractory to these agents.

**Commercial Relationships:** Roberto Gallego-Pinoza, Bayer (R), Novartis (R), Novartis (C), Carl Zeiss Meditec (R); Vinnie P. Shah, None; K Bailey Freund, Genentech (C), Regeneron (C), ThromboGenics (C), Bayer (C), DigiSight (C)

**Support:** None

Program Number: 3808 Poster Board Number: B0118

**Presentation Time:** 2:45 PM - 4:30 PM

**Bimonthly Ranibizumab for Exudative Age-related Macular Degeneration**

**Authors:** Salomon Y. Cohen, Bertrand Maloberti, Franck Fajkuch, Sylva Nghiem-Buffet, Corinne Delahaye-Mazza, Typhaine Grenet, Gabriel Quentin. Centre d’Imagerie Et de Laser, Paris, France.

**Purpose:** To evaluate the results of bimonthly intravitreal ranibizumab for exudative age-related macular degeneration.

**Methods:** Retrospective, monocentric, non-controlled study of AMD patients with naïve exudative AMD treated according to the following protocol:
- Monthly intravitreal ranibizumab during a 3-month loading phase
- Examination every 4 weeks during 52 weeks, including best-corrected ETDRS Visual acuity (BCVA), spectral-domain Optical Coherence Tomography, and fundus photography. Fluorescein angiography was performed at baseline, 24 and 52 weeks.
- Scheduled bimonthly intravitreal ranibizumab. Non-scheduled rescue intravitreal ranibizumab was possible in case of VA loss of 5 letters or more, new hemorrhage, and/or significant exudation. Baseline recorded data was: age and gender of patients, side of study eye, type of choroidal neovascularization (CNV), classified in type 1, 2 or 3. Primary end points were: proportion of patients maintaining vision (i.e. losing < 15 letters), and change in BCVA. Other end points were: proportion of patients gaining ≥ 15 letters, change in central retinal thickness, number of intravitreal injections performed.

**Results:** Thirty patients were included. Three patients did not complete the study, because of inability to consult each 4 weeks (one case), or non-related health problems (2 cases). Twenty-seven patients, 24 women and 3 men, aged from 68 to 90 years (mean: 81.2) were analyzed. At baseline, CNV subtypes were type 1 (n = 8), 2 (n = 7), 3 (n = 12). Twenty-five eyes (92.5%) lost < 15 letters. Two patients lost 26 and 28 letters, respectively because of RPE tear and subfoveal fibrosis. Mean BCVA changed from 58.3 (± 12.9) to 66.8 (± 14.3) letters. The mean visual gain was 8.40 ± 13.2 letters. Eleven patients (40.7%) gained ≥ 15 letters. Mean number of intravitreal injections was 8.77. More precisely, 19 patients received the 8
scheduled injections. Their mean visual gain was 11.7 letters. Eight patients required one to 5 non-scheduled injections. Their mean visual gain was limited to 0.75 letters.

**Conclusions:** Bimonthly ranibizumab after 3 initial monthly doses achieved satisfactory visual results, with a mean VA gain of 8.40 letters. However, patients who required additional injections did not have a significant visual gain.

**Commercial Relationships:** Salomon Y. Cohen, Novartis (C), Allergan (C), Bayer (C), Thea (C), Bausch and Lomb (C); Bertrand Maloberti, None; Franck Fajnkuchen, Novartis (C), Allergan (C); Sylvia Nghiem-Buffet, None; Corinne Delahaye-Mazza, None; Typhaine Grentel, None; Gabriel Quentel, novartis (C), allergan (C), zeiss meditec (C)

**Program Number:** 3809 Poster Board Number: B0119

**Presentation Time:** 2:45 PM - 4:30 PM

**Clinical outcomes of differing loading phase regimes in the management of neovascular age related macular degeneration (nVARM)

Jignesh Patel, Sharon L. Woollard, Nicola Hopkins, Asad Zaheer, Adil Salim, Giles Baggiony-Taylor, Bhamini Sellathurai, Vivek Bansal. Ophthalmology, Essex County Hospital, Colchester, United Kingdom.

**Purpose:** To assess the visual outcomes and retinal thickness of two different intravitreal ranibizumab loading phase regimes in the treatment of nVARM

**Methods:** Retrospective review of the clinical parameters (ETDRS Letters, Central Subfield Thickness (CSF) on SD-OCT) of patients managed using two different loading phase regimes of ranibizumab. One regime involved treatment along the definitions of the PRONTO clinical trial (Pronto method, loading phase of three monthly consecutive injections (n=40 eyes) and the second followed the management of the MARINA / ANCHOR trial (pseudo Marina method) with five loading phase injections and then PRONTO protocol (n=50 eyes).

**Results:** Baseline characteristics for PRONTO group was mean age 79 years and mean baseline vision 55 letters. At 12 and 24 months there was a mean gain of four and nine letters respectively compared to baseline but at 30 months no gain in vision in the PRONTO group whilst for the pseudo MARINA group mean letters gain was eight (at 12 months), six (at 24 months) and six (at 30 months). The mean CSF for PRONTO was 320 microns at baseline and 225, 203 and 250 microns at 12, 24 and 30 months compared to mean baseline of 321 microns and 244, 206 and 200 microns at 12, 24 and 30 months. The mean number of injections was 6 for the PRONTO group and 8 in the pseudo MARINA group in the first year whilst in the second year only a mean of 3 injections for both groups.

**Conclusions:** These results would suggest that an initial intensive loading phase in the management of nVARM can lead to gaining and maintaining vision through to 30 months from baseline compared to standard PRONTO loading phase of three consecutive injections.

**Commercial Relationships:** Jignesh Patel, Novartis (R); Sharon L. Woollard, Novartis (F); Nicola Hopkins, None; Asad Zaheer, None; Adil Salim, None; Giles Baggiony-Taylor, None; Bhamini Sellathurai, None; Vivek Bansal, Novartis (R)

**Program Number:** 3810 Poster Board Number: B0120

**Presentation Time:** 2:45 PM - 4:30 PM

**Evaluation of the accuracy and efficiency of an optometrist led stable AMD clinic in a regional Age Related Macular Degeneration (AMD) Centre

Nadeem Rob, Lorraine North, Gulrez Ansari, Fani Zacharaki, Manju N. Chandran, Geeta Menon. Eye Treatment Centre, Frimley Park Hospital, Frimley Park, United Kingdom.

**Purpose:** To assess the accuracy of clinical decision making in an optometrist led AMD clinic.

**Methods:** Constant increase in the number of wet AMD patients has posed a significant strain on the delivery of service in an NHS setting. Failure to provide the recommended four weekly follow-up can result in irreversible loss of vision. To address this problem, we decided that patients who had been stable for at least 6 months should be referred into a special optometrist led stable AMD clinic, run by three trained optometrists. This clinic is a part of the Hospital Eye Service (HES). Retrospective analysis of patients case notes and optical coherence tomography (OCT) images from 4 consecutive clinics was carried out by a senior ophthalmologist. The aim was to assess whether each clinical decision made by the optometrist was considered to be either correct or incorrect. In addition, the average appointment duration incurred by each patient was recorded.

**Results:** Total of 80 consecutive patient records who were first seen in this clinic were assessed by an independent ophthalmologist. The correct decision was made in 98.5% of cases seen by the optometrists. Only for 1 patient (1.5%) was a different follow-up plan suggested by the ophthalmologist. No adverse event related to this management deviation occurred. The average time for the patients to be seen in the stable clinic pathway from check-in to management was 58 minutes.

**Conclusions:** It can be concluded that specifically trained optometrists are capable of providing a safe and efficient stable AMD service in the hospital setting. This is an innovative way of reducing the burden on existing AMD services.

**Commercial Relationships:** Nadeem Rob, None; Lorraine North, None; Gulrez Ansari, None; Fani Zacharaki, Novartis Pharmaceuticals (F), Novartis Pharmaceuticals (R); Manju N. Chandran, None; Geeta Menon, NOVARTIS (R), ALLERGAN (R), BAYER (R)

**Program Number:** 3811 Poster Board Number: B0121

**Presentation Time:** 2:45 PM - 4:30 PM

**The Efficacy Of Biweekly Alternating Intravitreal Bevacizumab And Ranibizumab In Recalcitrant Choroidal Neovascularization Secondary To Age-Related Macular Degeneration

Radha Ram, Dilraj S. Grewal, Samira Khan, Manjot K. Gill, Department of Ophthalmology, Northwestern University, Feinberg School of Medicine, Chicago, IL.

**Purpose:** To evaluate the efficacy of biweekly alternate intravitreal bevacizumab and ranibizumab dosing for choroidal neovascularization (CNV) in age related macular degeneration (AMD), recalcitrant to prior monthly dosing of intravitreal anti-vascular endothelial growth factor (VEGF) therapy.

**Methods:** Review of AMD patients (identified after exclusion of other causes of CNV) with persistent or increased subretinal (SRF) or intraretinal fluid (IRF) fluid on spectral-domain OCT (SD-OCT) despite ≥12 previous monthly intravitreal bevacizumab or ranibizumab injections who were switched to biweekly alternating intravitreal 1.25mg bevacizumab and 0.5mg ranibizumab.

**Results:** Five eyes of five patients (mean age 80.6 ± 5.8 years) with recalcitrant AMD who had received an average of 39±8.2 prior ranibizumab or bevacizumab injections were included. BCVA, SD-OCT central subfoveal thickness (CFT) and macular volume (MV) were evaluated at baseline and at each subsequent biweekly treatment. The baseline BCVA was 0.52±0.07 logMAR, CFT μm was 413±150.7 (312-674 μm) and MV was 7.6±0.7mm³ (6.83-8.58mm³). After an average of 13.4±6.6 (range 6-21) alternating biweekly
Impact of using the aflibercept dosing regimen for wet macular degeneration on numbers of injections and monitoring visits over three years

Niro Narendra, Randhir Chavan, Swathi Panneerselvam, Yit C. Yang. Ophthalmology, Wolverhampton Eye Infirmary, Wolverhampton, United Kingdom.

Purpose: To model the three year impact of switching from ranibizumab to aflibercept therapy on injection and monitoring episodes for patients undergoing intravitreal therapy for wet macular degeneration.

Methods: 89 patients consecutively commenced ranibizumab therapy between May and October 2009, in a strict two stop model at a single site. The number of visits for injections and monitoring exams as well as the number of patients discharged from the programme were retrospectively analysed over a three year period up to end of October 2012. To estimate the effect of the recommended aflibercept dosing regimen, the number of patients actively managed in each twelve month period in year 1, 2 and 3 were assigned to fixed dosing every two months for first year but for years 2 and 3, a two monthly follow up regimen was followed with PRN dosing on a 1:1 replacement basis for aflibercept. The numbers of injection and monitoring visits were compared between actual numbers made on the ranibizumab programme and the number on an aflibercept programme estimated from the modelling.

Results: In the first year, 81 patients completed 12 month follow up, made 533 monitoring and 443 injection visits. 41 patients required fewer than six injections. Modelling for a two monthly fixed dosing aflibercept regimen there would have been 533 fewer monitoring visits but 41 patients would receive 86 more injections between them. 72 patients were followed to month 24 and 58 patients were followed to month 36. Over the second and third years, these patients made a total of 891 monitoring visits and received 531 injections. In the second and third year there could be a potential reduction of monitoring visits to about 445 visits by increasing follow up interval.

Conclusions: There is a significant natural attrition rate in numbers of patients beyond month 12. In the first twelve month a patient on aflibercept regimen would likely to experience more injections than on lucentis regimen but there should be a large reduction in monitoring visits. It should be possible to reduce the number of follow up visits in second and third year but whether the requirement for injections when using aflibercept on a PRN basis in the second and third year will be less than with ranibizumab is still uncertain.

Commercial Relationships: Niro Narendra. None; Randhir Chavan. None; Swathi Panneerselvam. None; Yit C. Yang. Novartis (R)

Program Number: 3814 Poster Board Number: B0124
Presentation Time: 2:45 PM - 4:30 PM

Patients prefer a fixed monthly dosing regimen in anti-VEGF treatment for neovascular age-related macular degeneration
Results: Forty-six men and 62 women were included. Mean time under anti-VEGF treatment was 35 months (range 11-83). The mean number of intravitreal injections was 19 (5-51). One eye was treated in 58.3 % of patients and 41.7 % of patients received injections in both eyes. Thirty- three percent of patients favoured a pro re nata regimen, 47 % of patients favoured continuous monthly injections, and 11 % of the patients abstained from the question of preference. The questionnaire from 8 % of the patients could not be analysed to a final conclusion.

Conclusions: The majority of patients favoured a fixed dosing regimen with monthly injections rather than monthly controls with a pro re nata regimen. However the patients in this cohort did not reflect and consider on the risk of endophthalmitis.

Commercial Relationships: Katharina Droge, None; Dirk Mueller, None; Albert Caramoy, Bausch & Lomb (F), Fluoron GmbH (F), Alamedics GmbH&Co. KG (F); Bernd Kirchhof, None; Sascha Fauser, None

Program Number: 3816 Poster Board Number: B0126
Presentation Time: 2:45 PM - 4:30 PM

RESULTS OF INTRAVITREAL RANIBIZUMAB WITH A PRN REGIMEN IN THE TREATMENT OF EXTRA AND JUXTAFOveal NEOVASCULAR MEMBRANES IN AGE-RELATED MACULAR DEGENERATION

Cinzia Mazzini, Lucia Finocchio, Daniela Bacherini, Giovanni Giacomelli, Ilaria Biagini, Lorenzo Vannozzi, None; Gianni Virgili, None; Ugo Menchini, None

Program Number: 3815 Poster Board Number: B0125
Presentation Time: 2:45 PM - 4:30 PM

RESULTS OF INTRAVITREAL RANIBIZUMAB WITH A PRN REGIMEN IN THE TREATMENT OF EXTRA AND JUXTAFOveal NEOVASCULAR MEMBRANES IN AGE-RELATED MACULAR DEGENERATION

Cinzia Mazzini, Lucia Finocchio, Daniela Bacherini, Giovanni Giacomelli, Fabrizio Giancanti, Ilaria Biagini, Lorenzo Vannozzi, Gianni Virgili, Ugo Menchini. Department of Specialist Surgical Sciences, Eye Clinic, University of Florence, Florence, Italy.

Purpose: To evaluate the efficacy of intravitreal ranibizumab with a pro re nata regimen (PRN) in the treatment of naïve extra or juxtafoveal neovascular membranes secondary to age-related macular degeneration (AMD).

Methods: Retrospective, non-comparative case series. 31 eyes of 31 patients (mean age 77.0 years, SD:6.7) with naïve neovascularization secondary to AMD were enrolled and treated with ranibizumab intravitreal injections with a PRN regimen. We reviewed 23 choroidal neovascular membranes (CNV) and 8 retinal angiomatosus proliferation (RAP). 16 lesions were extrafoveal and 15 were juxtafoveal. The follow-up was at least 12 months and it was performed monthly up to 6 months and then quarterly. Best corrected ETDRS visual acuity (BCVA) and lesion size analysis with fluorescein angiography (FA) were recorded before treatment and at 3, 6, 12 and 24 months after first injection.

Results: The mean baseline BCVA worsened from 0.28 LogMAR (SD:0.19) at baseline to 0.42 LogMAR (SD:0.33) at 1-year follow-up (P=0.02). BCVA was 0.53 LogMAR (SD:0.44) at 2-years follow-up. Overall visual acuity improved by at least one line in 7 cases(22.6%), it remained unchanged in 7 cases(22.6%) and it worsened in 17 cases(58.8%) at 1-year follow-up. 5 patients showed a slight improvement in visual acuity(20%), VA remained stable in 7 cases(28%) and it worsened in 13 cases(52%) at 2-years. The mean lesion size increased from 1.19 sq mm (SD:1.24 sq mm) at baseline to 2.07 sq mm(SD:2.21 sq mm) at 1-year follow-up (P=0.49), up to 2.47 sq mm(SD:2.56 sq mm) (P=0.01), 9 patients developed a recurrence at 6 months and 26 patients had one or more relapses at 1-year follow-up. Only in 5 cases the disease remained stable after 3 injections of loading phase. None of the 25 patients with 2-years follow-up was immune from relapse. The mean number of injections was 5.1(SD:1.4).

Conclusions: Intravitreal ranibizumab with a PRN regimen in nonsubbfoveal neovascular membranes was effective in maintaining BCVA level only up to 6 months of follow-up. However we registered a statistically significant VA decrease both at 1-year and at 2-years follow-up. Therefore we believe that controls have to be made monthly in a ranibizumab PRN regimen for nonsubbfoveal neovascular membranes secondary to AMD. A different regimen, such monthly injections or a treat and extend one, should be adopted.

Commercial Relationships: Cinzia Mazzini, None; Lucia Finocchio, None; Daniela Bacherini, None; Giovanni Giacomelli, None; Fabrizio Giancanti, None; Ilaria Biagini, None; Lorenzo Vannozzi, None; Gianni Virgili, None; Ugo Menchini, None

Program Number: 3812 Poster Board Number: B0122
Presentation Time: 4:30 PM - 6:00 PM

Effectiveness of quarterly (Q3M) versus monthly (QM) ranibizumab according to initial gains in visual acuity - an analysis of 12 month data from the EXCITE study

Vitor Chong, Winfried M. Amoaku, Jonathan Alsop, Aaron Osborne. Oxford Eye Hospital, Oxford University Hospitals, Oxford, United Kingdom.

Purpose: To investigate whether early visual acuity (VA) response to ranibizumab treatment in patients with neovascular AMD (nAMD) is predictive of VA outcomes at one year; and to to identify cohorts of patients (pts) in whom Q3M or more frequent follow-up may be required.

Methods: EXCITE was a 12-month, multicenter, double-masked, phase IIIB study of patients (N=353) with primary or recurrent nAMD (all lesion types) randomized 1:1:1 to treatment with three monthly initiating injections of loading phase. None of the 25 patients with 2-years follow-up was immune from relapse. The mean number of injections was 5.1(SD:1.4).

Conclusions: Intravitreal ranibizumab with a PRN regimen in nonsubbfoveal neovascular membranes was effective in maintaining BCVA level only up to 6 months of follow-up. However we registered a statistically significant VA decrease both at 1-year and at 2-years follow-up. Therefore we believe that controls have to be made monthly in a ranibizumab PRN regimen for nonsubbfoveal neovascular membranes secondary to AMD. A different regimen, such monthly injections or a treat and extend one, should be adopted.

Commercial Relationships: Cinzia Mazzini, None; Lucia Finocchio, None; Daniela Bacherini, None; Giovanni Giacomelli, None; Fabrizio Giancanti, None; Ilaria Biagini, None; Lorenzo Vannozzi, None; Gianni Virgili, None; Ugo Menchini, None
Impact of the vitreous configuration on the efficacy of quarterly, pro-re-nata and monthly treatment in multicenter trials evaluating ranibizumab for neovascular age-related macular degeneration

Sebastian M. Waldstein1, Ulrike Mayr-Sponer1, Markus Ritter1, Michael Kundi2, Christian Simader2, Ursula Schmidt-Erfurth3.
1Department of Ophthalmology, Medical University of Vienna, Vienna, Austria; 2Institute of Environmental Health, Medical University of Vienna, Vienna, Austria.

Purpose: Intravitreal administration of antiangiogenic drugs is the mainstream of current treatment of exudative macular diseases. However, the impact of the vitreous on the relevant pharmacokinetic mechanisms is unclear. The purpose of this study was to investigate the influence of the configuration of the vitreomacular interface (VMI) on the efficacy of quarterly, pro re nata (PRN) and monthly dosing of ranibizumab in the treatment of neovascular age-related macular degeneration (AMD).

Methods: Standardized monthly optical coherence tomography (OCT) examinations of 486 treatment-naïve patients, enrolled in two separate 12-month prospective randomized multicenter trials, were analyzed for the configuration of the VMI by certified graders of the Vienna Reading Center. Only patients with 10 or more available OCT-examinations, including baseline and month 12, were eligible for the analysis. The individual VMI readings from each visit were integrated to divide all patients into one of the following categories: (1) persistent vitreomacular adhesion (VMA); (2) progressive release of vitreomacular adhesion (RVA); (3) complete posterior vitreous detachment (PVD).

Results: At month 12, the mean change in best-corrected visual acuity (BCVA) from baseline was as follows: Quarterly treatment (n=163): VMA -0.3, RVA +3.2, PVD +4.7 letters; PRN treatment (n=128): VMA +6.3, RVA +4.3, PVD +3.7 letters; monthly treatment (n=84): VMA +7.5, RVA +12.7, PVD +4.9 letters. Quarterly treatment was non-inferior to monthly treatment in patients with PVD, p=0.001. Monthly treatment was superior to quarterly treatment in patients with VMA and RVA, p=0.035. In the PRN regimen, patients with PVD required significantly less dosing (mean 4.8 injections) compared to VMA and RVA (mean 5.3/6.6 injections, p<0.001). The functional outcomes of monthly treatment of patients with VMA and RVA surpassed those of all others.

Conclusions: The configuration of the VMI has a significant impact on the efficacy of therapeutic regimens. Patients with PVD appear to be less sensitive to dosing variations, while patients with VMA and RVA may derive optimal benefit from continuous intensive treatment. Our findings may serve as a base for individualized treatment decisions in neovascular AMD and potentially other indications.

Commercial Relationships: Sebastian M. Waldstein, None; Ulrike Mayr-Sponer, None; Markus Ritter, None; Michael Kundi, None; Christian Simader, None; Ursula Schmidt-Erfurth, Alcon (C), Bayer Healthcare (C), Novartis (C)

Clinical Trial: NCT00275821

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Program Number: 3818 Poster Board Number: B0129
Presentation Time: 2:45 PM - 4:30 PM
Treatment Patterns in Neovascular Age-Related Macular Degeneration between 2005-2010
Eleonora M. Lad1, Bradley G. Hammill2, Laura G. Qualls2, Fang Wang2, Scott W. Cousins3, Lesley H. Curtis4. 1Ophthalmology, Duke University Eye Center, Durham, NC; 2Duke Clinical Research Institute, Duke University School of Medicine, Durham, NC; 3GlaxoSmithKline, King of Prussia, PA.

Program Number: 3818 Poster Board Number: B0129
Presentation Time: 2:45 PM - 4:30 PM
Commercial Relationships: Gregory D. Lee, None; Jordana G. Fein, None; Elias Reichel, Thrombogenicins (F), Alimera (C), Ocular Instruments (F)

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Program Number: 3818 Poster Board Number: B0127
Presentation Time: 2:45 PM - 4:30 PM
Age-Related Macular Degeneration: Patient Response and Outcomes to Afiblercept using PRN Dosing Regimen
Gregory D. Lee, Jordana G. Fein, Elias Reichel. Ophthalmology, New England Eye Center, Tufts Medical Center, Boston, MA.

Purpose: To evaluate the response and outcomes in patients with age-related macular degeneration (AMD) treated with intravitreal afiblercept in a PRN dosing regimen.

Methods: Retrospective chart review of 19 eyes of 17 subjects, with a diagnosis of neovascular AMD, treated at the New England Eye Center, Tufts Medical Center, between February and December 2012 by one retina specialist. Patients were treated with intravitreal afiblercept using a PRN treatment regimen, with re-treatment criteria being the presence of new or persistent intra-retinal or sub-retinal fluid. All patients were followed with spectral domain optical coherence tomography (OCT) macular scans and a dilated ophthalmologic exam. Outcome measurements included anatomic response as measured on OCT, interval between follow-up visits, and interval between repeat injections.

Results: The 19 eyes received an average of 1.84 afiblercept injections over a mean follow-up time of 20.29 weeks. The mean interval between follow-up visits was 5.18 weeks and the mean interval between injections was 11.18 weeks. 14 eyes had been treated previously with ranibizumab or bevacizumab with an average of 6.62 prior injections (Range 1-57). Of these, 5 eyes (5/14, 36%) were non-responsive to other anti-vascular endothelial growth factor (anti-VEGF) medications, defined as persistent intra-retinal or sub-retinal fluid after previous injection; 4 of these non-responders (80%) responded to intravitreal afiblercept with anatomic resolution of fluid. This group of previous non-responders received a mean of 2 afiblercept injections, with a mean interval between injections of 11.20 weeks (Range: 7-18), and a total mean follow-up time of 25.91 weeks.

2 eyes of 2 patients were afiblercept non-responders (2/19 = 11%). One eye was a non-respondor to other anti-VEGF agents and the second eye was treatment naïve and failed both 2 afiblercept and 2 bevacizumab injections.

Conclusions: The results of this study, albeit limited due to small sample size and short duration of follow-up, suggest that the interval to repeat injection of afiblercept may be longer than with older anti-VEGF agents using a PRN dosing regimen. Furthermore, this study demonstrates the successful use of intravitreal afiblercept in patients who were previously non-responsive to either intravitreal ranibizumab or bevacizumab.

Commercial Relationships: Gregory D. Lee, None; Jordana G. Fein, None; Elias Reichel, Thrombogenicins (F), Alimera (C), Ocular Instruments (F)

Program Number: 3818 Poster Board Number: B0128
Presentation Time: 2:45 PM - 4:30 PM
Purpose: To describe the patterns of anti-VEGF therapy for 1 to 4 years following initial treatment for neovascular AMD (NVAMD) including the rate and frequency of treatment among Medicare beneficiaries.

Methods: We used claims from a 100% sample of Medicare beneficiaries diagnosed with NVAMD from 2005 to 2010. Anti-VEGF treatment was identified using claims for intravitreal injections (CPT 67028) of anti-VEGF with a supporting diagnosis of NVAMD (362.52). Identification of the specific medication received was determined using procedure codes and payment amounts.

Results: We identified 501,702 Medicare patients with NVAMD who initiated anti-VEGF treatment between 2005 and 2010. The mean number of anti-VEGF injections following the initial injection was 4.3 in the first year and decreased to 1.9 in the second year, 1.6 in the third year and 1.1 in the fourth year. Among patients who received a high frequency of injections (7+) during the first year, only 29% received comparable high frequency treatment at year 2, and 14% received no injections. Of the patients who received a low frequency of injections (1-3) during the first year, 76% received no injections and 18% received low frequency treatment during the second year. Between 2005 and 2009, the frequency of anti-VEGF injections in the first year was unchanged for the patients in the low frequency and high frequency cohorts (Table 1).

Conclusions: There is no evidence that the frequency of injections has increased since intravitreal anti-VEGF therapy became available for clinical use in 2005. The frequency of injections is significantly less than in the CATT and HORIZON clinical studies, suggesting general undertreatment of patients with NVAMD.

Table 1.

<table>
<thead>
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<th>Year</th>
<th>Low Frequency (1-3 injections)</th>
<th>High Frequency (&gt;4 injections)</th>
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<td>26.9%</td>
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<td></td>
<td>26.9%</td>
<td>High Frequency (≥4 injections)</td>
</tr>
</tbody>
</table>

Commercial Relationships: Eleonora M. Lad, None; Bradley G. Hammill, None; Laura G. Qualls, None; Fang Wang, GlaxoSmithKline (E); Scott W. Cousins, Alcon (F), Alcon (C), Heidelberg Engineering (C), Narrow River (C), Nordic Biotech (C), PanOptica (C), Pfizer (C), Salutaris Medical Devices (C), Sanofi-Fovea (C), Valeant Ophthalmics (C), Imagen Biotech (I); Lesley H. Curtis, GlaxoSmithKline (F), Johnson & Johnson (F) Support: The study was funded by GlaxoSmithKline. Dr. Lad is supported by a NEI Clinical Scientist Development (K12) award.

Program Number: 3821 Poster Board Number: B0131

Presentation Time: 2:45 PM - 4:30 PM

TWIN : Evolution of visual acuity in patients with wet AMD diagnosed since 2010 and treated with ranibizumab, in current practice - Comparison with LUMIERE study

Hassiba Oubrahim Mehroukine¹, Salomon Y. Cohen², Gerard Mimoun³, Eric H. Souied⁴, Stéphane Quéré⁵, Véronique Schneider⁶.

¹Office, Montargis, France; ²Private practice, Paris, France; ³Hospital, Creteil, France; ⁴Pharmaceutical industry, Rueil Malmaison, France.

Purpose: A previous retrospective study (LUMIERE) performed with 551 patients diagnosed and treated between 2007 and 2009 has suggested infrequent monitoring explaining why the visual function results were lower. The TWIN study was performed in the same centers to describe the evolution of visual acuity (VA) in patients with wet age-related macular degeneration (wAMD) diagnosed and treated since 2010.

Methods: Retrospective observational study sponsored by Novartis. 21 sites (included 13 of the 16 involved in LUMIERE) included 906 eyes of consecutive patients with wAMD diagnosed and treated since 2010 (from 01-2010 to 11-2011).

Results: In the TWIN study at baseline, most patients were female (67.7%), their mean age was 79.3 ± 7.8 years and their VA 56.8 ± 18.0 letters. The lesion was mostly occult (61.3%). The time from diagnosis to treatment improved from 12.6 ± 26.4 days to 7.7 ± 10.9 days. More patients received an induction phase with the first 3 injections every 4-5 weeks (56.6% vs 39.6%). No patient had a strict monthly monitoring over 12 months (visits every 30 days +/- 7 days) but about the same proportion of patients underwent "regular"
monitoring visits every 37 days +/- 14 days (6.5% vs 4.4%). The average visits number was lower (7.4 ± 2.0 vs 8.6 ± 2.0) for a greater average of injections (5.6 ± 2.3 vs 5.1 ± 2.1 injections). At 12 months, the VA gain was similar (4.3 ± 15.4 vs. 3.2 ± 14.8 letters), but a greater proportion of patients presented a gain greater than 5 letters (43.7% vs 37.0%) or between 0 and 15 letters (40.2% vs 33.4%).

Conclusions: The results suggest that compared to 2007-2009 (LUMIERE), physicians in the TWiN study achieve more VA gains by waiting less before first treatment and by complying more to the loading doses while monitoring less but giving more injections.

Commercial Relationships: Hassiba Oubraham Mebroukine, Novartis (R); Salomon Y. Cohen, Novartis (C), Allergan (C), Bayer (C), Thea (C), Bausch and Lomb (C); Gerard Minoum, None; Eric H. Souied, BAUSCH + LOMB (C), NOVARTIS (C), BAYER (C), THEA (C), ALLERGAN (C); Stéphane Quéré, Novartis Pharma SAS (E); Véronique Schneider, Novartis (E)

Support: Novartis

Program Number: 3822 Poster Board Number: B0132
Presentation Time: 2:45 PM - 4:30 PM

How bad are the long term results under real life conditions beyond 2 years of treatment for wet AMD with ranibizumab or bevacizumab? Results from a 4 year follow up of 77 patients Wolfgang F. Schrader, Adrian T. Bernhard, Clara Dietz, Karina Sommer, Ermioni Panidou, Ophthalmology, Maxmillians-Augenklinik, Nuernberg, Germany.

Purpose: Visual acuity (VA) can be preserved by 4-weekly intravitreal injections (IVI) of ranibizumab over >2 years (yrs). The CATT-trial showed that a PRN (pro re nata) Treatment (TX) based on a monthly follow up (FU) is not inferior to a monthly IVI TX. In Germany, most insurance companies do not reimburse a monthly FU based on OCT. However, a PRN-TX based on visual acuity (VA) changes rather than OCT changes has less favourable results. The aim of this study is to investigate the long term development of wet AMD under real life conditions.

Methods: Retrospective analysis of 77 patients with wet AMD, initially treated with either 3 IVI of bevacizumab (1.5mg) or ranibizumab (0.5mg), followed by PRN-IVI. Main outcome parameters were the VA change after a follow up (FU) of >4 yrs, the total number of IVI needed and the frequency of IVI in the 1st, 2nd, 3rd and 4th yr of TX.

Results: 88 eyes (77 patients, median age 78 yrs, mean 75.6 yrs, 45 females, 32 males) had a FU of >4yrs. Mean FU time was 4.33yrs. 12.6±7.3 IVI were performed within the FU-time. Mean no. of IVIs in 1st yr was 4.6±1.5 (range 3-8), in 2nd year 2.8±2.2 (range 0-8), in 3rd yr 2.7±2.5 (range 0-10) and in 4th yr 2.2±2.8 (range 0-10). 51/88 (58%) required 3 or more IVIs in yr 3, and 31/88 (35%) in yr 4. No significant increase of VA could be registered, as compared to a strict monthly OCT guided monitoring system. At least, VA remained stable over 2 yrs (LogMAR 0.64 at baseline, at 2 yrs 0.68), but then deteriorated to 0.84 at 4yrs. Patients younger than 78 yrs (mean 70.4±6.8 yrs) had a better baseline VA (LogMAR 0.54) and a better final VA (LogMAR 0.76) at 4yrs than those older than 77 (mean 82.4±3.1yrs, baseline VA 0.73, at 4yrs 0.92).

Conclusions: As in Germany neither monthly injections nor a monthly FU, based on OCT, was reimbursed by most insurance companies, our results based on a VA guided PRN TX were inferior to such a TX at 2 yrs. Younger patients have a more favourable outcome of VA after a 4yr TX of wet AMD. As a significant part of the patients require 3+ IVIs even in yr 3 and 4, we have to realize, that a close (monthly) monitoring is still necessary beyond two years of TX for a successful PRN-TX.

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Purpose: To report the 12-month outcomes of 1073 treatment-naive patients with exudative age-related macular degeneration (wet AMD) who were treated with anti-VEGF drugs audited in routine clinical practice. We tested the hypothesis that eyes treated in routine practice have similar results to those reported by the pivotal phase III studies, MARINA and ANCHOR.

Methods: This database study analyzed outcomes from a prospectively designed database of a cohort of patients with wet AMD. Index visit characteristics, such as lesion size and type, visual acuity (VA) (LogMAR letters), as well as treatments, outcomes (VA, change in lesion activity status) and ocular adverse events were continually and anonymously recorded in an electronic database for 12 months. Primary outcome measures were change in VA after 12 months and number of treatments administered. Secondary outcomes included ocular adverse events and predictors of 12-month outcomes.

Results: Data from 1073 patients that were contributed by 27 retinal specialists across Australia working in routine clinical practice were analyzed. Mean change in VA in the entire cohort was +3.7 letters (95% CI: 2.4-5) which was achieved with a mean of 7.3 injections. When cohorts of patients from the observational study were selected that matched entry criteria for the MARINA study, but not the ANCHOR study. No significant differences were found when results of change in VA and number of injections were analyzed with respect to lesion type or size. The median time to first the visit that the lesion was graded “inactive” was 191 days.

Conclusions: These findings indicate that VEGF inhibitors can achieve reasonably good outcomes for wet AMD when used in routine clinical practice. The comparison of matched patients from the observational cohort with the treatment groups of the two pivotal phase III studies indicated that the results of at least one of these may be achievable in the real world.

Commercial Relationships: Mark C. Gillies, Novartis (R), Pfizer (R), Allergan (F), Bayer (F); Daniel Barthelmes, None
Support: Australian National Health and Medical Research Council Project Grant

Program Number: 3825 Poster Board Number: B0135
Presentation Time: 2:45 PM - 4:30 PM
United Kingdom Neovascular AMD Database study: outcomes of over 92,000 intravitreal ranibizumab injections
Adnan Tufail, Ophthalmology, Moorfields Eye Hospital, London, United Kingdom.

Purpose: To evaluate the potential use of Electronic Medical Records (EMR) for rapid and high quality data capture. To study ranibizumab therapy for neovascular AMD (nAMD) in terms of baseline demographics, complications and visual outcome in a very large cohort of patients.

Methods: Participating centres prospectively collected clinical data using an EMR system, with automatic extraction of anonymized data to a database. Up to 5 years of data were collected from each centre. Centres using EMR systems that collected a minimum standard data set for eyes receiving ranibizumab therapy for nAMD including preoperative, visual acuity (ETDRS), operative and postoperative data set, were invited to submit data, which were remotely extracted, anonymised, assessed for conformity and completeness, and analysed.

Results: A total of 92,976 ranibizumab treatment episodes from 12952 treated eyes associated with over 300000 clinic visits were collated from treatment naive eyes within a month of starting the study. Mean age at first treatment was 79.1 (SD 8.4) with a female preponderance 1.7:1. Visual acuity changes were as follows: For eyes followed for at least 3 years the mean visual change from baseline in 0.58 (LogMAR) visual acuity changes were +4 letters at peak gain timepoint, +2 at 12 months, +1 letter at month 24 and them 0 at month 30. The proportion of eyes that avoided moderate vision loss (15 letters) were 90% by year 1, 84% year 2 and 82% at year 3. The proportion of eyes with visual acuity of 20/40 or better were 16% at baseline, 30% by month year 1, 30% year 2 and 29% year 3. The median number of treatments given were 5 in year one 4 in year 3 and 4 in year 3. The number of outpatient visit were in year 1 to 3 are 9, 2.8, 2 and 8.2 respectively.

Conclusions: EMR has the potential to collate very large volumes of high quality data rapidly. This study provides pooled, anonymized data on the demographics, and visual outcome and treatment and follow up burden of ranibizumab treatment for nAMD. This may enable retina specialist centres to benchmark their outcomes, and facilitate cost-benefit analyses.

Commercial Relationships: Adnan Tufail, Allergan (C), Bayer (C), GSK (C), OcuLogics (C), Pfizer (C), Thrombogenics (C), Amakem (C), Heidelberg Engineering (R), Novartis/Alcon (C), Sanofi/Genzyme (C)

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Purpose: To evaluate four year treatment results of visual outcome in patients with neovascular AMD treated with Ranibizumab and compare with landmark trials.

Methods: Retrospective data analysis of patients who first attended the AMD clinic between 2007-2008 with diagnosis of neovascular AMD and were treated with intravitreal Ranibizumab. Treatment involved 3 loading doses of Ranibizumab followed by strict four week review and retreatment on per re nata (PRN) basis. Data analysis included demographics, Best Corrected Visual Acuity (BCVA) and mean number of injections.

Results: A total of 143 treatment-naive patients first attended our AMD clinic between 2007-2008. Discontinuation rate was 21.7% (31 patients) compared with 22% in multi centre trials. Eleven patients were deceased, 10 missed follow-up due to change of residence location, and the remaining 10 for other reasons. 112 patients who completed 48 months follow-up were included in the analysis. Mean age was 83.54 years (SD 7.77). Mean BCVA at baseline was 47.72 ETDRS letters (SD 16.03). At 12 months, mean BCVA was 55.79 (SD 17.79) showing an improvement of 8.07 letters (P=0.01). Mean number of injections for this period was 5.78. This visual outcome was maintained at 24 months with a gain 9.5 letters (P=0.01) with a mean number of injections of 2.8. Similarly, at 36 months, mean BCVA was 55.83 (SD 19.9) and a gain of 8.11 letters was achieved. Mean number of injections for the third year was 2.47. Finally, at 48 months, our patients maintained a gain of 6.24 letters needed to determine the efficacy and long-term effects of aflibercept versus its anti-vascular endothelial growth factor predecessors.

Conclusions: We assessed the effect of switching from bevacizumab and/or ranibizumab to aflibercept in patients with age-related macular degeneration. On average, at the most recent aflibercept injection, 41% of eyes had improved visual acuity by 1 line or more on the Snellen visual acuity chart, and 57% of eyes had a decrease in central macular thickness. This study is limited by the small number of eyes studied. Ongoing data collection is currently being performed on a larger sample of patients at the same center. Further studies are needed to determine the efficacy and long-term effects of aflibercept.
logarithmic of the minimum angle of resolution visual acuity (Log MAR VA) was 0.978 (20/189) with a range of 0.1 to 2.6. Mean post treatment Log MAR VA was 0.93 (20/169; p = 0.68) after the first Aflibercept injection and 0.68 (20/96; p = 0.09) after the second Aflibercept injection. Mean pretreatment CMT was 288 microns; mean post treatment CMT was 261 microns after the 1st Aflibercept injection (p = 0.06), and 271 microns after the 2nd Aflibercept injection (p = 0.3). Analysis of the VFQ-25 answers revealed a trend towards improvement in general vision, near tasks, mental health, and reduced dependency from baseline treatment to three months following initial Aflibercept injection.

**Conclusions:** Since it gained FDA approval in 2011 for neovascular ARMD, Aflibercept has expanded the treatment options for this debilitating condition. Our findings suggest that in patients who have previously been treated with alternative VEGF inhibitors, there is a trend towards improvement in visual acuity, CMT, and, perhaps most importantly, quality of life. This can partly be explained by tachyphylaxis which develops in this cohort of patients. Further follow up of these patients is warranted to understand fully the relative efficacy of Aflibercept in neovascular ARMD.

**OCT following treatment with 7 Ranibizumab injections and 1 Pegaptanib injection**

**OCT of same patient after one Aflibercept injection.**

**Program Number:** 3829  **Poster Board Number:** B0139  **Presentation Time:** 2:45 PM - 4:30 PM

**Early vs Delayed 15-Letter Responders to Ranibizumab Treatment in Year 1 of the Phase III HARBOR Trial**

**Richard Dreyer¹, Gregg T. Kokame², Glenn Stoller³, Howard Shapiro⁴, Dafeng Chen⁵, Lisa Tuomi⁶.**

¹Retina Northwest, Portland, OR; ²The Retina Center at Pali Momi, Aiea, HI; ³Ophthalmic Consultants of Long Island, Lynbrook, NY; ⁴Genentech, Inc., South San Francisco, CA; ⁵Genentech, Inc., South San Francisco, CA; ⁶Genentech, Inc., South San Francisco, CA.

**Purpose:** This subanalysis of the phase III HARBOR study examined patterns of visual acuity (VA) response over time to ranibizumab 0.5 mg or 2.0 mg administered on a monthly or as-needed (PRN) basis in patients with subfoveal neovascular age-related macular degeneration (wet AMD). Potential baseline predictors of treatment response in early 15-letter responders vs delayed 15-letter responders were also identified.

**Methods:** Patients (n=1097) were randomized to receive intravitreal ranibizumab 0.5 mg or 2.0 mg monthly or PRN after three monthly loading doses. Best-corrected visual acuity (BCVA), as observed, was measured at baseline (n=1097), and at Months (M) 3 (n=1057), 6 (n=1028), 9 (n=1013), and 12 (n=1000). Patients were categorized based on VA changes as “early responders” (ie, gained ≥15 letters from baseline at M3; n=266) or “delayed responders” (did not gain ≥15 letters from baseline at M3, but did so at M12; n=138).

**Results:** At M3, the proportion of patients who gained ≥15 letters from baseline in BCVA was: 24% (0.5 mg monthly), 25% (0.5 mg PRN), 26% (2.0 mg monthly), and 26% (2.0 mg PRN). Some patients who did not achieve a ≥15 letter gain at M3 continued to experience VA increases throughout treatment, as the proportion of patients who gained ≥15 letters from baseline in BCVA at M12 was 36%, 32%, 37%, and 35%, respectively. At M12 (n=256), early responders maintained their ≥15 letter gain in 83%, 76%, 86% and 82% of patients, respectively. Compared with the M3 visit, an additional 11-12% of patients treated with ranibizumab monthly and 7-9% of patients treated with ranibizumab PRN gained 15 letters of vision at M12. Compared with delayed responders, those that were early responders tended to have worse mean VA at baseline, with significant differences observed in the 0.5 mg monthly (P=0.0013) and 2.0 mg monthly (P=0.022) treatment groups.

**Conclusions:** A subset of patients who do not experience significant gains (ie, ≥15 letters) in BCVA at M3 can, with continued ranibizumab treatment, achieve significant gains at M12. A ≥15 letter gain in vision at M3 may indicate sustained efficacy with a less-than-monthly dosing regimen, as 76-82% of PRN patients maintained these gains at M12.

**Commercial Relationships:** Richard Dreyer, Genentech (F), Genentech (F), Allergan (F), Regeneron (F); Gregg T. Kokame, Santen (C), Allergan (C), Genentech (C), Regeneron (C), Regeneron (R), Alimera (C); Glenn Stoller, Lpath (C), Regeneron (F), Lpath (P), SKS (I); Howard Shapiro, Genentech, Inc. (E); Dafeng Chen, Genentech/Roche (F), Genentech/Roche (C); Lisa Tuomi, Genentech (E)

**Clinical Trial:** NCT00891735

**Program Number:** 3830  **Poster Board Number:** B0140  **Presentation Time:** 2:45 PM - 4:30 PM

**Comparison of outcome of anti-vascular endothelial growth factor (anti-VEGF) treatment in exudative Age-related Macular Degeneration (AMD) in the presence and absence of Vitreomacular Adhesion (VMA)**

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**Purpose:** To compare the outcome of anti-VEGF treatment in exudative AMD in the presence and absence of VMA.

**Methods:** We retrospectively analysed medical records and Optical Coherence Tomography (OCT) scans of 38 patients (38 eyes) who were receiving intravitreal injections of Ranibizumab for exudative AMD. We included 19 patients in Group A (presence of VMA) and 19 patients in the control Group B (no VMA). Both groups were comparable in respect of age distribution, Best Corrected Visual Acuity (BCVA) and central macular thickness (CMT) at baseline. BCVA and CMT were compared between the two groups at baseline and at 12 months.

**Results:** Mean BCVA (ETDRS letters) in Group A at baseline was 57.79 and showed a statistically significant improvement at 12 months by 8.74 letters (P=0.043). In Group B there was a significant improvement in BCVA from baseline 59.47 over 12 months by 8.16 letters (P=0.040). Baseline CMT in Group A was 311.11 microns and showed a significant reduction by 62.27 microns (P=0.016), and Group B showed a reduction in CMT from baseline of 310.48 microns by 54.89 microns (P=0.022) at 12 months review.

**Conclusions:** Our results with a small number of patients showed both groups responded equally well to the anti-VEGF treatment. Presence of vitreomacular adhesion in wet macular degeneration did not seem to affect the response to anti-VEGF treatment, and prompt treatment on diagnosis helps to achieve better visual outcome. Further prospective studies with larger groups of patients over a longer period are needed to fully evaluate if presence of VMA is an indicator for poor response to anti-VEGF treatment in wet AMD.

**Commercial Relationships:** Seena Nambiar, None; Manju N. Chandran, None; Narendran Nair, None; Sidharth Praveen, None; Malpreet Liddar, None; Geeta Menon, NOVARTIS (R), ALLERGAN (R), BAYER (R).

**Program Number:** 3831 Poster Board Number: B0141

**Presentation Time:** 2:45 PM - 4:30 PM

**LUMINOUS:** baseline characteristics of the first cohort of patients treated with ranibizumab 0.5 mg in routine clinical practice

**Christopher Brand.** Royal Hallamshire Hospital, Sheffield, United Kingdom.

**Purpose:** LUMINOUS is a 5-year, global, prospective, observational, long-term study being conducted to evaluate the safety and effectiveness of ranibizumab 0.5 mg in patients with age-related macular degeneration (AMD), diabetic macular edema (DME) and retinal vein occlusion (RVO) in routine clinical practice, treated in accordance with the local product label.

**Methods:** The study aims to enrol 30,000 patients from approximately 500 centres in 34 countries worldwide. Here we report the baseline characteristics of the first cohort of patients enrolled from March 2011 to February 2012.

**Results:** A total of 1915 patients in this recruitment period were included in the analysis. Since majority of the patients (n=1877) have neovascular (n) AMD, here we report the baseline characteristics of nAMD patients. The mean age of these patients is 79.2 years, 61.7% are female, and 93.0% are Caucasian. Demographic characteristics such as age, gender and race are well-balanced between treatment-naive (T1) and treatment non-naive (T2) groups. Fifty-eight percent of patients are treatment non-naive; median time since nAMD diagnosis to baseline is 0.9 years for T1 patients and 1.9 years for T2 patients. At baseline, mean visual acuity was 55.8 (T1) and 57.7 (T2) letters and central retinal thickness was 283.0 (T1) and 251.0 (T2) μm. Overall, 31.0% of patients had predominantly classic type of lesion, 42.0% had pigment epithelium detachment, 2.2% had polypoidal choroidal vasculopathy and 3.1% had retinal angiomatic proliferation at baseline.

**Conclusions:** LUMINOUS trial is successfully enrolling patients (more than 7726 patients recruited by Dec, 2012), and the overall baseline characteristics are as expected in a real-world setting.

**Support:** Novartis Pharma AG

**Clinical Trial:** NCT01318941

**Program Number:** 3832 Poster Board Number: B0142

**Presentation Time:** 2:45 PM - 4:30 PM

**Visual outcomes of ranibizumab treatment in fellow eyes of exudative AMD

Jamie Chew1-3, Geoffrey Broadhead1-2, Haitao Li1, Meidong Zhu2-4, Andrew A. Chang5-6. 1Sydney Retina Clinic & Day Surgery, SYDNEY, NSW, Australia; 2Save Sight Institute, University of Sydney, SYDNEY, NSW, Australia. **Purpose:** To evaluate 12 month visual acuity outcomes of fellow eyes compared to first eyes in patients receiving intravitreal ranibizumab for exudative age-related macular degeneration (AMD).

**Methods:** Retrospective review of patients with exudative AMD initiated on ranibizumab treatment between June 2007 and March 2008 at a tertiary retinal clinic. Patients who were diagnosed with choroid neovascularisation (CNV) bilaterally and were anti-VEGF treatment naïve were included in the study. All patients were followed for 12 months in both eyes. Best corrected visual acuity (BCVA) was converted to visual acuity score (VAS). Eyes with VAS > 85 letters (“Good vision group”, Snellen VA >6/12) at baseline in both the first and fellow eyes were further analysed for BCVA change.

**Results:** 46 patients met inclusion criteria. Mean interval of CNV differentiation was 3.1 months (range 0.3-10 months). Mean interval of CNV recurrence was 6.2 months (range 0.2-37 months). Mean interval of the first anti-VEGF treatment was 1.3 months (range 0.1-2.4 months).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Treatment-naive (T1)</th>
<th>Treatment non-naive (T2)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), Mean (SD)</td>
<td>78.4 (8.7)</td>
<td>79.2 (8.5)</td>
<td>78.9 (8.6)</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>295 (37.7)</td>
<td>421 (38.4)</td>
<td>716 (38.1)</td>
</tr>
<tr>
<td>Female</td>
<td>486 (62.1)</td>
<td>673 (61.5)</td>
<td>1159 (61.7)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (0.1)</td>
<td>1 (0.1)</td>
<td>2 (0.1)</td>
</tr>
<tr>
<td>Prior ocular treatment, n (%)</td>
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<tr>
<td>Ranibizumab</td>
<td>0 (0.0)</td>
<td>1088 (99.4)</td>
<td>1088 (98.0)</td>
</tr>
<tr>
<td>Bevacizumab</td>
<td>0 (0.0)</td>
<td>72 (6.6)</td>
<td>72 (3.8)</td>
</tr>
<tr>
<td>Verteporfin</td>
<td>0 (0.0)</td>
<td>17 (1.6)</td>
<td>17 (0.9)</td>
</tr>
<tr>
<td>Non-drug phototherapy</td>
<td>0 (0.0)</td>
<td>13 (1.2)</td>
<td>13 (0.7)</td>
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<tr>
<td>Pegaptanib sodium</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Visual acuity (average ETDRS letter score), Mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central retinal thickness (μm), Mean (SD)</td>
<td>282.8 (104.84)</td>
<td>251.0 (65.70)</td>
<td>261.5 (93.60)</td>
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<td>Lesion type, n (%)</td>
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<tr>
<td>Predominantly Classic</td>
<td>260 (33.2)</td>
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<td>All others</td>
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<td>767 (70.6)</td>
<td>1283 (68.4)</td>
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<td>Missing</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Lesion size, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1 DA</td>
<td>297 (38.0)</td>
<td>385 (35.2)</td>
<td>682 (36.3)</td>
</tr>
<tr>
<td>≥1 DA</td>
<td>480 (61.4)</td>
<td>704 (64.7)</td>
<td>1184 (63.3)</td>
</tr>
</tbody>
</table>

*Patients included in the treatment non-naive group are those who had prior experience to ranibizumab and/or other ocular treatments.

**Commercial Relationships:** Allergan (C), Allergan (D), Bayer (C), Merck (R), Pfizer (F), Quark Pharmaceuticals (F), Novartis (C), Novartis (F), Novartis (R), Sharp (R), Dohme (MSD) (R).

**Clinical Trial:** NCT01318941

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diagnosis between the fellow eye and the first eye was 461+/−378 days, and the mean time between the fellow eye diagnosis and the previous clinical review was 47+/−20 days. There was no statistically significant difference in the mean baseline VAS between these two groups (First eye=70 letters, Snellen acuity 6/17 and the second eye=77 letters, Snellen 6/13) (p=0.101), nor with the 12-month mean BCVA (VAS=72 letters in the first eye and 76 letters in the fellow eye) (p>0.05).

At baseline, 15 first eyes and 22 fellow eyes were categorised in the “Good Vision Group”. Of these patients, 8 first eyes (53%) and 18 fellow eyes (82%) remained in this group at 12 months. Mean VAS change at 12 months compared to baseline was −9 letters in the first eyes (p=0.024) and −3 letters in the fellow eye group (p=0.206).

Conclusions: Intravitreal ranibizumab was able to maintain sight in both first and second eyes. In the subcategory of patients with good baseline VA, the first eyes significantly declined at 12 months, whilst the majority of fellow eyes maintained their baseline visual level at 12 months. Regular assessment of the fellow eye may result in early detection of CNV and better treatment outcomes.

Commercial Relationships: Jamie Chew, None; Geoffrey Broadhead, None; Haitao Li, None; Meidong Zhu, None; Andrew A. Chang, Alcon (C), Bayer (C), Novartis (C), Alcon (R), Bayer (R), Novartis (R), Bayer (F)

Program Number: 3833 Poster Board Number: B0143
Presentation Time: 2:45 PM - 4:30 PM

Short-term Effectiveness of Intravitreal Aflibercept for Persistent Exudative Age-Related Macular Degeneration

Andrew A. Chang1, 2, Geoffrey Broadhead1, 2, Jamie Chew1, 2, Meidong Zhu, Haitao Li. 1Ophthalmology, Sydney Retina Clinic Sydney Eye Hosp, Sydney, NSW, Australia; 2Save Sight Institute, The University of Sydney, Sydney, NSW, Australia.

Purpose: To evaluate the short-term effectiveness of intravitreal Aflibercept for patients with persistent exudative age-related macular degeneration (AMD) despite previous treatment with ranibizumab or bevacizumab.

Methods: Fifty eyes from 50 exudative AMD patients who were poorly responsive to previous anti-VEGF therapies were prospectively recruited (ANZCTR registered: ACTRN12612000666820, registered 21/06/12, commenced 15/7/2012). All participants had at least 4 consecutive anti-VEGF intravitreal injections within the preceding 6 months. Each patient received a single intravitreal aflibercept injection (2.0 mg) and was followed up to 1 month after the baseline treatment. Best-corrected visual acuity (BCVA) was measured by ETDRS vision chart and central macular thickness (CMT) was measured by spectral domain optical coherence tomography.

Results: The average age of participants was 77.1±7.6 years and 22 out of 50 (44%) were male. Mean number of previous ranibizumab or bevacizumab injections was 4.8±0.4 in the 6 months prior to the study enrollment. Baseline BCVA was 60.8±16.2 letters and baseline CMT was 449.3±146.8μm. Mean BCVA improvement from baseline was 3 letters at week 1 and 5 letters at month 1 (both p<0.0001). Mean CMT reduction was 91.0μm at week 1 and 107.3μm at month 1 compared to baseline (both p<0.0001). At month 1, 48.0% of the participants had at least one line (5 letters) improvement in BCVA and 12% of patients had at least 2-line improvement. No patient experienced vision loss greater than one line. At month 1, 79.6% of participants had CMT reduction at least 10% of their baseline measurement and 57.1% of the participants had a reduction of more than 20%. None of the participants had increased CMT more than 5% of their baseline. There were no moderate or severe adverse events associated with aflibercept injection within the observed period.

Conclusions: Intravitreal aflibercept was observed to produce a rapid improvement in visual acuity and reduction in CMT in eyes with persistent macular fluid. No significant safety concerns were noted during the observed period. The long-term anatomical changes and visual acuity outcomes remain to be assessed.

Commercial Relationships: Andrew A. Chang, Alcon (C), Bayer (C), Novartis (C), Alcon (R), Bayer (R), Novartis (R), Bayer (F); Geoffrey Broadhead, None; Jamie Chew, None; Meidong Zhu, None; Haitao Li, None

Support: Unrestricted Bayer Support Grant

Clinical Trial: ACTRN12612000666820

Program Number: 3834 Poster Board Number: B0144
Presentation Time: 2:45 PM - 4:30 PM

Visual And Anatomical Outcomes Following Intravitreal Aflibercept In Eyes With Recalcitrant Neovascular Age Related Macular Degeneration

Dilraj S. Grewal, Daniel Saretsky, Rukhsana Mirza, Manjot K. Gill, Alice T. Lyon. Ophthalmology, Northwestern University, Chicago, IL.

Purpose: To assess the efficacy of intravitreal aflibercept (2mg/0.05ml) on visual and anatomical outcomes in patients with neovascular age-related macular degeneration (AMD) with persistent disease activity recalcitrant to monthly intravitreal bevacizumab or ranibizumab injections.

Methods: Neovascular AMD patients with evidence of persistent exudation on SD-OCT (Spectralis HRA+OCT, Heidelberg Engineering, Heidelberg, Germany), despite having received ≥6 prior intravitreal injections of 0.5 mg/0.05 ml ranibizumab or 1.25 mg/0.05 ml bevacizumab in the prior 12 months were included. Persistent exudation on SD-OCT was defined as presence of either intraretinal fluid/cysts (IRF), or subretinal fluid (SRF), or both. Non-AMD causes of choroidal neovascularization were excluded on the baseline angiogram.

Results: Twenty-eight eyes of 24 patients (11 males, 13 females; mean age 80.6±4.6 years) with recalcitrant AMD who had received an average of 28.5±16.7 (range 6-70) prior ranibizumab or bevacizumab injections over a mean duration of 32.1±18.6 months were included. None of the eyes had evidence of vitreomacular traction or an epiretinal membrane at baseline. Best corrected visual acuity (BCVA), central subfoveal thickness (CFT) and macular volume (MV) using SD-OCT were evaluated at baseline and at each subsequent treatment visit. At baseline, BCVA was 0.38±0.29 logMAR (range 0-0.9), CFT was 315.04 ± 94.15μm (216-637μm) and MV was 7.62±1.23mm3 (4.83-10.15mm3). Twenty-three of these 28 eyes (82.1%) had SRF at baseline, 12/28 had IRF (42.9%) and 8/28 (28.6%) had both. After an average of 5±0.7 aflibercept injections over 6 months, mean logMAR BCVA was 0.37±0.28 (p=0.5), mean CFT decreased to 295.5±77.77μm (range 206-609μm; p=0.008) and MV improved to 7.49±1.09 mm3 (range 5.23 to 9.02mm3; p=0.003). At 6 months follow-up there was a significant reduction in the percentage of eyes with persistent SRF to 14/28 eyes (50%, p=0.02, Fishers exact test) and IRF in 3/28 eyes (10.7%, p=0.01).

Conclusions: In patients with recalcitrant neovascular AMD, intravitreal aflibercept led to statistically significant anatomic improvement as measured by CFT and MV and reduction in the percentage of eyes with persistent IRF or SRF. However, these anatomic gains did not translate into a significant visual improvement at 6 months follow-up.

Commercial Relationships: Dilraj S. Grewal, None; Daniel Saretsky, None; Rukhsana Mirza, None; Manjot K. Gill, None; Alice T. Lyon, None

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Support: An Unrestricted Grant From Research To Prevent Blindness, Inc., New York, New York

Program Number: 3835 Poster Board Number: B0145
Presentation Time: 2:45 PM - 4:30 PM

Outcomes of anti-VEGF therapy for exudative macular degeneration with retinal pigment epithelial tears
Joshua Robinson, Caesar Luo, Bruce Garretson. Associated Retinal Consultants, Royal Oak, MI.

Purpose: To report outcomes of eyes with exudative macular degeneration undergoing anti-VEGF injections following a retinal pigment epithelial tear (RPET) and to assess the prognostic utility of various OCT findings at diagnosis of RPET.

Methods: OCT images of a consecutive series of patients receiving anti-VEGF injections for persistent subretinal fluid associated with RPET were characterized according grade of RPET, absence of subfoveal fibrosis and presence of subfoveal residual RPE. These characteristics were correlated with visual acuity at diagnosis of RPET and at last followup. Statistical significance was set at p<0.05 by Student's t-test.

Results: A retrospective chart review yielded 23 eyes of 23 patients with an average of 15.4 months followup from the time of diagnosis of RPET. Average baseline logMAR visual acuity immediately prior to RPET was 0.691 (SD=0.43). All eyes but one underwent previous intravitreal injection with bevacizumab (N=7), ranibizumab (N=11) or a combination of these drugs (N=3) with an average of 2.2 injections prior to RPET. Average visual acuity decreased to 0.946 (SD=0.63) at diagnosis of RPET, and improved to 0.828 (SD=0.60) at last followup. Visual acuity results by OCT characteristics are shown in Table 1. All subgroups were associated with trending improvement in visual acuity except for eyes with grade 4 RPET. While no subgroup demonstrated a statistically significant change in visual acuity, a significant difference was noted at last followup between Grade 2 (0.419) and Grade 4 eyes (1.209; p=0.034). All 23 eyes presented with subretinal fluid on OCT at diagnosis of RPET, and at last followup 19 (83%) demonstrated improvement in subretinal fluid with complete resolution in 9 (39%) eyes following an average of 9.4 PRN injections of bevacizumab, ranibizumab or aflibercept. No differences were noted in outcomes between anti-VEGF agents.

Conclusions: Long-term visual outcomes in eyes with exudative macular degeneration with RPET are highly variable. Better outcomes are associated with smaller, extrafoveal tears (grade 2). Continued treatment with anti-VEGF agents is associated with improvement or resolution of subretinal fluid in most eyes. Baseline OCT characteristics of RPET grade, subfoveal fibrosis or subfoveal RPE were not predictive of visual improvement with continued anti-VEGF treatment.

Table 1. Changes in logMAR visual acuity by OCT characteristics

<table>
<thead>
<tr>
<th>OCT Findings</th>
<th>Number of eyes</th>
<th>Visual acuity at diagnosis of RPET</th>
<th>Visual acuity at last followup</th>
<th>p-value</th>
<th>Average logMAR change</th>
<th>Visual acuity difference vs. eyes only</th>
</tr>
</thead>
<tbody>
<tr>
<td>All eyes</td>
<td>23</td>
<td>0.946 (SD=0.63)</td>
<td>0.288 (SD=0.10)</td>
<td>0.27</td>
<td>0.113 (SD=0.499)</td>
<td></td>
</tr>
<tr>
<td>Grade 1 RPET (≤30um)</td>
<td>0</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>Grade 2 RPET (30um to 1 disc diameter)</td>
<td>5</td>
<td>0.531 (SD=0.385)</td>
<td>0.419 (SD=0.118)</td>
<td>0.43</td>
<td>0.111 (SD=0.284)</td>
<td></td>
</tr>
<tr>
<td>Grade 3 RPET (&gt;1 disc diameter)</td>
<td>8</td>
<td>0.972 (SD=0.612)</td>
<td>0.501 (SD=0.677)</td>
<td>0.77</td>
<td>0.072 (SD=0.071)</td>
<td></td>
</tr>
<tr>
<td>Grade 4 RPET (&gt;1 disc diameter involving fovea/cortical)</td>
<td>6</td>
<td>1.180 (SD=0.688)</td>
<td>1.229 (SD=0.692)</td>
<td>0.81</td>
<td>0.228 (SD=0.279)</td>
<td></td>
</tr>
<tr>
<td>Subfovealfibrosis absent</td>
<td>15</td>
<td>0.698 (SD=0.332)</td>
<td>0.739 (SD=0.352)</td>
<td>0.40</td>
<td>0.041 (SD=0.483)</td>
<td></td>
</tr>
<tr>
<td>Subfoveal/RPE present</td>
<td>13</td>
<td>0.662 (SD=0.320)</td>
<td>0.716 (SD=0.379)</td>
<td>0.57</td>
<td>0.087 (SD=0.340)</td>
<td></td>
</tr>
</tbody>
</table>

Commercial Relationships: Joshua Robinson, None; Caesar Luo, None; Bruce Garretson, None

Program Number: 3836 Poster Board Number: B0146
Presentation Time: 2:45 PM - 4:30 PM

Retrospective analysis of the real-world utilization of ranibizumab in wAMD
Sobha Sivaprasad1, Ramin Tadayoni2. 1Biomedical Research Centre, King's College Hosp NHS Fdn Trust, Camberley, Surrey, United Kingdom; 2Ophthalmology, Lariboisiere University Hospital, Paris, France.

Purpose: Clinical studies demonstrate that optimal outcomes are achieved with monthly ranibizumab treatment for wet, age-related macular degeneration (wAMD). In clinical practice, in order to reduce management burdens, as-needed or treat-and-extend dosing regimens have been adopted. The AURA study examines the real-world utilization and related outcomes of ranibizumab.

Methods: Retrospective, international (Canada, France, Germany, Ireland, Italy, Netherlands, UK, Venezuela), non-interventional, observational study. Target enrollment was 444 patients per country. Consecutive AMD patients who were prescribed ranibizumab by their physicians and started treatment between January 1, 2009, and August 31, 2009, were included, with a follow-up period of up to 2.5 years. Primary outcomes were change in visual acuity and resource utilization (number of treatment and monitoring visits, treatment use). Data are presented as descriptive statistics.

Results: 253, 489, 54, 445, 436, 490, and 49 patients were enrolled from Canada, France, Germany, Ireland, Italy, Netherlands, UK, and Venezuela, respectively. To date, results for France and Germany are available. The mean change in visual acuity from baseline at Year 1 and Year 2 was 0.8 ± 17.3 and 0.1 ± 18.2 letters, respectively, in France, and -0.4 ± 16.0 and -2.4 ± 17.7 letters, respectively, in Germany. The mean number of monitoring visits was 8.5 in Year 1 and 4.9 in Year 2 in France, and 7.8 and 3.1, respectively, in Germany. The mean number of treatment visits was 4.7 in Year 1 and 2.1 in Year 2 in France, and 4.5 and 1.4, respectively, in Germany. The mean number of injections was 4.4 in Year 1 and 1.9 in Year 2 in France, and 4.2 and 1.1, respectively, in Germany. The clinical management, utilization patterns, and outcomes obtained with the use of ranibizumab for the treatment of wAMD from the remaining countries will also be presented.

Conclusions: The data show that in France and Germany patients undergoing treatment with ranibizumab for wAMD are, on average, having poorer than expected visual outcomes due to less than monthly monitoring and low numbers of treatments per year. Even though these results are much better than the untreated evolution of the disease, consideration should be given to closer adherence to published clinical trial protocols, to try to improve visual outcomes in wAMD patients.

Commercial Relationships: Sobha Sivaprasad, Allergan (F), Bayer (F), Novartis (F); Ramin Tadayoni, Alimera (R), Alcon (C), Novartis (C), Allergan (C), DORC (R), Bausch + Lomb (R), FCI-Zeiss (C), Takeda (R), Alimera (R), Bayer (C)

Support: Study sponsored by Bayer

Clinical Trial: NCT01447043

Program Number: 3837 Poster Board Number: B0147
Presentation Time: 2:45 PM - 4:30 PM

The efficacy of ranibizumab for polypoidal choroidal vasculopathy in a long-term follow-up
Keiko Azuma1, Hidenori Takahashi2, Ryo Obata1, Yasuo Yanagi1.
1Ophthalmology, Tokyo university, Tokyo, Japan; 2Jichi Medical University, Tochigi, Japan.
**Purpose:** The aim of this study was to investigate the long-term efficacy of intravitreal injections of ranibizumab for polypoidal choroidal vasculopathy (PCV), especially focusing on the vascular changes.

**Methods:** A database review was performed for treatment-naïve symptomatic PCV with at least 12 months’ follow-up period. After three monthly injections of ranibizumab, re-treatments were administered when fluid or hemorrhage was present with monthly monitoring. The main outcome measures were the change of the best-corrected visual acuity (BCVA), the diameters of branching vascular networks as measured by indocyanine green angiography (ICGA) and classification of the polypoidal lesion. ICGA was performed at baseline and at least three months after the initial treatment. BCVA was measured by Landolt C-chart and converted to LogMAR units for statistical analysis.

**Results:** Twenty eyes of twenty patients with PCV were included. Mean baseline BCVA before treatment was 0.27 LogMAR, and mean baseline BCVA at the last follow up was -0.35 LogMAR (P=0.20 with Student’s t-test). Mean greatest linear dimension (GLD) of the branching vascular networks were 3.20 mm at baseline and 3.92 mm at the last follow up (P<0.0001 with Student’s t-test), and enlarged by an average of 30.7% in all 20 eyes. Polypoidal lesions were completely obliterated in 7 eyes (35%), partially obliterated in 6 eyes (30%), and stable or increased in 7 eyes (35%).

**Conclusions:** Although the visual acuity was maintained by intravitreal injections of ranibizumab, the branching vascular networks enlarged in nearly all cases and polypoidal lesions remained in 65% of the eyes. “As needed” re-treatment protocol might be limited in preventing the growth of branching networks and polypoidal lesions. More effective treatment plans are needed to control PCV.

**Commercial Relationships:** Keiko Azuma, None; Hidenori Takahashi, None; Ryo Obata, None; Yaso Yu Yagi, None

**Program Number:** 3838 Poster Board Number: B0148
**Presentation Time:** 2:45 PM - 4:30 PM
**Comparison of Intravitreal Afiblercept with Bevacizumab and Ranibizumab for the Treatment of Wet Age-related Macular Degeneration**

Adeel Shaikh1,2, Daniel M. Miller1,2, Michael R. Petersen1, Robert E. Foster1, Christopher D. Riemann1, Robert A. Sisk1,2. 1Vitreous Retinal Surgery, Cincinnati Eye Institute, Cincinnati, OH; 2Ophthalmology, University of Cincinnati, Cincinnati, OH.

**Purpose:** For the past 5 years, intravitreal injections of bevacizumab and ranibizumab have been the conventional treatment of wet age-related macular degeneration (wAMD). Afiblercept is a recently FDA-approved drug indicated for the treatment of wAMD. Recent investigation suggests afiblercept may potentially have a longer biologic effect in vivo in wAMD compared to ranibizumab. We hypothesize that afiblercept may reduce injection frequency in patients with a maintenance anti-VEGF injection requirement for control of wAMD, and despite fewer office visits it will increase treatment healthcare cost per patient.

**Methods:** The records of patients seen at Cincinnati Eye Institute for wAMD between 2011 to 2012 were retrospectively reviewed. Patients receiving intravitreal injections of bevacizumab (IVA) or ranibizumab (IVL) for at least 6 months whose regimen was subsequently changed to afiblercept (IVE) and continued for at least 6 months were included in the study. Demographic data, ocular characteristics, interval between treatments, and cost per injection were collected and analyzed.

**Results:** Thirty three eyes of 30 patients with wAMD were included in the study. There were 17 right and 16 left eyes in the series. Mean patient age was 79 years. There were 15 females and 15 males. Mean follow-up was 12 months. Indication for intravitreal therapy at each office visit was active wAMD. Eight eyes received IVL and 25 eyes received IVA injections initially. Subsequently all eyes received IVE injections. Average duration between IVA or IVL was 29 days, where as it was 34 days between IVE injections (p<0.0004). No complications were noted. Total cost over 6 months of treatment with the IVA injections was $3700, $96600 for IVL injections and $366300 for IVE injections.

**Conclusions:** Afiblercept may be considered in the management of wAMD in select patient population to reduce frequency of injections, office visits and possibly complications. Our retrospective study suggests that afiblercept injections may offer a decreased injection frequency compared to IVA or IVL injections but does add a considerable healthcare cost per patient. Further studies need to be carried out comparing efficacy and visual outcomes in these groups.

**Commercial Relationships:** Adeel Shaikh, None; Daniel M. Miller, Genentech (F), Regeneron (F), Ophthotech (F), Alcon (F), Neovista (F); Michael R. Petersen, Regeneron (F), Genentech (F), Alcon (F), Aerie Therapeutics (F), Ophthotech (F), Neovista (F), Novartis (F); Robert E. Foster, None; Christopher D. Riemann, None; Robert A. Sisk, None

**Support:** 1) Unrestricted Departmental Grant from Research to Prevent Blindness, Inc., New York, NY, to University of Cincinnati Department of Ophthalmology (James J. Augsburger, Chairman), 2) The Cincinnati Eye Institute Foundation, Cincinnati Eye Institute, Ohio (Funding)

376 Macular Miscellaneous

Tuesday, May 07, 2013 2:45 PM-4:30 PM
**Program #/Board # Range:** 3839-3853/B0233-B0247
**Organizing Section:** Retina

**Program Number:** 3839 Poster Board Number: B0233
**Presentation Time:** 2:45 PM - 4:30 PM
**Comparison of Retinal Atrophy after Laser, Anti-vasogenin Injections, or Combination Therapy in the Treatment of Branch Retinal Vein Occlusion**

Quraish Ghadiali1,2, Sabah Shaq1,2, Jane S. Myung1,2, Ken Wald1,2. 1Ophthalmology, NYU, New York, NY; 2Ophthalmology, Manhattan Eye and Throat Hospital, New York, NY.

**Purpose:** To determine the extent of retinal atrophy in patients with branch retinal vein occlusion (BRVO) receiving either laser treatment, intravitreal anti-vascular endothelial growth factor (anti-VEGF) treatment or combination therapy for the treatment of macular edema (ME).

**Methods:** 33 eyes with a history of BRVO treated with focal/grid laser alone, intravitreal anti-VEGF injections alone, or combination therapy for center-involving ME were reviewed in this retrospective study. Cirrus high definition optical coherence tomography Macular Cube Analysis was used to measure the retinal thickness from internal limiting membrane to retinal pigment epithelium using the Early Treatment Diabetic Retinopathy Study macular grid centered over the fovea. Retinal thinning was defined as a statistically significant difference between the affected and unaffected hemispheres of the same eye. Far paracentral and mid paracentral measurements from the grid were compared between the affected and unaffected hemispheres. The most recent OCT analysis with maximally resolved edema was used.

**Results:** 10 eyes received anti-VEGF injections alone with a mean of 5.5 injections per eye, 16 eyes received laser treatments alone with a
Treatment of Radiation Maculopathy with Bevacizumab versus Alternating Bevacizumab and Intravitreal Triamcinolone

Kelly M. Bui, Mark S. Dikopf, Joelle Hallak, Daniel F. Kiernan, Clement C. Chow, William F. Mieler

Purpose: Radiation maculopathy (RM) is the most common cause of severe vision loss following radiotherapy for uveal melanoma. To date, no proven therapy for RM exists. This study compares the treatment efficacy of bevacizumab to alternating therapy with bevacizumab and intravitreal triamcinolone (IVTA).

Methods: This was a retrospective case series of patients who underwent I-125 brachytherapy for uveal melanoma and were treated for RM by one surgeon, WFM, from February 2009 to May 2012. Radiation maculopathy was defined as macular edema with associated exudation and capillary bed disruption. Outcome measures were changes in logMar visual acuity (VA) and central foveal thickness (CFT) between bevacizumab group and IVTA group on a monthly basis and between monotherapy group (bevacizumab) and alternating therapy group (bevacizumab and IVTA) at 6 months.

Results: Forty-eight patients underwent I-125 brachytherapy and 5 developed RM. Four additional patients were referred to WFM for treatment of RM (total N=9). Five patients received monotherapy and 4 received alternating therapy after failing an initial bevacizumab monotherapy trial. The mean age was 63 years (39-79); all were Caucasians. Average tumor basal diameter was 10.6mm; height 5mm. Mean apex dose was 88.6 Gray. Patients developed RM at a mean of 21 months following brachytherapy. The mean change in VA was 0.12 logMar in both the bevacizumab and IVTA groups (p=0.49); the mean reduction in CFT was 68 microns in the bevacizumab group compared to 200 microns in the IVTA group (p=0.048). At 6 months, the monotherapy group had a 0.34 logMar change in VA compared to 0.067 in the alternating therapy group (p=0.17). Mean reduction in CFT was 174 microns in the monotherapy group compared to 151 microns in the alternating therapy group (p=0.38). Adverse events included increased intraocular pressure controlled on topical glaucoma agents and posterior subcapsular cataracts.

Conclusions: The use of IVTA resulted in a statistically significant reduction in CFT without corresponding change in VA. Alternating therapy did not lead to statistically significant improvement in VA or CFT compared to monotherapy. However, the results are confounded by a selection bias as patients in the alternating therapy group had failed initial bevacizumab monotherapy. Alternating bevacizumab and IVTA may be beneficial in recalcitrant cases of RM.

Commercial Relationships: Kelly M. Bui, None; Mark S. Dikopf, None; Joelle Hallak, None; Daniel F. Kiernan, Allergan (C), Allergan (R); Clement C. Chow, None; William F. Mieler, Genentech (C), Alcon (C), Allergan (C)

Program Number: 3842 Poster Board Number: B0236
Presentation Time: 2:45 PM - 4:30 PM

CENTRAL SEROUS CHORIORETINOPATHY IN WOMEN
Donatella Musetti, Massimo Nicolo, Carlo E. Traverso
Di.N.O.G.Mi., University Eye Clinic, Genova, Italy.

Purpose: To describe the clinical features of central serous chorioretinopathy (CSC) in women by Optical Coherence Tomography (OCT), Fluorescein angiography (FA) and Indocyanine green angiography (ICG). To evaluate preliminary results of different types of treatment

Methods: Prospective cross-sectional study. Twenty-seven eyes from 22 women (19 Caucasians and 3 Hispanics) with active CSC were included in the study. Inclusion criteria were the presence of a

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neurosensory retinal detachment of the macula (NSRD) and/or a pigment epithelial detachment (PED) as detected by OCT examination together with reduced visual acuity (VA). The fellow eyes of each patient were classified as normal when they showed physiological retinal profiles and VA was normal. Historical factors and medical records of each patient were evaluated. Subjects were divided into three groups based on three different treatment options: phacoemulsification, photodynamic therapy (half doses, HD or half fluence, HF) or no treatment (complete spontaneous recovery), respectively.

**Results:** CSC was associated with steroid use in 10 patients, while it was idiopathic in the other 12. Five patients reported no associated medical condition, 5 reported hypertension as their only medical condition, 3 unspecified autoimmune disease, 2 hyperthyroidism, 1 asthma, 1 organ transplant and 7 were heavy smokers. The most frequent symptoms were decreased VA and metamorphopsia. Seventeen eyes had a NSRD alone, whereas another 5 eyes had an associated PED. Two eyes were treated by argon laser photocoagulation; 14 eyes with photodynamic therapy (10 HD and 4 HF) and 6 recovered spontaneously. With a follow up of 2 years, both laser treatment and photodynamic therapy (PDT) yielded similar results with a trend for the HD-PDT treated patients to perform better. Mean age of onset in women was 50 ± 9.7 (mean ± SD) years, later than that reported in literature for men.

**Conclusions:** Although predominantly found in men, our study shows that CSC in women has similar features and similar response to treatment. As steroids were used by a significant number of study subjects, the cortisol may play a role in the development of CSC in women. The mechanism by which other causes influence the development of CSC is worth further investigations.

**Commercial Relationships:** Donatella Musetti, None; Massimo Nicolò, None; Carlo E. Traverso, None

**Support:** none in the support

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**Program Number:** 3843 Poster Board Number: B0237

**Presentation Time:** 2:45 PM - 4:30 PM

**Intravitreal Bevacizumab for choroidal neovascularization secondary to angioid streaks: five-year follow-up**

**Fedra Kort, Ahmed Chebil, Mejda Bouladi, Bourouai Rim, El Matri Leila.** Hedi Rais Institute of ophthalmology, Tunis, Tunisia.

**Purpose:** To report the five-year results of intravitreal bevacizumab for the treatment of choroidal neovascularization (CNV) complicating angioid streaks.

**Methods:** A retrospective interventional case series of 10 patients (10 eyes) with subfoveal or juxtafoveal active CNV secondary to angioid streaks treated with intravitreal bevacizumab injections (1.25mg/0.05ml), was conducted. All patients were followed-up for at least 5 years. Retreatment was given every four to six weeks in case of persistent symptoms or CNV activity on OCT. Efficacy of treatment was determined by changes in best corrected visual acuity (BCVA) and central retinal thickness on OCT.

**Results:** The mean number of injections was 7.2 during the first year and 4.4 during the fifth year. The mean BCVA at baseline was 20/62 (range 20/400 to 20/32) and improved to 20/52 (range 20/160 to 20/20) at five years (p=0.052). The BCVA improved by three or more lines in three eyes (30%) and remained within two lines of baseline in seven eyes (70%). Mean central retinal thickness was 404.2µm (range 160 to 602 µm) at baseline and decreased significantly to 332.5µm (range 150 to 523 µm) at five years. Intraretinal cysts persisted in 6 eyes (60%) with subfoveal CNV. No ocular or systemic complications were observed.

**Conclusions:** Our study suggests intravitreal bevacizumab to be an efficient and safe treatment for eyes with CNV secondary to angioid streaks at 5 years. Further long term studies are required to confirm these findings.

**Commercial Relationships:** Fedra Kort, None; Ahmed Chebil, None; Mejda Bouladi, None; Bourouai Rim, None; El Matri Leila, None

**Program Number:** 3844 Poster Board Number: B0238

**Presentation Time:** 2:45 PM - 4:30 PM

**The effect of BEST1 mutations on cellular protein degradation pathways in a BD hiPSC-RPE model**

**David Kuai1, Molly Smith1, Jessica M. Martin1, Wei Shen1, Amelia Verhoeven1, Kyle Wallace1, David M. Gamm2, Ruchira Singh1.** 1Waisman Center, University of Wisconsin - Madison, Madison, WI; 2Dept. of Ophthalmology and Visual Sciences, University of Wisconsin - Madison, Madison, WI; 3Mc Pherson Eye Research Institute, University of Wisconsin - Madison, Madison, WI.

**Purpose:** Best disease (BD) is an inherited macular degeneration caused by mutations in the BEST1 gene. We have recently shown perturbed calcium homeostasis and delayed degradation of photoreceptor outer segment (POS) in a human induced pluripotent stem cell (hiPSC)–derived retinal pigment epithelium (RPE) model of BD (hiPSC-RPE). Given that intracellular calcium signaling modulates multiple protein degradation processes, in this study using a BD hiPSC-RPE model, we sought to determine if alterations in specific protein degradation pathways contribute to the pathophysiology of BD.

**Methods:** Monolayers of hiPSC-RPE were derived from two BD patients and unaffected siblings. To assess whether the rate of global protein degradation was delayed in BD, we compared the amount of oxidized and poly-ubiquitinated proteins in BD and control hiPSC-RPE using ELISA and Western blot analyses. To determine if a specific protein degradation pathway was affected in BD hiPSC-RPE, we evaluated the expression and activity of key enzymes involved in lysosomal, ubiquitin-proteasomal and autophagy-mediated protein degradation. We also quantified lysosomal pH in BD and control hiPSC-RPE using lysosensor yellow/blue dye. Furthermore, to investigate whether lipofuscin accumulation in BD is due to altered exocytosis, we quantified the amount of exosome release and its protein composition in BD and control hiPSC-RPE.

**Results:** An increased amount of oxidized proteins, but not polyubiquitinated proteins, was seen in BD hiPSC-RPE compared to control hiPSC-RPE. Of the lysosomal and proteasomal enzymes tested, the protein levels of cathepsin-D and mono-ubiquitin were lower in BD hiPSC-RPE compared to control hiPSC-RPE. Baseline levels of autophagy markers (LC3 I, LC3 II, P62) were at the lower limit of detection in both control and BD hiPSC-RPE, and no difference in lysosomal pH was observed between them. However, differences were seen in the amount of exosome released from BD vs. control hiPSC-RPE.

**Conclusions:** Our current evidence suggests that defective protein processing and degradation in the lysosomal and/or proteasomal pathways contributes to delayed degradation of POS and subsequent lipofuscin accumulation in the BD hiPSC-RPE model.

**Commercial Relationships:** David Kuai, None; Molly Smith, None; Jessica M. Martin, None; Wei Shen, None; Amelia Verhoeven, None; Kyle Wallace, None; David M. Gamm, Cellular Dynamics international (C); Ruchira Singh, None

**Support:** Foundation Fighting Blindness Wynn-Gund Translational Research Award, Macula Vision Research Foundation, Retina Research Foundation

**Program Number:** 3845 Poster Board Number: B0239

**Presentation Time:** 2:45 PM - 4:30 PM

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Mapping visual distortions in macular disease
Gerard McGowan1, Tsveta Ivanova1, David B. Yorston1, Niall C. Strang2, Velitchko Manahilov3,4 1Tennent Institute of Ophthalmology, Glasgow, United Kingdom; 2Visual Science, Caledonian University, Glasgow, United Kingdom.

Purpose: To develop a test for mapping visual distortions (metamorphopsia) within the central visual field in patients with macular disease.

Methods: Metamorphopsia testing was carried out pre- and post-operatively. The test uses octagonal grids formed by black elements (squares) of various densities (Fig. 1) These cardboard-like charts (D-charts) contain grids at eccentricities of 0.5-1.5, 1.5-3.5, 3.5-7 and 7-11.5 deg. Patients were presented monocularly with D-charts at 40 cm distance. They were instructed to look at the fixation disk in the centre of the D-charts and report if the grid appeared distorted (irregular) by indicating with their finger the sectors (45 deg apart) of apparent distortion. The metamorphopsia score (the maximal element separation which produces perception of grid distortion) was determined for each ring and sector. The results provide a two dimensional map of metamorphopsia severity.

Results: 13 patients (mean age 72; SD 8.1 years) with epiretinal membrane (ERM) and 16 patients (mean age 70; SD 7.4 years) with macular hole (MH) were tested. Mean LogMAR visual acuity for MH was 0.9 (SD 0.4) and 0.5 (SD 0.3), for ERM. Pre-operatively, mean values of total metamorphopsia score and metamorphopsia area were significantly larger than zero (p<0.05, t-tests Bonferroni corrections) in the near peripheral regions (eccentricities of 0.5-3.5 deg for ERM and 0.5-7 deg for MH). Following surgery patients showed a significant reduction in the total metamorphopsia score and in the area of metamorphopsia, even if visual acuity was unchanged.

Conclusions: D-Charts allow quantification of metamorphopsia severity and localization in ERM and MH patients with a wide range of visual acuities. The area of visual distortion in MH patients was greater than that for patients with ERM. The results suggest that the D chart is an effective tool to map changes in metamorphopsia pre- and post-surgically, and may be useful in selecting which patients will benefit from surgery.

Sight threatening complications in Sickle Cell Retinopathy
Gabriella De Salvo, Pearse A. Keane, Dawn A. Sim, Catherine A. Egan. Medical Retina, Moorfields Eye Hospital, London, United Kingdom.

Purpose: Sickle cell retinopathy (SCR) is a hemoglobinopathy that can present with mild to severe proliferative retinal findings. In this abstract we describe features of non-proliferative and proliferative SCR and sight threatening complications of this disorder.

Methods: Clinical and imaging data were retrospectively collected from patients attending medical retina clinics at Moorfields Eye Hospital. Color fundus photographs, Optical Coherence Tomography (OCT), Fluorescein angiography (FA) and health records were reviewed. Clinical features noted included: abnormalities of the vitreoretinal interface at the macula [vitreomacular traction (VMT), macular hole (MH), epiretinal membrane (ERM)] and features related to the proliferative retinopathy [vitreous hemorrhage (VH), tractional retinal detachment (TRD)]. Final visual outcome was collected.

Results: 260 eyes from 130 patients with SCR were reviewed retrospectively. 24 eyes (9.23%) had no apparent ocular disease. Complications of the vitreoretinal interface were seen in 77 eyes: 29.62% (TRD 18.85%, MH 5.38%, VMT 1.54%, ERM 3.85%). A total of 66 eyes (25.4%) underwent one or more vitreoretinal procedures (12.7% for TRD, 3.5% for MH, 8.1% for VH). The final visual outcome was as follows: 80% had a visual acuity (VA) equal or better than 6/12, while 20% had a final VA equal or worse than 6/18 [No light perception in 4 eyes (1.54%), light perception in 4 (1.54%), hand motion in 5 (1.92%), count fingers in 3 (1.15%), and 36 eyes (13.85%) had VA between 6/18 to 6/60].

Conclusions: SCR, both non-proliferative and proliferative disease, can present with sight threatening complications. A higher than expected number of patients had significant visual loss from abnormalities of the vitreoretinal interface at the macula or related to proliferative disease that ultimately required surgical intervention.

Commercial Relationships: Gabriella De Salvo. None; Pearse A. Keane. None; Dawn A. Sim. None; Catherine A. Egan. Bayer (S), Oculogics (S), Novartis (S), Allergan (S), Novartis (F)

MacTel Inhibition Prevents the Formation of Outer Retinal Neovascularization in a Murine Model of Macular Telangiectasia

Purpose: The pathogenesis of macular telangiectasia (MacTel) is unclear and currently no approved treatment is available. We have previously characterized the very low density lipoprotein receptor knockout mouse (VLDLR−/−) crossed with the knock-in transgenic mouse expressing GFP under the control of a CX3CR1 promoter (VLDLR−/−;CX3CR1GFP/− mice). These mice have MacTel-like outer retinal neovascularization and GFP-positive myeloid cells associated with the neovascular tufts. (Aguilar E et al. ARVO 2012). Macrophage colony-stimulating factor (M-CSF) plays an important role in the differentiation and maintenance of macrophages. To examine the function of macrophages in this animal model of MacTel, we suppressed M-CSF signaling using a selective M-CSF receptor tyrosine kinase inhibitor.

Methods: The M-CSF inhibitor is administered daily to VLDLR−/− mice, CX3CR1GFP/− mice, or VLDLR−/−;CX3CR1GFP/− mice intraperitoneally. The administration was started when the pathological neovascularization is first observed (postnatal day 10;
P10) and continued until the day before sacrifice. Mice are examined at varying time points, and tuft formation and macrophage distribution in the retina are evaluated by confocal microscopy of wholemount preparations.

**Results:** GFP positive myeloid cells in the retinas of CX3CR1 \(^{GFP/+}\) mice and VLDLR \(^{-/-}\) CX3CR1 \(^{GFP/+}\) mice are effectively eliminated after daily administration of the M-CSF inhibitor. Tuft formations in VLDLR \(^{-/-}\) mice or VLDLR \(^{-/-}\) CX3CR1 \(^{GFP/+}\) mice are significantly reduced compared to vehicle treated littermate controls observed at P17 and P25 (p=0.00062 and p=0.00021, respectively).

**Conclusions:** The systemic administration of a M-CSF inhibitor depletes retinal macrophages and prevents MacTel-like outer retinal neovascular tuft formation in the VLDLR \(^{-/-}\) mouse, an animal model resembling MacTel. The results of this study suggest that macrophages contribute to outer retinal neovascularization in an animal model of MacTel and this observation may be used to develop novel therapeutic strategies for treating MacTel.

**Commercial Relationships:** Edith Aguilar, None; Toshihide Kurihara, None; Peter D. Westenskow, None; Stephen Bravo, None; Carli M. Wittgrove, None; Liliana Paris, None; Martin Friedlander, None

**Support:** NEI EY017540, NEI EY11254, The Lowy Medical Institute (MacTel)

**Program Number:** 3848 Poster Board Number: B0242
**Presentation Time:** 2:45 PM - 4:30 PM

**Surgical removal of idiopathic epiretinal membrane with or without post-membrane peel intravitreal triamcinolone: A comparison of anatomical and functional outcomes**

Steven A. Agemy, Johnstone M. Kim, Ankur N. Mehta, Chaesik Kim, Asheesh Tewari. Kresge Eye Institute, Detroit, MI.

**Purpose:** Our goal was to determine whether the addition of intravitreal triamcinolone at the end of vitrectomy with membrane peel improves functional and anatomical outcomes in patients with an epiretinal membrane with associated macular edema.

**Methods:** This is a retrospective chart review of patients who underwent pars plans vitrectomy with membrane peel by a single vitreoretinal surgeon (A.T.) for idiopathic epiretinal membrane with macular edema at the Kresge Eye Institute from 1/2009 to 2/2012. Patients were divided into two groups: the group that received intravitreal injection of 4mg of triamcinolone acetonide at the end of surgery and the group that did not. All patients were followed for a minimum of 3 months. Best-corrected visual acuity, central macular thickness by optical coherence tomography and intraocular pressure were recorded from each follow-up visit.

**Results:** Our study consisted of 20 eyes of 20 patients in total including 10 eyes in the triamcinolone group and 10 eyes in the control group. The mean change from preoperative best-corrected visual acuity (logMAR) in the injected group at 1, 3, 6, and 9 months was +0.09, +0.10, -0.02 and +0.22; mean change in the control group was -0.09, +0.24, +0.20, and -0.05. There was no statistically significant difference in the change from preoperative best-corrected visual acuity at each visit between the two groups. The mean decrease from preoperative central macular thickness (µm) of the injected group at 3, 6, and 9 months was 109.2, 146.0, and 152.5; mean decrease in the control group was 104.0, 137.4, and 133.3. There was no statistically significant difference in the decrease from preoperative central macular thickness at each visit between the two groups. The mean change from preoperative intraocular pressure (mmHg) of the injected group at 1, 3, 6, and 9 months was -3.1, +3.6, +1.0, and +2.0; mean change in the control group was -0.6, -0.3, -1.8, and -2.7. There was a statistically significant difference in the mean change from preoperative IOP between the two groups at 1 month (p=0.04) and 3 months (p=0.04).

**Conclusions:** Pars plana vitrectomy with membrane peel resulted in improvement in visual acuity and macular thickening while the addition of intravitreal triamcinolone at the end of the surgery did not improve postoperative anatomical and functional outcomes.

**Commercial Relationships:** Steven A. Agemy, None; Johnstone M. Kim, None; Ankur N. Mehta, None; Chaesik Kim, None; Asheesh Tewari, None

**Program Number:** 3849 Poster Board Number: B0243
**Presentation Time:** 2:45 PM - 4:30 PM

**Structured Method for Assessing Macular Holes by OCT and Correlations with Visual Outcomes**

Zabrina Abdool, \(^{1,4}\) Jan M. Provis, \(^{3,4}\) William G. Campbell, \(^{2}\) Alex P. Hunyor, \(^{2}\) Ian L. McAllister, \(^{2}\) Rohan W. Essex, \(^{2,5}\) Toshihide Friedlander, \(^{2}\) John Curtin School of Medical Research, Australian National University, Canberra, ACT, Australia; \(^{2}\)Department of Ophthalmology, The Canberra Hospital, Canberra, ACT, Australia; \(^{3}\)ANU Medical School, Australian National University, Canberra, ACT, Australia; \(^{4}\)ARC Centre of Excellence for Vision Sciences, Australian National University, Canberra, ACT, Australia; \(^{5}\)Vitreoretinal Unit, Royal Victorian Eye and Ear Hospital, East Melbourne, VIC, Australia; \(^{6}\)Retina Associates, Sydney Eye Hospital, Sydney, NSW, Australia; \(^{7}\)Center for Ophthalmology and Visual Science, Lions Eye Institute, Perth, WA, Australia.

**Purpose:** To develop an objective method to assess pre- and postoperative macular holes (MH) using optical coherence tomography (OCT) in a single surgeon cohort, and to explore the association between OCT parameters and visual outcomes.

**Methods:** Horizontal OCT B-scans at baseline and 3 months postoperative were analysed in 50 eyes undergoing surgery for idiopathic macular hole. Visual acuity (VA) was assessed pre-operative and at 3 months post-operative using VA letter score. In addition to various linear measurements, the cross-sectional area of the pre- and post-operative central 3mm macular region was measured, sub-divided into 4 layers: Layer 1: Inner limiting membrane (ILM) to the outer border of the inner plexiform layer (IPL); Layer 2: from layer 1 to the mid-line of the outer plexiform layer (OPL); Layer 3: from layer 2 to the external limiting membrane (ELM); and Layer 4: from layer 3 to the inner-border of the retinal pigment epithelium (RPE). The presence of inner nuclear layer (INL) or Henle’s layer cysts was noted. Correlations between change in area, presence of cysts and change in vision were calculated.

**Results:** Post-operatively, the percentage change in cross-sectional area of layers 1 thru 4 were -4.4%, -7.4%, -18% and +6% respectively. Change in layer 2 (the layer containing the inner nuclear layer (INL)) was significantly negatively correlated to change in vision (i.e. better improvements in visual acuity with greater loss of area, P=0.028). No significant correlation was observed between change in vision and change in the other layers. The presence of INL cysts pre-operatively, but not of Henle’s layer cysts, was significantly correlated with a greater postoperative improvement of vision (P = 0.013).

**Conclusions:** Conclusions: The pre-operative presence of inner retinal cysts, and a decrease in INL cross-sectional area at 3 months postoperative were associated with greater improvements in VA following macular hole surgery. In contrast, although outer retinal cross-sectional area, decreased more following surgery, this was not associated with greater visual acuity improvements.

**Commercial Relationships:** Zabrina Abdool, None; Jan M. Provis, EyeCo (C); William G. Campbell, None; Alex P. Hunyor, Zeiss (R); Ian L. McAllister, None; Rohan W. Essex, None

**Support:** ORIA project
Clinical characteristics of responders to intravitreal Bevacizumab in central serous chorioretinopathy patients

Gyu Ah Kim, Tyler Hyung Taek Rim, Christopher S. Lee, SungChul lee. Ophthalmology, Yonsei Univ College of Medicine, Seoul, Republic of Korea.

Purpose: Bevacizumab has been reported to be effective in central serous chorioretinopathy (CSC). We investigated the clinical factors associated with response to intravitreal bevacizumab (IVB) in CSC patients.

Methods: We retrospectively reviewed the medical charts of 48 eyes of 48 patients with CSC who received IVB (0.05ml, 1.25mg) and followed up for at least 3 months from November 2009 through December 2012. “Good responder” was defined as complete resolution of subretinal fluid (SRF) on spectral domain optical coherence tomography (SD-OCT) within 1 month following a single session of IVB. Eyes that showed partial or no resolution of SRF were grouped as “poor responder”. Subfoveal choroidal thickness and basal diameter of detached retina were measured on SD-OCT. Number of leakage sites, distance of leaking point from foveal center, and CSC type classification (“classic” or “diffuse retinal pigment epitheliopathy”) were analyzed using fluorescein angiography (FA).

Results: There were 10 (20.8%) good responders and 38 (79.2%) poor responders. The mean follow-up was 4.3 months. No significant difference was noted between the 2 groups with respect to demographic characteristics including age, gender, and spherical equivalent except preoperative visual acuity (p=0.01). There was no statistical difference between 2 groups with respect to CSC types, number of leakage sites, and distance to the nearest leakage site. The largest basal diameter of detached retina was significantly smaller in good responders than poor responders (1215±383µm vs. 1605±469µm; p=0.03). Subfoveal choroidal thickness was significantly thicker in good responders than poor responders (485.0±104.2µm vs. 379.2±137.5µm; p=0.04). According to receiver operator characteristic (ROC) analysis, subfoveal choroidal thickness was characterized parameter of good responder with area under the curve of 0.74. The cut-off value of 434µm were determined by ROC curve with 77.8% sensitivity and 70.0% specificity. Subjects with ≥434µm of choroidal thickness were more likely to be a good responder (Odds ratio = 5.43, 95CI, 1.06-27.8).

Conclusions: We found that thicker choroid and smaller basal diameter of the detached retina in CSC predict good response to IVB. This may imply an important role of choroid in CSC.

Commercial Relationships: HEESEONG YOON, None; Sun Young Lee, None; Woo Seok Lee, None; Kyung Hun Lee, None

Program Number: 3850 Poster Board Number: B0246
Presentation Time: 2:45 PM - 4:30 PM
Development of BEST1 reporter constructs for use in iPSC based high throughput drug screens and disease modeling

Allison Songstad1, Erin R. Barnright1, Robert F. Mullins1, Edwin M. Stone1,2, Jeanane L. Andorf1, Luuan M. Strelb1, Xiaoying Lu1, Bud A. Tucker1,2. Ophthalmology, Inst for Vision Resrch, Univ of Iowa, Iowa City, IA; 1Investigator, Howard Hughes Medical Institute, Iowa City, IA.

Purpose: Best disease, a rare inherited form of dominant juvenile onset macular dystrophy, is characterized by electrophysiological dysfunction of the retinal pigment epithelium (RPE), accumulation of vitelliform material, death of the overlying photoreceptor cells and a subsequent irreversible loss of central vision. Although it is clear that mutations in the RPE gene BEST1 are responsible for this disease, the molecular pathophysiology of mutations in this gene is poorly understood. Induced pluripotent stem cell (iPSC) derived RPE cells are morphologically and biochemically similar to RPE cells in vivo, and iPSC-derived RPE cells generated from patients with Best disease can be used to elucidate the biological function of BEST1 mutations. Likewise, iPSC-derived RPE cells make an attractive cell type for testing of potential therapeutics in a high throughput fashion. The purpose of this study was to develop BEST1 reporter constructs to be used in RPE cells generated from patients with Best disease for both elucidation of disease mechanism and as surrogate markers of therapeutic efficacy.

Methods: Keratinocyte-derived iPSCs were generated from patients with molecularly confirmed Best disease. Human iPSCs were differentiated into RPE cells using our previously developed step-wise differentiation protocol. Human BEST1 reporter constructs were synthetically generated and directionally cloned into an AAV vector. RT-PCR analysis was used to validate sequence and insert orientation.

Results: Human constructs containing a fluorescent reporter (GFP or tdTomato) flanked by 3' and 5' BEST1 UTRs, driven under control of the BEST1 promoter were generated, directionally cloned into AAV vectors, and packaged into AAV2 particles (Best1R-AAV2).

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Program #:Board # Range: 3854-3864/B0318-B0328
Organizing Section: Retina

Program Number: 3854 Poster Board Number: B0318
Presentation Time: 2:45 PM - 4:30 PM
Choroidal Neovascularization Associated with Birdshot Chorioretinopathy
Jessica Shantha1, Vincent Y. Ho1, Purnima Patel1, Farzin Forooghian2, Steven Yeh3. 1Emory University, Atlanta, GA; 2St. Paul’s Hospital, Vancouver, BC, Canada.
Purpose: Birdshot chorioretinopathy (BCR) is a rare cause of bilateral posterior uveitis associated with HLA-A29-positivity and represents less than 10% of posterior uveitis cases referred to tertiary care centers. Complications leading to loss of visual acuity (VA) include macular edema, optic disk edema, epiretinal membrane, and choroidal neovascular membrane (CNV) formation. Since its first description in 1983, the association of CNV with BCR has rarely been reported in the literature. The purpose of this study was to review our experience in the management of CNV associated with BCR.
Methods: A retrospective case review of 37 BCR patients from the Emory Eye Center and St. Paul’s Hospital (Vancouver, BC) was performed. Patients with clinical and fluorescein angiographic evidence of CNV were reviewed. Descriptive data collected included demographic data, ophthalmic exam findings, and immunosuppressive therapy. Main outcomes measured included initial and final visual acuity, mechanism of treatment, number of anti-VEGF injections, and spectral domain optical coherence tomography (SD-OCT).
Results: Four of 37 BCR patients (10.8%) were identified to have CNV. Two were female and two were male, and one patient had bilateral CNV. The average age was 57 years at the time of CNV diagnosis. The mean follow-up was 18.5 months (Range 2-36 months). Mean logMAR VA improved from 0.41 (Snellen VA 20/50) to 0.26 (Snellen 20/30-20/40, p=0.09). All eyes maintained or improved vision during follow-up. Three of four BCR patients had macular lesions at the time of CNV diagnosis. Three patients were treated with systemic immunosuppression including mycophenolate mofetil (2), cyclosporine (1), and tacrolimus (1) and one patient received a fluocinolone acetonide implant. Identification of CNV in all patients prompted anti-VEGF medications including bevacizumab (3) or ranibizumab (1). Affected eyes received a mean of 2.8 injections (Range 2-5). SD-OCT findings at the time of diagnosis included pigment epithelium detachment, photoreceptor disruption, cystoid macular edema, and subretinal fluid. Mean central subfield thickness improved from 352 microns to 228 microns (p=0.17) at final follow-up.
Conclusions: CNV, a rare complication of BCR, may be treated successfully with anti-VEGF medications. A combination of systemic or local immunosuppression and anti-VEGF therapy may be implemented for the management of CNV associated with BCR.
Commercial Relationships: Jessica Shantha, None; Vincent Y. Ho, None; Purnima Patel, None; Farzin Forooghian, None; Steven Yeh, Bausch and Lomb (C)
Support: Unrestricted Grant for Research to Prevent Blindness, Emory Eye Center

Program Number: 3855 Poster Board Number: B0319
Presentation Time: 2:45 PM - 4:30 PM
Role of Periostin in Choroidal Fibrovascular Membrane Formation

377 CNV
Tuesday, May 07, 2013 2:45 PM-4:30 PM
Exhibit Hall Poster Session

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Purpose: The pathogenesis of choroidal fibrovascular membrane (FVM) formation remains unclear. Periostin is a matricellular protein involved in tissue and vascular remodeling. We previously reported the increased expression of periostin in FVMs obtained from patients with proliferative diabetic retinopathy (Yoshida et al IOVS 2011). The purpose of this study was to investigate the role of periostin in choroidal FVM formation.

Methods: We generated mouse laser-induced choroidal neovascularization model (CNV) using C57BL/6 wild type (WT) and periostin knock out (KO) mice. The concentration of periostin in retinal pigment epithelium (RPE)/choroid complex from WT CNV mice were measured by ELISA. Periostin localization in choroidal FVM obtained from CNV mice and from patients with age-related macular degeneration (AMD) was evaluated by immunohistochemical analysis. We also quantified the volume of CNV and the degree of fibrosis in FVM using choroidal flat mount of WT and periostin KO mice at 7 or 21 days after laser injury.

Results: ELISA showed that periostin concentrations in mouse CNV increased and reached a peak at 14 days after laser coagulation. Immunohistochemical analysis showed that periostin was expressed in RPE cells in choroidal FVM of both CNV mice and AMD patients. At 7 days after laser injury, the volume of CNV and the degree of fibrosis didn’t differ between WT and periostin KO mice. At 21 days after laser injury, the amount and density of collagen type 1 in FVM were significantly reduced in periostin KO mice compared to WT mice (p<0.01), while the volume of CNV was not significantly altered.

Conclusions: These results suggest that periostin plays a role in fibrosis of choroidal FVM formation.

Commercial Relationships: Takahito Nakama, None; Shigeo Yoshida, None; Keijiro Ishikawa, None; Ryo Asato, None; Takeshi Kita, None; Shintaro Nakao, None; Yukio Sassa, 1,2, Yuji Oshima, None; Hiroshi Enaida, None; Tatsuro Ishibashi, None

Program Number: 3856 Poster Board Number: B0320
Presentation Time: 2:45 PM - 4:30 PM

Long-term Effect of Intravitreal Bevacizumab on Chorioretinal Atrophy Progression in Myopic Choroidal Neovascularization Paolo Lanzetta, Daniele Veritti, Valentina Sarao, Sara Macor. Dept of Ophthalmology, University of Udine, Udine, Italy.

Purpose: To investigate the long-term progression of chorioretinal atrophy (CRA) in patients with myopic choroidal neovascularization (mCNV) treated with intravitreal bevacizumab (IVB).

Methods: We retrospectively reviewed the clinical records of mCNV patients. Inclusion criteria were: (1) presence of subfoveal or juxtafoveal CNV, (2) refractive error ≥ 6.0 diopters or axial length ≥ 26.5 mm, (3) treatment with intravitreal injection of 1mg/0.04 ml of bevacizumab, (4) minimum follow-up of 24 months. Patients underwent digital fundus photography at baseline and every 12 months. Development or enlargement of CRA was judged and measured independently by two investigators (VS, SM), blinded to the other characteristics of patients. The main outcome was the change of total CRA area calculated as the sum of peripapillary atrophy area and CRA area at the posterior pole. Correlation between CRA progression and the number of injections was statistically analyzed.

Results: Ninety-four eyes of 84 patients met the inclusion criteria. CRA did increase significantly (+7.82 mm²) (p < 0.0001) after two years of follow-up. A post hoc comparison test showed that the CRA change was significant at both 12 and 24 months (p < 0.001). Patients received an average of 4.3 treatments in 24 months. No correlation was found between the number of IVB and CRA enlargement at the posterior pole (p=0.85), in the peripapillary area (p=0.74), in both regions (p=0.83). Eighteen eyes reached 5 years of follow-up. After 60 months CRA enlarged significantly (+14.15 mm²) (p < 0.0001). The mean number of injections was 6.3 in 60 months. No correlation was found between the number of IVB and CRA progression at the posterior pole (p=0.13), in the peripapillary area (p=0.46), in both regions (p=0.29).

Conclusions: A significant enlargement of CRA frequently occurred in patients affected by mCNV and treated with IVB. This condition doesn’t seem to be influenced by the number of anti-VEGF intravitreal injections.

Commercial Relationships: Paolo Lanzetta, Alimera (C), Allergan (C), Bayer (C), Novartis (C), Novartis (R), Roche (C), Iridex (P); Daniele Veritti, None; Valentina Sarao, None; Sara Macor, None

Program Number: 3857 Poster Board Number: B0321
Presentation Time: 2:45 PM - 4:30 PM

Development of an Objective Measurement Technique for Choroidal Neovascularization Based on Fluorescein Angiography Christian R. Osswald, 1 Mitch J. Guthrie, 1 Nicole L. Vallo, 1 William F. Mieler, 1 Jennifer J. Kang Mieler, 1 1Biomedical Engineering, Illinois Institute of Technology, Chicago, IL; 2Biological and Chemical Sciences, Illinois Institute of Technology, Chicago, IL; 3Ophthalmology & Visual Sciences, University of Illinois at Chicago, Chicago, IL, IL.

Purpose: To develop an objective method of quantifying choroidal neovascularization (CNV) areas based on fluorescein angiography (FA) images obtained from a confocal scanning laser ophthalmoscope (SLO) and to determine the method’s accuracy at various stages of CNV growth.

Methods: Five CNV lesions per eye were induced in Long-Evans rats using an Ar-green laser (400 mW, 50 μm, 0.1 sec). To test different stages of CNV, two groups received 5μl of 40mg/ml triamcinolone acetonide (TAC) or 40 mg/ml dexamethasone sodium phosphate (DSP) solution immediately after the laser treatment. A third group received no drug and served as control. FA was performed weekly for 5 weeks using SLO. To quantify CNV areas, late-phase FA images of each lesion were processed using the “multi-Otsu threshold” plug-in for ImageJ software. Three regions were defined: background, diffuse leakage, and CNV. Areas were calculated using a pixel-scaling factor based on the dimensions of the eye and field of view of the image. Each lesion was compared to its corresponding histological area.

Results: The “background” threshold output contained only the background of the picture (deep choroidal vessels). The “diffuse leakage” output included the hyperfluorescence around the CNV lesion and often major and small vessels adjacent to the lesion. The “CNV” output included the bright center of the CNV lesion and occasionally major blood vessels. CNV lesions from control animals increased in size until week 3 and did not significantly change thereafter (p=0.02); at week 5, the corresponding CNV area was 0.046 mm². Histology confirmed significant CNV in these animals. The multi-level Otsu thresholding technique consistently yielded CNV areas 68% the size determined via histology (0.068 mm²). TAC-treated lesions were initially well-defined and comparable in size to the original laser burn; by week 5, lesions resolved and lacked CNV. The method was able to track weekly changes in CNV areas. DSP-treated CNV lesion areas were 3.5 times smaller at week 4.

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Compared to week 2 (p=0.05). Histology confirmed less CNV growth in DSP-treated eyes than control.

**Conclusions:** A quantitative area measurement technique has been developed to monitor the progression of CNV in vivo. This approach provides the ability to objectively quantify CNV lesion growth and can be applied to determine the efficacy of various therapeutics on treating CNV.

**Commercial Relationships:** Christian R. Osswald, None; Micah J. Guthrie, None; Nicole L. Valio, None; William F. Mieler, Genentech (C), Alcon (C), Allergan (C); Jennifer J. Kang Mieler, None

**Support:** EY020807-01

**Program Number:** 3858 Poster Board Number: B0322

**Presentation Time:** 2:45 PM - 4:30 PM

**Retinal Protection by Lactoferrin in the Murine Laser Model of Choroidal Neovascularization**

Luke Dolezal¹, Kevin Mar², Abrar A. Rageh³, Michael Jordan³, Deborah A. Ferrington², Sandra R. Montezuma³. ¹University of Minnesota Medical School, Minneapolis, MN; ²Department of Ophthalmology and Visual Neurosciences, University of Minnesota, Minneapolis, MN; ³University of North Dakota, School of Medicine and Health Sciences, Grand Forks, ND.

**Purpose:** The purpose of this study is to determine if endogenous and exogenous administered Lactoferrin (LF) can protect the retina from choroidal neovascularization (CNV) in the murine laser model of CNV. Endogenous murine LF was evaluated by comparing the response of Wild Type (WT) vs Lactoferrin knock out (LFKO) mice in the CNV laser model. The potential protective effect of exogenous LF was evaluated following intraperitoneal (IP) administration of bovine lactoferrin (bLF) in LFKO mice.

**Methods:** Four 532-nm argon laser spots were placed between the retinal vessels of each WT and LFKO mouse. At Day 7, CNV was measured both clinically and microscopically. Fluorescein Angiography (FA) was performed to grade the lesions based on the degree of hyperfluorescence/leakage from images taken using a Micron III (Phoenix Research Lab Inc) color digital camera. The CNV lesions were imaged using an Olympus FV1000 confocal microscope and analysis of the images was performed manually using Image J software. The first experiment compared a group of WT to LFKO mice with no treatment. The second experiment compared a group of LFKO mice treated with intraperitoneal (IP) injections of bLF to a control group of LFKO mice treated with PBS.

**Results:** Experiment #1: WT mice demonstrated a 31% smaller lesion volume (p=0.015) and 14% smaller height (p=0.009) than LFKO mice (n=5/group).

Experiment #2: LFKO mice treated with bLF demonstrated a 26% smaller lesion volume (p=0.053) and 13% smaller lesion height (p=0.051) compared with the LFKO mice treated with PBS (n=8 bLF, n=9 PBS). FA demonstrated clinically significant leakage in 13% of the lesions in the LFKO group treated with PBS and 2% of the lesions in the LFKO treated with bLF.

**Conclusions:** Our results demonstrate the endogenous and exogenous LF anti-angiogenic activity in reducing the volume of the lesions in the CNV laser-induced animal model. Further study is needed to assess the LF clinical utility in the treatment of eye diseases in which neovascularization is involved.

**Commercial Relationships:** Luke Dolezal, None; Kevin Mar, None; Abrar A. Rageh, None; Michael Jordan, None; Deborah A. Ferrington, None; Sandra R. Montezuma, None

**Support:** Unrestricted grant from Research to Prevent Blindness to Department of Ophthalmology and Visual Neurosciences, Minnesota Lions Club. VitroRetinal Surgery Foundation Research Award.

**Program Number:** 3859 Poster Board Number: B0323

**Presentation Time:** 2:45 PM - 4:30 PM

**Intravitreal Bevacizumab for Non-Subbfoveal Choroidal Neovascularization Associated with Angioid Streaks**

Mauricio B. Parodi¹, Pierluigi Iacono², Ugo Introni², Carlo La Spina³, Luigi Berchicci³, Anita Leys³, Francesco Bandello³. ¹Department of Ophthalmology, Scientific Institute San Raffaele, Milano, Italy; ²Fondazione G. B. Bietti for the Ophthalmology, IRCCS (Istituto di Ricovero e Cura a Carattere Scientifico), Rome, Italy; ³Department of Ophthalmology, University Hospital Leuven, Leuven, Belgium.

**Purpose:** To assess the effects of intravitreal bevacizumab injections in the treatment of non-subfoveal choroidal neovascularization (CNV) associated with angioid streaks (AS). Design: Retrospective study.

**Methods:** Fifteen patients (15 eyes) affected by juxtapfoveal or extrafoveal CNV secondary to AS were considered in the study. All patients underwent a complete ophthalmologic examination, including ETDRS best corrected visual acuity (BCVA) measurement, optical coherence tomography (OCT), and fluorescein angiography (FA). The protocol treatment included a first injection, followed by repeated injections over a 12-month follow-up period on the basis of the detection of any type of fluid on OCT and/or presence of leakage on FA.

Primary outcome measures: Mean changes in BCVA and proportion of eyes gaining at least 10 letters (2 ETDRS lines) at the end of the follow-up.

Secondary outcomes: Mean changes of central macular thickness (CMT) and extension to the fovea.

**Results:** Mean BCVA did not change throughout the follow-up period, being 0.2±0.2 LogMAR at baseline and 0.2±0.3 LogMAR at the 12-month examination. A functional improvement of at least 2 ETDRS lines was achieved by 5 eyes (33%), with 3 eyes (20%) gaining 3 lines.

Mean CMT at baseline was 215±13µm and 225±85µm at the 12-month examination. Two eyes (13.3%) showed CNV extension to the fovea.

**Conclusions:** Intravitreal bevacizumab injection can be regarded as a beneficial approach for the management of non-subfoveal CNV secondary to AS over a one-year follow-up. Further studies are warranted to confirm our preliminary results.

**Commercial Relationships:** Maurizio B. Parodi, None; Pierluigi Iacono, None; Ugo Introni, None; Carlo La Spina, None; Luigi Berchicci, None; Anita Leys, novartis (F), théa (R), bayer (R); Francesco Bandello, ALLEGAN Inc. (S), NOVARTIS PHARMACEUTICALS CORPORATION (S), FARMILA-THEA (S), BAYER SCHERING PHARMA (S), PFIZER Inc. (S), ALCON Inc. (S), BAUSCH AND LOMB (S), GENENTECH Inc. (S), ALIMERA SCIENCES Inc. (S), SANOFI AVENTIS (S), THROMBOGENICS (S)

**Program Number:** 3860 Poster Board Number: B0324

**Presentation Time:** 2:45 PM - 4:30 PM

The incidence of neovascularization in the fellow eye of patients with unilateral choroidal neovascularization: a survival analysis

Sara Boschinio, Roberta Secondi, Alba Xhepa, Alessandra Acquistapace, Andrea Giani, Mario V. Cigada, Giovanni Staurenghi. Eye Clinic, Department of Biomedical and Clinical Science “Luigi Sacco”, Luigi Sacco Hospital, Milan, Italy.

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**Purpose:** To compare the survival of unaffected fellow eye between choroidal neovascularization (CNV) and retinal angiomatous proliferation (RAP).

**Methods:** A retrospective review of 239 consecutive patients enrolled in our Eye Clinic between February 2006 and November 2012, showing naïve unilateral forms of CNV (choroidal, n=202, retinal angiomatous proliferation, n=37). Mean follow-up time was 2.9 years (range 131-2214 days) for choroidal CNV and 2.6 years (range 519-1340 days) for RAP. Survival was estimated by Kaplan-Meier analysis and Logrank test was used to compare the two curves.

**Results:** Kaplan Meier analysis showed that the 50% of the fellows eyes with choroidal CNV survived healthy for about 4.4 years while eyes with RAP survived healthy for about 2.7 years. Logrank test showed a high significant difference between the two curves (p < 0.002).

**Conclusions:** This study found that the incidence of neovascularization in the unaffected fellow eye increase with time and the development of RAP is more premature than choroidal CNV, as studies previously reported.

**Purpose:** To evaluate the visual and anatomical outcomes of intravitreal bevacizumab in patients with idiopathic choroidal neovascularization.

**Methods:** Twenty seven eyes of 27 patients with idiopathic choroidal neovascularization were treated with a single intravitreal injection of bevacizumab, followed by as-needed dosing based on spectral domain-optical coherence tomography findings including intraretinal edema, subretinal fluid, or pigment epithelial detachment. Changes in best-corrected visual acuity (BCVA), central foveal thickness, and subfoveal choroidal thickness were evaluated. The subfoveal choroidal thickness of the normal fellow eye were measured for comparative analysis. 17 eyes for normal control were collected for comparative analysis of subfoveal choroidal thickness.

**Results:** The mean number of injections was 2.74 (±2.30) for 27 eyes during the mean follow-up of 1.18 (±11.47) months. The mean logarithm of the minimum angle of resolution BCVA improved from 0.36 ± 0.32 to 0.23 ± 0.28 (Wilcoxon signed-ranks test; p=0.09). The mean central foveal thickness decreased from 375.20 ± 93.40 μm to 264.79 ± 29.38 μm (Wilcoxon signed-ranks test; p<0.0001) At presentation, the subfoveal choroidal thickness of affected eyes was significantly thinner than the subfoveal choroidal thickness of the unaffected fellow eye (255.94 ± 39.02 vs. 283.24 ± 48.93 μm, respectively; p=0.036). When compared to the normal controls, the subfoveal choroidal thickness of affected eyes was significantly thinner (255.94 ± 39.02 vs. 274.06 ± 48.49 μm, respectively; p=0.34). No change in the subfoveal choroidal thickness was seen in the affected eye between initial and final measurements (p=0.079). Of 27 eyes, 26 (96.3%) had maintained or improved their best-corrected visual acuity at their last visit.

**Conclusions:** Intravitreal bevacizumab resulted in significant visual and anatomical benefit for patients with idiopathic choroidal neovascularization. The thin subfoveal choroidal thickness is associated with idiopathic choroidal neovascularization.

**Commercial Relationships:** Kahyun Lee, None; SungChul lee, None; Sungsoo Kim, None; Suk Ho Byeon, None; Christopher S. Lee, None
favorable with more than half of patients having driving vision (>20/50) in the treated eye after an average of 28 months of follow-up. Number of treatments per episode was low (2.5) with recurrence being on average 1.6 episodes over the total 28 months.

**Commercial Relationships:** Michelle V. Carle, None; Homayoun Tabandeh, Alcon (C), Allergan (C); Francesco Boscia, None; David S. Boyer, Alcon (C), Allegro (C), Allergan (C), Bayer (C), Genentech (C), Glaukos (C), GSK (C), Neurotech (C), Optos (C), Regeneron (C); Thomas G. Chu, None; Firas M. Rahhal, None

**Program Number:** 3863 Poster Board Number: B0327
**Presentation Time:** 2:45 PM - 4:30 PM
**Treatment with Intravitreal Anti-VEGF for Choroidal Neovascular Membrane secondary to Sorsby’s Fundus Dystrophy: A 24-Month Analysis**

Guillermo Fernandez Sanz1, Rafael Alonso-Gonzalez2, Pearse A. Keane1,3, Ester Carreno1, Gerald Liew1, Dawn A. Sim1,4, Praveen J. Patel1, Andrew R. Webster1,3, Catherine A. Egan1,3, Adnan Tufail1,3.

1Medical Retina, Moorfields Eye Hospital, London, United Kingdom; 2Adult Congenital Heart Disease & Pulmonary Hypertension Centre, Royal Brompton Hospital, London, United Kingdom; 3UCL Institute of Ophthalmology, London, United Kingdom.

**Purpose:** To evaluate the safety and efficacy of 24-month intravitreal therapy with anti-vascular endothelial growth factor (VEGF), bevacizumab or ranibizumab, for treatment of choroidal neovascular membrane (CNV) secondary to Sorsby’s fundus dystrophy.

**Methods:** All patients with bilateral CNV related to Sorsby’s fundus dystrophy and treated with intravitreal anti-VEGF agents (bevacizumab/ranibizumab) at Moorfields Eye Hospital (May 2006 to October 2010) were included in this study. All affected patients were heterozygous for the pSer204Cys missense mutation in exon 5 of the TIMP3 gene.

Best Corrected Visual Acuity (BCVA) was assessed at 1, 3, 6, 12, 18 and 24 months from treatment by Snellen chart with logMAR conversion. Significant visual loss was defined as an increase ≥0.3 logMAR units. Fellow eyes not treated with anti-VEGF agents were used as a control. Clinical data were retrieved from medical records. Cox-proportional-hazards regression was performed to investigate the association between anti-VEGF and significant visual loss.

**Results:** A total of 9 eyes in 8 patients were treated with intravitreal anti-VEGFs, of whom 62.5% were male. Mean age at diagnosis was 45.3±6.9 years (y) in the treatment group and 54.0±8.4y in the control group. Mean BCVA at baseline was 0.40±0.41 and 0.60±0.67 logMAR in control and treatment group respectively (p=0.60).

**Conclusions:** Intravitreal anti-VEGF treatment for CNV related to Sorsby’s disease is safe and effective. In these patients, the risk of developing significant visual loss is reduced by 96% at 24 months.

**Program Number:** 3864 Poster Board Number: B0328
**Presentation Time:** 2:45 PM - 4:30 PM
**CHOROIDAL THICKNESS IN PATHOLOGIC MYOPIA**

Cláudia Farinha1, Alda Balar2, Sandrina Nunes3, Ana Rita Santos2, Maria da Luz Cachulo2,1, Isabel Pires1,2, João Figueira1,2, Rufino Silva1,2,3, Ophthalmology unit, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal; 2Association for Innovation and Biomedical Research on Light and Image, Coimbra, Portugal; 3Faculty Medicine, University Coimbra, Coimbra, Portugal.

**Purpose:** To evaluate macular choroidal thickness (CT) in pathologic myopic eyes without CNV and with CNV treated with photodynamic therapy (PDT), intravitreal ranibizumab (IVR), or both (PDT+IVR).

**Methods:** The medical records of patients with high myopia treated with PDT and/or IVR in our Department were reviewed. All eyes with history of CNV that met the inclusion criteria were assigned to three groups according to treatment received: PDT, IVR and PDT+IVR. A fourth group - “dry myopic maculopathy group” - included the contralateral highly myopic eyes that never developed CNV. All patients underwent complete ophthalmologic examination with best-corrected visual acuity (BCVA), measurement of axial length, color fundus photography and enhanced depth imaging optical coherence tomography (EDI OCT). Both the horizontal and vertical sections passing through the center of the fovea were used for the choroidal thickness measurements on EDI OCT. Type of myopic maculopathy found in each point measured was recorded, using the classification system proposed by Hayashi et al.

**Results:** Forty-two eyes (21 patients) were included: 11 eyes (26.2%) in PDT group, 8 (19.0%) in IVR group, 9 (21.4%) in PDT+IVR group, and 14 (33.3%) in dry maculopathy group. Mean age was not statistically different between groups. Mean subfoveal CT was 69.4±33.6 μm in PDT group, 80.9±50.5 μm in IVR group,

Figure 1: Probability of not having a significant visual loss (defined as an increase ≥0.3 logMAR units) over 24 months follow-up.
106.2±52.0 μm in PDT+IVR group, and 119.4±81.4 μm in dry maculopathy group, with no significant differences between groups (p>0.05). A positive but weak correlation was found between BCVA and macular CT (r=0.293, p<0.001). The tessellated fundus lesion had the thickest choroid (194.3±57.0 μm) followed by macular atrophy (82.0±55.8 μm), diffuse chorioretinal atrophy (70.3±49.1 μm), and patchy chorioretinal atrophy (62.5±9.2 μm). Regression analysis showed that age (p<0.001), axial length (p<0.001), gender (p=0.001), and myopic lesions such as tessellated fundus (p=0.046) and patchy atrophy (p=0.008) were predictive of choroidal thickness.

Type of treatment used for myopic CNV was not predictive of choroidal thickness.

**Conclusions:** Older age and greater axial length are the major factors associated with macular choroidal thinning. No significant differences in subfoveal CT between treatment groups were found, and type of treatment used for myopic CNV showed no predictive value for choroidal thickness.

**Commercial Relationships:** Claudia Farinha, None; Alda Baltar, None; Sandrina Nunes, None; Ana Rita Santos, None; Maria da Luz Cachulo, None; Isabel Pires, None; João Figueira, Alcon (C), Novartis (C), Allergan (C), Pfizer (C), Alimera (C), Bayer (C); Rufino Silva, Thea (C), Novartis (C), Bayer (C), Allergan (C), Alimera (C)

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**403 Retinitis Pigmentosa II**

Wednesday, May 08, 2013 8:30 AM-10:15 AM
6C Paper Session

**Program #/Board # Range:** 4016-4022

**Organizing Section:** Retina

**Program Number:** 4016

**Presentation Time:** 8:30 AM - 8:45 AM

**Long-term efficacy and safety of treatment of retinitis pigmentosa with valproic acid**


**Purpose:** The purpose of this study was to examine the long-term safety and efficacy of valproic acid (VPA) use in patients with retinitis pigmentosa (RP) and other retinal degenerative disorders that were offered off-label use of this drug by a previous investigator at the University of Florida. More recently, any patients currently seen at the University of Florida who had not already self-terminated use of VPA were asked to stop this drug until further prospective data on safety and efficacy is released.

**Methods:** This study was a retrospective chart review of all patients with retinal dystrophies who had been prescribed VPA at the University of Florida Ophthalmology Department clinic between January 2009 and April 2012. Visual field (VF), visual acuity (VA), length of treatment, liver enzymes, and side effects were analyzed. Visual field (VF) areas were defined using Goldmann visual field (GVF) tracings recorded before, during, and after VPA treatment using the V4e isotherm for each eye. Areas determined by isotherm V4e were converted into areas of functioning retina, as shown in figure 1.

**Results:** Five of the patients (10 eyes) had two GVF tracings, allowing comparison between baseline and follow-up VF. After 9.8 months of VPA, VF decreased by 0.145 cm2 (26.478%) (p=0.432) as shown in Figure 2. For 22 of the patients (41 eyes), VA data was available, and logMAR score changed by 0.056 log units (representing a decline in VA) after 14.9 months on VPA (p=0.002). Twelve patients (38.7%) reported negative side effects related to VPA use and 9 (29%) patients discontinued VPA due to these side effects.

**Conclusions:** We found that VPA may not be an appropriate treatment for all retinal dystrophies. After an average of 9.8 months on VPA, visual field areas showed a declining trend in four out of five patients and visual acuity significantly worsened during treatment with VPA. VPA plays a complex role in patients with pigmentary retinopathy and may be associated with visual acuity and field decline as well as adverse side effects. Physicians should use caution with using VPA for pigmentary retinopathies. Effective treatment options likely depend on first identifying the disease-causing mutation and then optimizing treatment targeting genotype-specific pathology.
Purpose: Retinitis pigmentosa (RP) patients are motivated to try alternative therapies to slow disease progression. Basic science, clinical research and patients’ self-reports support the hypothesis that electroacupuncture may improve visual function in RP, which we explored in a case series study.

Methods: A standard protocol involving electroacupuncture to the forehead and below the eyes, and acupuncture to the body, was administered to 12 RP patients at 10 half-hour sessions over 2 weeks. Pre- and post-treatment tests included ETDRS visual acuity (VA), Pelli-Robson contrast sensitivity (CS), Goldmann visual fields, dark-adapted full-field stimulus test (FST)(n=9), SST-1 dark-adaptometry (n=2), and Heidelberg Spectralis spectral domain optical coherence tomography (SD-OCT). We measured ocular blood flow (OBF) in the ophthalmic artery (OA), central retinal artery (CRA), and posterior ciliary artery (PCA) with color Doppler imaging (Philips iU-22) in the last 2 subjects.

Results: Eight of 12 subjects had a measurable, significant visual function improvement post-treatment. Three of the first 9 subjects had a significant 10.3-17.5dB (i.e. 13-53 fold) improvement in FST in both eyes at 1 week, maintained for at least 4-6 months, well outside typical test-retest variability (95% CI: 3-3.5dB) in RP. Dark-adaptation with the SST-1 was shortened in both subjects tested on average by 44% at 1 week (range 36-62% across 10-30dB), outside typical coefficients of variation of <30% previously determined in RP and normals. Three subjects had ≥0.1 logMAR VA improvement, and another subject had 0.55 logCS improvement. Both subjects with cystoid macular edema (CME) pre-treatment developed a reduction. At 1-2 weeks post-treatment, there was a significant reduction in the OA resistance index (RI) in both subjects, as well as in the CRA and PCA RI in subjects 11 and 12, respectively. Subject 11 had increased OA and CRA end diastolic velocities (EDV), and subject 12 had increased CRA and PCA peak systolic and EDV. Electro- and standard acupuncture was well tolerated by all, without adverse events or vision loss.

Conclusions: Electro- and standard acupuncture entails minimal risk and may have measurable benefits on residual visual function, while other promising treatments are developed. Current findings support the need to explore potential mechanisms and more rigorous methodology in the continued study of electroacupuncture for RP.

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Heckenlively et al. reported that 90% of 30 RP patients who presented with CME had circulating anti-retinal antibodies. Further characterization of retinal inflammation in RP may provide a target for future therapy.

Leaking peripheral vasculature in a patient with retinitis pigmentosa captured by Optos wide-field fluorescein angiography

Commercial Relationships: Matthew B. Kaufman, None; Carlos A. Medina-Mendez, None; Thomas R. Friberg, 13/581,518 (P); Andrew W. Eller, None

Support: National Institutes of Health CORE Grant P30 EY008098, Research to Prevent Blindness, Eye and Ear Foundation of Pittsburgh, PA

Program Number: 4019
Presentation Time: 9:15 AM - 9:30 AM
Inheritance of Retinitis Pigmentosa: Update in the Era of Genetic Testing
Kari E. Branham, Jillian Huang, Kanishka T. Jayasundera, John R. Heckenlively. Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, MI.

Purpose: To determine how often inheritance of RP varied between information gathered from pedigree analysis and results of genetic testing.

Methods: Pedigrees from 104 probands with RP who had positive and informative genetic test results were reviewed. The analysis of the pedigree included the number of individuals affected, gender, familial relationships, and (when available) age of onset of RP. Pedigrees were classified as AD if there were two or more generations of affected individuals and there was male to male transmission or affected males and females with similar disease severity/age of onset. Pedigrees were considered AR pedigrees if there was a single generation of more than one person affected (males and females or only males) or if there was parental consanguinity. Pedigrees were considered XL if there was no evidence of male to male transmission and only males affected or males affected severely and females affected mildly or at a later age of onset. Pedigrees not fitting into one of those categories were descriptively described as male siblings only affected or isolate cases. Genetic testing results were also recorded.

Results: Among the 37 AD families, five families were determined to be XL through genetic testing. In the eight AR families tested, one family had an AD mutation. In the 38 XL pedigrees, two had mutations in AD genes and 36 in XL. In the 17 isolated cases tested, six had mutations in AR genes and 11 in XL genes. Finally, in the four families with male siblings affected, all had mutations in XL genes. In summary, 8/83 (9.6%) of patients had a different inheritance for their RP based on genetic testing than what was suggested based on pedigree analysis alone. Moreover, the inheritance could be clarified for an additional 21 families where there were isolated cases or only male siblings affected in which inheritance was ambiguous based on pedigree analysis alone.

Conclusions: While pedigree analysis is an essential aspect of providing care to patients with inherited retinal dystrophies, successful genetic testing provides the ability to perform more precise genetic counseling to patients.

Commercial Relationships: Kari E. Branham, Arctic DX (P); Jillian Huang, None; Kanishka T. Jayasundera, None; John R. Heckenlively, None

Support: Foundation Fighting Blindness

Program Number: 4020
Presentation Time: 9:30 AM - 9:45 AM
Ultra wide-field autofluorescence is useful to evaluate residual retinal functions in patients with Retinitis Pigmentosa
Shuntaro Ogura, Tsutomu Yasukawa, Munenori Yoshida, Yuichiro Ogura. Department of Ophthalmology, Nagoya City Univ Medical School, Nagoya, Japan.

Purpose: To investigate the correlation between the visual field (VF) tested by Goldmann perimetry (GP) and ultra wide-field fundus autofluorescence (FAF) in patients with retinitis pigmentosa (RP).

Methods: In this pilot study, 20 eyes of 10 patients diagnosed as RP were enrolled. GP and ultra wide-field FAF images with Optos®200Tx (Optos) were evaluated for each eye. The areas of absent autofluorescence in FAF were correlated with the areas of scotoma in GP. GP and FAF images were then superimposed and the agreement ratio in the central 60 degrees of VF was evaluated.

Results: The areas of absent autofluorescence in FAF were significantly correlated with the areas of scotoma (I4e/V4e isopters) in GP (R=0.86, P<0.000001). The agreement ratio of absent autofluorescence and the scotoma in the central 60 degrees was 88.7±11.5% of VF. In addition, the agreement ratio of normal autofluorescence and remaining VF (V4e) was 87.1±8.7% of VF as well. Irregular or abnormal autofluorescence was seen in 7 eyes at the border of normal and absent autofluorescence while the VF was normal in those areas.

Conclusions: These results suggested that FAF imaging by Optos is very useful to evaluate residual retinal functions in patients with RP. Abnormal fundus autofluorescence might precede the loss of retinal functions and be helpful to monitor for the progression of the disease.

Commercial Relationships: Shuntaro Ogura, None; Tsutomu Yasukawa, None; Munenori Yoshida, None; Yuichiro Ogura, None

Program Number: 4021
Presentation Time: 9:45 AM - 10:00 AM
Recombinant Human Nerve Growth Factor Protects Photoreceptor Degeneration in a Rat Model of Inherited Retinitis Pigmentosa
Luigi Aloe1, Patrizia Bianchi1, Maria Luisa Rocco1, Alessandra Micera2, Alessandro Lambiase3, Stefano Bontini4. 1Institute of Neurobiology and Molecular Medicine, National Research Council, Rome, Italy; 2G.B. Bietti IRCCS, Rome, Italy; 3Department of Ophthalmology, University of Rome, Campus Biomedico, Rome, Italy.

Purpose: Since its discovery nerve growth factor (NGF), a naturally occurring protein involved in the differentiation, growth and maintenance of neurons, has been considered a potential treatment for neurodegenerative disorders. Recent evidence suggests NGF may also be beneficial in ocular neurodegenerative diseases such as retinitis pigmentosa (RP) and glaucoma. A major limitation in the development of NGF for the treatment of ophthalmic diseases is the adequate production of a formulation capable of penetrating the globe...
or crossing the blood retinal/brain barrier. Herein, we report the effect of recombinant human NGF (rhNGF) administered intravitreally and topically on the progression of photoreceptor degeneration in a well-characterized model of RP.

**Methods:** Royal College of Surgeons (RCS) rats were allocated 1 of 5 treatment groups (no treatment, rhNGF eye drops (200µg/ml) 3 times daily for 20 days, or one 5 µl intravitreal injection of either saline, murine NGF or rhNGF) with all treatments initiated at day 20, the onset of the retinal degeneration. At day 40 treated eyes were collected and evaluated using histopathology, immunohistochemistry, confocal microscopy, western blot and immunoenzymatic analysis.

**Results:** Compared to controls, eyes treated with NGF (murine and rhNGF) showed a lower expression of apoptotic markers, reduced numbers of dead retinal cells and a greater number of surviving photoreceptors. Compared to controls and murine NGF treated eyes, rhNGF treated eyes showed the higher levels of intraretinal NGF and activated NGF receptors (TrkA). No differences were observed comparing eyes treated with topical and intravitreal rhNGF.

**Conclusions:** In an animal model of retinitis pigmentosa NGF was effective for reducing the progression of the retinal neurodegeneration. Notably, topical administration of rhNGF seemed to be equally as effective as intravitreal rhNGF. These data suggest that a topical formulation of rhNGF could be a promising treatment for range of ocular neurodegenerative disease in which apoptosis plays a pathogenic role.

**Commercial Relationships:** Luigi Aloe, Dompé S.p.A. (F); Patrizia Bianchi, None; Maria Luisa Rocco, None; Alessandra Micera, None; Alessandro Lambiase, Dompè (C); Stefano Bonini, Dompè (C)

**Program Number:** 4022  
**Presentation Time:** 10:00 AM - 10:15 AM  
**Nonsyndromic RP Due to BBS2 Mutations**  
Meghan J. Marino\(^1\), Gayle J. Pauer\(^1\), John Chiang\(^1\), Stephanie A. Hagstrom\(^2\), Elias I. Traboulsi\(^1,3\).  
\(^1\)Ophthalmic Research, Cole Eye Institute, Cleveland Clinic, Cleveland, OH; \(^2\)Ophthalmology, Cleveland Clinic Lerner College of Medicine Case Western Reserve University, Cleveland, OH; \(^3\)Casey Eye Institute Molecular Diagnostics Laboratory, Portland, OR.  
**Purpose:** To describe a family with nonsyndromic retinitis pigmentosa (RP) due to BBS2 mutations.  
**Methods:** The proband was evaluated in retinal dystrophy clinic. Family and medical histories were reviewed. Fundus photographs, visual fields, and OCT were obtained. Molecular analysis via Next Generation Sequencing (NGS) found BBS2 variants, which were confirmed by Sanger Sequencing. Segregation analysis of the variants was performed among available family members. In silico analysis of the identified missense change was evaluated using the PolyPhen-2, pMut, and SIFT algorithms.  
**Results:** A 41 year-old Caucasian female presented with a diagnosis of RP. Eye exam showed significant visual field constriction, nystagm, and peripheral pigmented changes. Family history at the time was non-contributory. Her brother, age 39, had no visual complaints, and both of her parents were asymptomatic. DNA analysis for the recessive RP panel was negative. Later analysis via NGS of the RetNet genes found 2 variants in the BBS2 gene. R275X is known to be pathogenic and P134R is a novel mutation. Co-segregation analysis determined that the variants were inherited independently from each parent. The proband’s brother also carried both mutations. Subsequent clinical evaluation of her brother showed evidence of retinal degeneration and peripheral visual field constriction. He remains asymptomatic; however, he is infertile. His medical history is otherwise unremarkable. Kidney function tests and ultrasound are pending.  
**Conclusions:** This family illustrates the high degree of variability in patients with BBS mutations and describes a novel BBS2 mutation. Mutations in BBS2 may be an under-recognized cause of apparently nonsyndromic recessive RP.
regardless of the underlying retinal vascular disease process, high levels of VEGF are associated with closure of retinal vessels which is prevented by neutralization of VEGF with injections of RBZ.

**Commercial Relationships:** Peter A. Campochiaro, Advance Cell Technology (C), Aerpio (C), Elan (C), Gene Signal (C), Genentech (C), GlaxoSmithKline (C), LPath, Inc (C), Norvox (C), Regeneron (C), Genentech (F), Genzyme (F), GlaxoSmithKline (F), Oxford Biomedica (F); Charles Wykoff, Genentech (R), Regeneron (R), Bayer (C); Dafeng Chen, Genentech/Roche (F), Genentech/Roche (C); Howard Shapiro, Genentech, Inc. (E); Jason S. Ehrlich, Genentech (E), Roche (I); Roman Rubio, Roche (E), Roche (I)

**Clinical Trial:** RIDE (NCT00473382) and RISE (NCT00473330)

**Program Number:** 4024

**Presentation Time:** 8:45 AM - 9:00 AM

**Intensive Diabetes Therapy Reduces Ocular Surgeries in Patients with Type 1 Diabetes: twenty-eight year followup of the Diabetes Control and Complications Trial / Epidemiology of Diabetes Interventions and Complications study (DCCT/EDIC)**

Lloyd P. Aiello,1-2, Wanjie Sun,3, Patricia A. Cleary,1 John M. Lachin,4 Sappna Gangaputra,6, Ronald Klein,6 Arup Das,2 Szillard Kiss,4, Anitha Domalpally,1 Ronald P. Danis1

1Beethem Eye Institute, Joslin Diabetes Center, Boston, MA; 2Department of Ophthalmology, Harvard Medical School, Boston, MA; 3Fundus Photograph Reading Center, University of Wisconsin, Madison, WI; 4Department of Ophthalmology and Visual Sciences, University of Wisconsin School of Medicine and Public Health, Madison, WI; 5Biostatistics Center, George Washington University, Rockville, MD; 6Clinical Research, Weill Cornell Medical College, New York, NY; 7University of New Mexico School of Medicine, Albuquerque, NM.

**Purpose:** The DCCT/EDIC study established the beneficial impact of intensive diabetes therapy (INT) on retinopathy onset and progression. However, the effects of diabetes treatment on the incidence of ocular surgery have not been explored. This report compares the long-term effect of former INT vs. conventional therapy (CON) on the incidence of ocular surgeries 28 years after the initiation of DCCT (1983-2011).

**Methods:** Annual visits recorded the history of surgical procedures in either eye over the 28 years after initiation of the DCCT.

**Results:** During DCCT (1983-93), HbA1c was ~7% in INT and 9% in CON, but during EDIC there were no statistical differences from Year 4 to date. Over the 23-year median followup, 63 of 711 INT and 98 of 730 CON subjects had at least one ocular surgery for an incidence of 3.95 and 6.24 per 1000 subject-years (P=0.0001). Ocular surgeries included cataract extraction (42 INT, 61 CON subjects), vitrectomy (29, 50), glaucoma-related (9, 14), other cornea-related (2, 3), posterior capsulotomy (3, 4) andenucleation (1, 1). Total surgeries in both eyes were 138 (INT) and 180 (CON) for an incidence of 8.01 and 6.64 per 1000 subject-years, respectively (P<0.0001). INT subjects had fewer overall surgeries (P=0.035) and fewer different surgery types (p=0.015) than CON subjects. INT was associated with a 48% risk (hazard) reduction in experiencing any ocular surgery (95% confidence interval [CI], 28 to 62%; P=0.0001) after adjustment for age, gender, diabetes duration, HbA1c, retinopathy and visual acuity at DCCT baseline. INT was associated with 48% (P=0.002) and 44% (P=0.016) adjusted risk reduction of cataract extraction and vitrectomy, respectively (CI 22-66% and 10-65%). The beneficial effect of INT on the risk of any ocular surgery or cataract extraction or vitrectomy was fully accounted for by adjustment for updated mean HbA1c or retinopathy level. Higher A1c, retinopathy, macular edema, poorer visual acuity, nephropathy, neuropathy and hypertension were each independently associated with increased risk of ocular surgery.

**Conclusions:** Intensive insulin therapy reduces the long-term risk of ocular surgery in patients with type 1 diabetes.
unsatisfactory therapeutic effect in 11% of the laser arm (n=82), 3% of the combination arm (n=78) and 1% of the ranibizumab arm (n=81). 11% of safety patients experienced an SAE (n=214). No fatal event was reported

**Conclusions:** This preliminary analysis shows ranibizumab (alone or with laser) to be an effective and safe treatment option for visual impairment due to DME.

**Commercial Relationships:** Thomas Sheidow, Novartis (F); Alan R. Berger, None; Frederica deTakacsy, Novartis Pharmaceuticals Canada Inc. (E); Ruiling Li, Novartis Pharma (E); Bonita Relié, Novartis Pharmaceuticals Canada Inc. (C); AnneSophie Courseau, Novartis Pharmaceuticals Canada Inc. (E), Sanofi Canada Inc. (E)

**Support:** Novartis Pharmaceuticals Canada

**Clinical Trial:** NCT01135914

**Program Number:** 4026

**Presentation Time:** 9:15 AM - 9:30 AM

**Baseline Predictors of improvement in self-reported visual function following treatment with ranibizumab in patients with diabetic macular edema**

Rohit Varma1, Neil M. Bressler2, Chantal Dolan3, Linda Yau3, James F. Ward3, Shoshana Colman1, 1Ophthalmology and Visual Sciences, University of Illinois at Chicago Eye and Ear Infirmary, Chicago, IL; 2Retina Division, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, MD; 3Genentech, Inc., South San Francisco, CA.

**Purpose:** To identify predictors of improvement in patient-reported visual function following 24 months of every 4 week treatment with ranibizumab in patients with diabetic macular edema (DME) enrolled in the RIDE and RISE clinical trials.

**Methods:** Data from RIDE and RISE were pooled to identify predictors of overall composite score improvement from baseline to 24 months in patient-reported visual function measured by the National Eye Institute Visual Function Questionnaire-25 (NEI VFQ-25). Predictors were chosen from a set of 28 candidate variables considered to be potentially important predictors by the authors using two approaches: 1) a multivariate stepwise selection procedure from the full set of 28 candidate variables (P<0.05 criterion for inclusion) and 2) a univariate selection procedure identifying variables one at a time (P<0.10 criterion for inclusion) to be included in a final multivariate model utilizing stepwise selection procedure (p<0.05 criterion for inclusion). Parameter estimates and associated p-values for a combined screening model derived from (1) and (2) were obtained using the SAS GLM procedure.

**Results:** There were 605 study participants with NEI VFQ-25 scores at both baseline and month 24. Predictors of improvement in patient-reported vision function in the combined screening model included the following: treatment with ranibizumab vs sham (P = 0.03), higher baseline contrast sensitivity in the untreated eye (P<0.001), lower baseline systolic blood pressure (P<0.03) and lower baseline NEI-VFQ-25 composite score (P<0.0001).

**Conclusions:** These data suggest that treatment with ranibizumab and lower self-reported visual function at baseline are associated with improved patient-reported visual function. No features have been identified which would preclude ranibizumab treatment for DME based on patient-reported visual function outcomes. Of particular note, baseline visual acuity in the treated eye does not necessarily predict improvement in self-reported visual function.

**Commercial Relationships:** Rohit Varma, Allergan (C), AqueSys (C), Genentech (C), Merck & Co. Inc (C), Replchenish (C), Genentech (F), National Eye Institute (F); Neil M. Bressler, Abbott Medical Optics, Inc (F), Alimera Sciences (F), Allergan (F), Bausch & Lomb, Inc (F), Bayer (F), Carl Zeiss Meditec, Inc (F), ForSight Labs, LLC (F), Genentech, Inc (F), Genzyme Corporation (F), Lumenis, Inc (F), Notal Vision (F), Novartis Pharma AG (F), Pfizer, Inc (F), Regeneron Pharmaceuticals, Inc (F), Roche (F), Thrombogencis (F); Chantal Dolan, None; Linda Yau, Genentech, Inc. (E); James F. Ward, Genentech, Inc. (C); Shoshana Colman, Genentech (E)

**Support:** Genentech

**Clinical Trial:** RISE: NCT00473330, RID: NCT00473382

**Program Number:** 4027

**Presentation Time:** 9:30 AM - 9:45 AM

**Effect of Statins and Diabetes Therapy (Oral Hypoglycemics and Insulin) on the Outcomes of Patients Treated with Ranibizumab and/or Laser Therapy**

Mohammad A. Sadiq1, Muhammad Hassan1, Yasir J. Sepah1, Graeme K. Loh2,1, Saleema Kherani3, Mostafa Hanout4, Rachel E. Annam1, Mehreen Ansari1, Diana V. Do1, Quan Dong Nguyen1,1. Retinal Imaging Research and Reading Center, Wilmer Eye Institute. Johns Hopkins University, Baltimore, MD; 2Division of medicine, University College London Medical School, London, United Kingdom.

**Purpose:** To evaluate the role of concomitant use of statins, oral hypoglycemics or insulin, and the status of diabetic retinopathy, in determining the outcomes of patients with diabetic macular edema (DME) who were treated either with laser, ranibizumab (RBZ), or a combination of RBZ and laser.

**Methods:** Data from the READ-2 study was utilized for this study. For the purpose of analysis, data from the three study groups was combined and then stratified based on the severity of diabetic retinopathy (DR) and the use of statins, oral hypoglycemics, or insulin. Baseline characteristics were analyzed for each subgroup. The outcome variables assessed were mean change in BCVA (ETDRS scores) and foveal thickness. The effect of each parameter on the outcome variables was assessed using the Mann-Whitney U test. The number of RBZ injections given after month 6 (based on retreatment criteria) was also compared between patients receiving oral hypoglycemics and insulin therapy.

**Results:** Baseline characteristics (age, race, gender, weight and hypertension) were found to be similar across all subgroups. No significant association was seen between the use of statins, insulin, or oral hypoglycemic agents on the outcome variables: foveal thickness and BCVA at month 6, 24, or 36 (P-values are shown in table 1). The severity of DR was also not associated with a significant change in the outcome. Mean number of injections required after month 6 were 5.51, 7.68, and 6.90 for patients on oral hypoglycemics alone, insulin alone, or a combination of both, respectively (p>0.05).

**Conclusions:** No significant association was detected between the use of concomitant medications such as statins, oral hypoglycemics, or insulin with the outcome of DME patients treated with RBZ, laser, or combination. Grade of DR was also not significantly associated with the outcome. Therefore, severity of DR and presence of co-morbidities should not affect treatment decisions for DME, as comparable visual benefits can still be achieved.
Table: Effect of Statins, Oral Hypoglycemics, Insulin and Severity of NPDR on outcome variables at month 6, 24 and 36

<table>
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<tr>
<th>Study</th>
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<th>Month 24</th>
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<td>0.18</td>
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<td>0.008</td>
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</table>

Conclusions: These data, derived from two large randomized controlled trials of ranibizumab for DME, provide strong evidence that ranibizumab is effective in reducing DR severity and can inhibit clinical progression to PDR evaluated by composite outcomes. However, prolonged delays in initiation of ranibizumab therapy, as in the RIDE/RISE sham group, may limit this therapeutic effect.

Commercial Relationships: Jason S. Ehrlich, Genentech (E), Roche (I); Amitha Domalpally, None; Linda Yau, Genentech, Inc. (E); J J. Hopkins, Genentech, Inc. (E); Michael S. Ip, Eye Technology Ltd. (C), Genentech, Inc. (C), NicOx (C), Notal Vision (C), QLT Phototherapeutics, Inc. (C), Regeneron (C), Sirion (C), Allergan, Inc (F), Regeneron (F)

Support: Genentech, Inc.

Clinical Trial: NCT00473330 and NCT00473382

Program Number: 4029

Presentation Time: 10:00 AM - 10:15 AM

RELIGHT - Ranibizumab treatment of diabetic macular oedema with bimonthly monitoring after a phase of initial Treatment Ian A. Pearce. Royal Liverpool University Hospital, St Paul's Eye Unit, Liverpool, United Kingdom.

Purpose: In patients with visual impairment due to DME (VI-DME) treated with ranibizumab 0.5mg, the 18-month RELIGHT study investigates whether extending follow-up intervals to bimonthly following initial monthly follow-up for 6 months, will provide and maintain improvements in vision. Data is presented from the primary end-point at month-12.

Methods: This is a prospective, open-label, multicenter, single-arm study. It evaluates three monthly initiation doses of ranibizumab 0.5mg, followed by individualised retreatment. Retreatment criteria are based on reductions in VA of >5 letters and / or OCT ≥225 micrometers with monthly review for three months following initiation, and subsequent bi-monthly review out to 18 months. Laser treatment was permitted after 6 months.

Results: Of 139 patients screened, 110 initiated treatment. The primary endpoint was reached for the last patient in October 2012. Preliminary analyses show at baseline, patients had a median age 64 (range 37.1 to 82), median hBAlc 7.6% (range 5.4 to 11.7), and mean BP 139/78 mmHg. Median VA improved from 65 letters (6/15) (range 34 to 84) at baseline to 70 letters (6/12) (range 3 to 85), a median change of 5 letters (range 5 to 27) at 12 months. Median central subfield thickness improved from 452.5µm to 293 µm, representing a median change of -127.5µm. A median of seven (range 3-9) injections were given, with 23.1% of patients achieving ≥10 letter gain and 4.6% demonstrating ≥10 letter loss.

Conclusions: This regimen provided VA gains and central subfield thickness improvements consistent with those in the pivotal RESTORE and DRCR.net studies. The reduction in monitoring frequency in RELIGHT supports that seen in year three of the DRCR.net study in which there was a median of 7 to 8 appointments, with at least 25% of patients being reviewed on the protocol mandated minimum of 4 occasions, while maintaining vision with a median of 1 to 2 injections.

Commercial Relationships: Ian A. Pearce, Novartis (C)
The Effects of Docosahexaenoic Acid (DHA) Dietary Supplementation on Retinal Lipid Profile in a Mouse Model of Stargardt-like Macular Dystrophy (STGD3)

Mandy Hong, Sharee Kuny, Rachel Bryant, Frederic Gaillard, Miyoung Suh, Yves Sauve - Ophthalmology, University of Alberta, Edmonton, AB, Canada; Human Nutritional Sciences, University of Manitoba, Winnipeg, MB, Canada.

Purpose: Accumulating evidence demonstrate that docosahexaenoic acid (DHA) can delay the progression of age-related macular degeneration (AMD); however, the underlying mechanisms remain unknown. Using the ELOVL4 mouse, an animal model of early onset macular degeneration (Stargardt-like, STGD3), we examined the impact of DHA supplementation on retinal anatomy, function, and lipid profile. We hypothesized that antenatal DHA supplementation in ELOVL4 mice would optimize DHA’s rescue effect on the retina as evidenced by preserved function, anatomy and lower AA/DHA ratios.

Methods: Wildtype (WT) and transgenic (TG) mice were provided DHA+ (1% over total fatty acid content), DHA- (DHA replaced with oleic acid), or chow (0.19% omega-3 fatty acid, standard laboratory diet) antenatally. Electroretinograms (ERG), cross-sectional staining, and ultrahigh-pressure liquid chromatography coupled with mass spectrometry coupled with mass-spectrometry (UPLC-MS-MS) allowed assessment of retinal function, anatomical integrity, and fatty acid profiles, respectively. ERGs were recorded at 1 and 3 months of age, while the other outcome measures were obtained at 3 months.

Results: ERG and anatomical results showed rod dysfunction (at 1 and 3 months) and photoreceptor loss (at 3 months only) in TG versus WT mice. Diet did not affect retina function in WT or TG mice. Paradoxically, the number of photoreceptors was reduced and the AA/DHA ratio increased in DHA versus non-DHA supplemented TG mice. This effect was not observed in WT animals.

Conclusions: Expression of the human mutated ELOVL4 in mice exerts a negative impact on retinal function and anatomy, occurring as early as 1 and 3 months, respectively. While exogenous DHA intake is essential for eye development, dietary levels of 1% or more might be associated with negative effects on photoreceptor survival and function during development in subjects with STGD3.

Commercial Relationships: Mandy Hong, None; Sharee Kuny, None; Rachel Bryant, None; Frederic Gaillard, None; Miyoung Suh, None; Yves Sauve, None

Program Number: 4084 Poster Board Number: A0002
Presentation Time: 8:30 AM - 10:15 AM

In vivo Evaluation of Surface Modified Expanded-polytetrafluoroethylene (ePTFE) Substrate as a Permanent Substrate for Cell Transplantation

Shen Nian1, Zhongjie Fu1, Carl M. Sheridan1, Victoria Kearns1, Rachel Williams2, Sai Hung David Wong3, Krasimir Vasiliev4, Akash Bachhuka4, Amy C. Lo2, Wico W. Lai1, Ophthalmology, University of Hong Kong, Hong Kong, Hong Kong; 2Research Centre of Heart, Brain, Hormone and Healthy Aging, University of Hong Kong, Hong Kong; 3Eye and Vision Science, University of Liverpool, Liverpool, United Kingdom; Mawson Institute and School of Advanced Manufacturing, University of South Australia, Mawson Lakes, SA, Australia.

Purpose: Age-related macular degeneration (AMD) is the leading cause of severe and permanent visual loss in patients above 55 years of age with no effective treatments. Transplantation of a functional cell monolayer grown on the substrate into the subretinal space may help rescue the photoreceptors and in turn treating AMD. However, degradation of biodegradable substrates may cause the breakdown of functional cell monolayer and produce toxic byproducts. Therefore, synthetic non-degradable materials have been employed as the permanent underlying substrate to establish an intact functional cell monolayer for subretinal transplantation. We aimed to investigate the host response of surface modified ePTFE substrates after subretinal transplantation.

Commercial Relationships: Mandy Hong, None; Chan Ho Cho, None; Min Sagong, None; Hyun Ju Oh, None; Jae Whi Park, None; Dong Geun Park, None; Mi Rae Kim, None; Won Mo Gu, None; Jun Hyuk Son, None

Program Number: 4083 Poster Board Number: A0001
Presentation Time: 8:30 AM - 10:15 AM

Pars Plana Vitrectomy, Subretinal Injection of Recombinant Tissue Plasminogen Activator and Intraocular Gas Tamponade for Thick Submacular Hemorrhage with Polypoidal Choroidal Vasculopathy

Woohyuk Chang, Chan Ho Cho, Min Sagong, Hyun Ju Oh, Jae Whi Park, Dong Geun Park, Mi Rae Kim, Won Mo Gu, Jun Hyuk Son - Department of Ophthalmology, Yeungnam Univ College of Medicine, Daegu, Republic of Korea.

Purpose: To evaluate the efficacy of pars plana vitrectomy, subretinal injection of tissue plasminogen activator (t-PA) and intraocular gas tamponade for thick submacular hemorrhage caused by polypoidal choroidal vasculopathy.

Methods: Retrospective review of 13 eyes of 13 consecutive patients with polypoidal choroidal vasculopathy and thick submacular hemorrhage who underwent pars plana vitrectomy with subretinal t-PA injection and fluid-gas (20% SF6) exchange with postoperative facedown positioning. Outcome measures included degree of blood displacement from the fovea, postoperative corrected visual acuity.

Results: All patients were followed for a minimum of 3 months. (mean 6.8 months, range 3 to 20). The mean age was 63.9 years, and the average symptom duration of submacular hemorrhage before surgery was 16.2 days. In all 13 eyes, the procedure resulted in complete displacement of thick submacular hemorrhage from the fovea within 1 month. Mean preoperative visual acuity at baseline was 20/893 (1.65±0.92 logMAR). The visual acuity improved to 20/252 (1.10±0.84 logMAR, p=0.085) at month one, 20/148 (0.87±0.87 logMAR, p=0.019) at month 3 and 20/142 (0.85±1.00 logMAR, p=0.019) at final visit. The polyp was located in the macular region in 10 eyes (76.9%) and extramacular region in 3 eyes (23.1%), which was identified by postoperative indocyanine green angiography. No significant correlation was found between location of polypoidal lesion and postoperative final visual acuity. (p=0.573) Postoperative complications included one case of rebleeding and one case of retinal pigment epithelium tear.

Conclusions: Pars plan vitrectomy with subretinal t-PA injection and gas tamponade was found to be relatively effective procedure for displacement of thick submacular hemorrhage with a significant visual acuity improvement in patients with polypoidal choroidal vasculopathy.

Commercial Relationships: Woohyuk Chang, None; Chan Ho Cho, None; Min Sagong, None; Hyun Ju Oh, None; Jae Whi Park, None; Dong Geun Park, None; Mi Rae Kim, None; Won Mo Gu, None; Jun Hyuk Son, None

Program Number: 4083 Poster Board Number: A0001
Presentation Time: 8:30 AM - 10:15 AM

413 AMD II, RE
Wednesday, May 08, 2013 8:30 AM-10:15 AM
Exhibit Hall Poster Session
Program #/Board # Range: 4083-4129/A0001-A0047
Organizing Section: Retina

Support: Novartis Pharmaceuticals sponsored study
Clinical Trial: NCT01257815
Methods: Fibronectin coated n-heptylamine modified (F-HA) ePTFE substrate was transplanted into the subretinal space of 4-week-old Royal College of Surgeons (RCS) rat eyes. Fundus was photographed and intraocular pressure (IOP) was measured immediately before and after surgery and weekly thereafter until RCS rats were sacrificed. 1 and 4 weeks after surgery, eyes were isolated and examined by H&E-stained retinal sections. Inflammatory responses were evaluated by immunostaining of tumor necrosis factor α (TNFα) and interleukin-1β (IL1β). Glial cell responses were assessed by immunostaining of glial fibrillary acidic protein (GFAP).

Results: Retinal detachment was only observed immediately after surgery in fundus photos. IOP of rat eyes remained at about 10 mmHg except a drop to 7 mmHg immediately after transplantation. Retinal morphology was similar with/without substrate transplantation. Expression of pro-inflammatory cytokines (TNFα and IL1β) and GFAP was not significantly increased in the F-HA ePTFE substrate-transplanted eyes at 1 and 4 weeks. The F-HA ePTFE substrates remained flat beneath the neural retina up to 4 weeks after transplantation. Some cells were found to attach to F-HA ePTFE substrates and were positively stained with isocitrin but negatively with RPE65.

Conclusions: F-HA ePTFE substrate showed good biocompatibility and lack of host inflammatory and glial cell responses, suggesting that it is a suitable permanent underlying substrate for subretinal transplantation.

Commercial Relationships: None; Akash Bachhuka, None; Carl M. Sheridan, None; Victoria Kearns, None; Rachel Williams. None; Sai Hung David Wong. None; Krasimir Vasilev. None; Akash Bachhuka. None; Amy C. Lo. None; Wico W. Lai, None

Support: None; The University Development Fund and Seed Funding from The University of Hong Kong

Program Number: 4086 Poster Board Number: A0004

Presentation Time: 8:30 AM - 10:15 AM

Prevalence of Subretinal Drusenoid Deposits in Age-Related Macular Degeneration with Newly Diagnosed Choroidal Neovascularization

Sandrine A. Zweifel, Roman A. Rieder, Myrtha M. Kohler, Reto Gambon. Department of Ophthalmology, University Hospital Zurich, Zurich, Switzerland.

Purpose: To analyze the prevalence of subretinal drusenoid deposits (SDD) in patients with treatment naïve newly diagnosed choroidal neovascularization (CNV) in age-related macular degeneration (AMD).

Methods: We studied 114 consecutive patients (125 eyes) with treatment naïve CNV in AMD seen during 11 months. Multimodal imaging were reviewed for druse type (soft drusen, SDD, mixed) and type of CNV. Classification for neovascularization was based on our earlier proposed grading system incorporating multimodal imaging including fluorescein angiography (FA), spectral-domain optical coherence tomography (SD-OCT), and, where necessary, indocyanine green angiography. The following types of CNV were differentiated: Type 1 (or usually described as occult or poorly defined with FA), Type 2 (or usually described as well-defined or classic with FA), Type 3 (or retinal angiomatosus proliferation (RAP)) and polypoidal choroidal vasculopathy (PCV). SDD was considered present when there was OCT evidence ≥ 3 definite drusenoid deposits above the retinal pigment epithelium (RPE) in > 1 B-scan, with consistent changes in either near-infrared imaging or the blue light channel as previously described. Soft drusen were determined from color fundus photographs and confirmed by SD-OCT.

Results: In 30 eyes with newly diagnosed CNV without prior treatment there were too advanced exudative changes with subretinal fibrosis which made a classification impossible. In 94 eyes (mean patient age 79.4 years) type of neovascularization and druse type were graded. The types of neovascularization were Type 1 for 39 eyes, Type 2 for 33, Type 3 for 18 and PCV for 4 eyes. SDD only without the presence of soft drusen were detected in 14 of 94 eyes (14.9%) with a treatment naïve CNV secondary to AMD. In eyes with SDD only, type 1 was identified in 0 eyes, type 2 in 13 eyes, type 3 in 1 eyes and PCV in 0 eyes.

Conclusions: SDD represent a common phenotypic characteristic in eyes with treatment naïve CNV in AMD. The prevalence of SDD only in type 2 neovascularization was higher than for other types. The high incidence of SDD in type 2 might be explained by their location in the subretinal space. The predominant druse type either SDD or soft drusen might be relevant in the development of either sub-retinal pigment epithelium (RPE) neovessels or proliferation vessels above the RPE in the subneurosensory location.

Commercial Relationships: Sandrine A. Zweifel. None; Roman A. Rieder. None; Myrtha M. Kohler. None; Reto Gambon, None

Program Number: 4087 Poster Board Number: A0005

Presentation Time: 8:30 AM - 10:15 AM

Autofluorescence and OCT of Retinal pigment epithelial tears

Naoto Hanyuda, Taku Sato, Ryo Mukai, Shoji Kishi. Gunma University, Maebashi, Japan.

Purpose: To determine using optical coherence tomography (SD-OCT), fundus autofluorescence (FAF) that factors of poor visual acuity of retinal pigment epithelial tear (RPE tear) after treatment for exudative age-related macular degeneration (AMD).

Methods: A total of 182 patients (183 eyes) who were treated by PDT combined with anti-VEGF for exudative AMD. 7 eyes (3.8%) developed RPE tear following therapy. 5 eyes of 7 eyes were observed using optical coherence tomography (SD-OCT), fundus autofluorescence (FAF). We evaluated characteristics of the onset of RPE tear, and the changes of the findings.

Results: In all cases FAF showed absence of autofluorescence in the area of denuded RPE and showed hyperfluorescence in the role of the RPE. In 3 eyes of 5 eyes the area of denuded RPE changed hypoautofluorescence area in FAF. In 2 eyes of 5 eyes proliferation of RPE was observed in SD-OCT.

Conclusions: RPE tears changed from absence of autofluorescence in the area of denuded RPE to hypoautofluorescence area in FAF. We confirmed re-growth of RPE in SD-OCT.

Commercial Relationships: Naoto Hanyuda. None; Taku Sato. Alcon Japan Ltd. (F); Ryo Mukai. None; Shoji Kishi, None

Program Number: 4088 Poster Board Number: A0006

Presentation Time: 8:30 AM - 10:15 AM

Anatomic patterns and clinical presentation of recurrence in ‘stable’ wet Age Related Macular Degeneration (AMD) patients

Fani Zacharaki, Manju N. Chandran, Narendran Nair, Priyanga Vijayakumar, Geeta Menon. Frimley Park Hospital NHS Foundation Trust, Frimley, United Kingdom.

Purpose: To determine anatomic features and clinical presentation of recurrence in patients under anti-Vascular Endothelial Growth Factor (VEGF) treatment for wet AMD, who had an untreated observation period of more than 6 months.

Methods: We reviewed data of AMD patients on Ranibizumab treatment that had not had an injection for a period of at least 6 months, therefore characterized as ‘stable’. Only patients fulfilling the National Institute of Clinical Excellence (NICE) guidelines for treatment were included in the study. Stability criteria were: complete resolution of Intraretinal fluid (IRF) or Subretinal fluid (SRF), or...
existence of stable cysts of IRF. In our clinic these patients were still followed-up monthly. On each visit, they were asked to report any subjective changes in visual function and they underwent oculard examination including Best Corrected Visual Acuity (BCVA), macular Optical Coherence Tomography (OCT) using Heidelberg Spectralis, and dilated Fundus Biomicroscopy. Retreatment criteria were: SRF; IRF; or new intra- or subretinal haemorrhage.

**Results:** 75 eyes (66 patients, 46 female and 20 male) were reviewed that met stability criteria. Mean treatment-free period was 17 months (range 6–42 months). Mean number of previous injections was 6.8 (range 3–24). Twelve patients (16%) met the retreatment criteria and received an injection. Mean injection-free period for retreated patients was similar to the general group (mean 16.6 months, range 7–37). Three of the retreated patients (25%) reported visual distortion on that visit, and the majority (n=9) remained asymptomatic. In 5 patients a decrease in VA was documented, whereas 7 had stable VA compared with their last visit. In all 12 retreated cases, presence of fluid was documented in the OCT. 10 cases presented with new SRF, 1 case with new IRF and 1 with increased IRF. Only in 1 patient (8.3%) was there clinical evidence of recurrence on biomicroscopy (new macular haemorrhage).

**Conclusions:** With the increasing pressure of new and follow up patients in Medical Retina clinics, it has been suggested that extending follow up might be considered for ‘stable’ patients. Our data imply that anatomic changes usually precede functional deterioration in recurrences of wet AMD. This should be taken under consideration when a decision of further management of stable AMD patients is to be made.

**Commercial Relationships:** Fani Zacharaki, None; Novartis Pharmaceuticals (F); Novartis Pharmaceuticals (R); Manju N. Chandran, None; Narendran Nair, None; Priyanga Vijayakumar, None; Geeta Menon, NOVARTIS (R), ALLERGAN (R), BAYER (R)

**Program Number:** 4089 Poster Board Number: A0007
**Presentation Time:** 8:30 AM - 10:15 AM
Detection and Quantification of Autofluorescence Abnormalities in Patients with Neovascular Macular Degeneration using a Fully Automated Image Analysis Algorithm

**Kathryn L. Pepple, Qing Nie, Sally S. Ong, Scott W. Cousins.** Ophthalmology, Duke Eye Center, Durham, NC.

**Purpose:** To develop a fully automated fundus autofluorescence (AF) image analysis algorithm and evaluate the occurrence of retinal pigment epithelium abnormalities (RPE) in patients with neovascular macular degeneration.

**Methods:** A retrospective chart review was performed to identify patients with NVAMD that had fundus AF images obtained at presentation and at follow up at least one year later. A custom Matlab algorithm was designed to allow fully automated segmentation and quantification of hypo-AF and hyper-AF. The computer segmentation results were compared against the boundaries defined by three expert graders who performed manual segmentation. The baseline area of abnormal AF was compared to the follow up area and a rate of change was calculated.

**Results:** 22 eyes of 16 patients with NVAMD were identified. The computer algorithm successfully identified areas of hyper-AF and hypo-AF in all eyes. The area identified by the computer algorithm had good agreement with the area identified by the human graders. In all eyes at baseline, abnormal hypo-AF was present, and on average, the area increased in size by the final follow up. The average size of the hyper-AF area also increased from baseline, but less than the area of hypo-AF. An example of the output from the automated software is included below.

**Conclusions:** Image analysis of fundus AF using a fully automated algorithm can provide rapid, objective information about RPE pathology in patients with NVAMD. This software has the potential to allow for monitoring of RPE changes to detect disease progression and in response to medical therapy.
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0.5 mg, -2.19; 2 mg, -2.54; PRN: 0.5 mg, -1.80, 2 mg, -2.02). At 12 months, complete regression in total CNV area (reduction of 100% in the total CNV area from baseline) was observed in 66% of patients in the monthly groups compared with 55% in the PRN groups, while complete regression in classic CNV area was seen in 97% of patients in all groups.

**Conclusions:** Ranibizumab treatment (monthly or PRN) induced reductions in total CNV area as measured by fluorescein angiography that differed based on location and type of CNV. Monthly treatment led to greater reduction in total CNV area; however, complete regression in total CNV area was also observed in greater than 50% of patients in the PRN groups.

**Commercial Relationships:** None; Paul E. Tornambe, None; Linda Yau, Genentech, Inc. (E); Jeffrey A. Nau, Genentech (E); Lisa Tuomi, Genentech (E)

**Clinical Trial:** NCT00891735

**Program Number:** 4091 Poster Board Number: A0009

**Presentation Time:** 8:30 AM - 10:15 AM

**Anti-VEGF Gene Therapy for Wet AMD: Phase II/II Safety and Pharmacology Results**

Elizabeth P. Rakoczy1, 2, May Lai1, 2, Cora Pierce2, Aaron L. Magno2, Richard Samulski2, Thomas W. Chalberg2, Mark S. Blumenkranz3, Ian Constable1, 2, 3'Centre for Ophthalmology and Visual Sciences, The University of Western Australia, Perth, WA, Australia; 2Molecular Ophthalmology, Lions Eye Institute, Perth, WA, Australia; 3Gene Therapy Centre, University of North Carolina, Chapel Hill, NC; 4Avalanche Biotechnologies, San Francisco, CA; 5Byers Eye Institute at Stanford, Palo Alto, CA.

**Purpose:** To assess the safety and tolerability of rAAV.sFlt-1 following subretinal injection in subjects with exudative age-related macular degeneration (AMD).

**Methods:** 8 subjects with longstanding and extensively treated exudative AMD were randomized to treatment (6 subjects) or control (2 subjects). All subjects received 0.5 mg ranibizumab at baseline and day 30 to provide anti-VEGF therapy during the initial ramp-up period. Following day 30, ranibizumab was given when a subject met criteria for re-treatment based on visual acuity (VA) and optical coherence tomography (OCT). Seven days after baseline, 6 subjects received rAAV.sFlt-1 (3 low dose: 10E10 vg and 3 high dose: 10E11 vg), administered in 100 ul volume via subretinal injection.

**Results:** The average age of the patients enrolled for the trial was 79±4.6 years. In all 6 treated subjects, subretinal injection was successfully performed and bleb formation was observed. Serial ophthalmic examinations over time revealed no superficial, anterior segment, or vitreous inflammatory signs in any of the subjects. There was no significant intraocular pressure elevation, retinal detachment, or significant intraocular or systemic inflammation in any patient. Vector sequence was found in the tear of two subjects at one day following rAAV.sFlt-1 injection that cleared by the next sampling time point (14 days post-injection). Vector sequence or AAV capsid were not detected in any other samples. Clinical laboratory assessments, including blood biochemistry, complete blood count, and lymphocyte subsets, remained without any significant change from baseline. Although 50% of subjects had neutralizing antibodies to AAV at baseline, this did not appear to affect safety. Secondary endpoints included apparent visual acuity gains and a 10+ fold reduction in as-needed anti-VEGF injection frequency, with 5/6 treated patients requiring no further injections.

**Conclusions:** These initial results suggest that subretinal injection of rAAV.sFlt-1 is safe and well-tolerated, and is not associated with systemic or ophthalmic complications even among the elderly.

**Commercial Relationships:** Elizabeth P. Rakoczy, Avalanche Biotechnologies (C), Lions Eye Institute (P); May Lai, Lions Eye Institute (P); Cora Pierce, None; Aaron L. Magno, Avalanche Biotechnologies, Inc. (F), Avalanche Biotechnologies, Inc. (R); Richard Samulski, Asklepios BioPharmaceutical, Inc. (I); Thomas W. Chalberg, Avalanche Biotechnologies, Inc. (E), Avalanche Biotechnologies, Inc. (I), Avalanche Biotechnologies, Inc. (P), Avalanche Biotechnologies, Inc. (S); Mark S. Blumenkranz, avalanche biotechnologies (I), avalanche biotechnologies (P), optimedica (I); Ian Constable, Lions Eye Institute (P), Avalanche Biotechnologies (C)

**Support:** National Health and Medical Research Council of Australia

**Clinical Trial:** NCT01494805

**Program Number:** 4092 Poster Board Number: A0010

**Presentation Time:** 8:30 AM - 10:15 AM

**Polyoidal choroidal vasculopathy in Caucasian patients**

Stephen Davis, Andreas Lauer, Christina J. Flaxel, Oregon Health and Science University, Casey Eye Institute, Portland, OR.

**Purpose:** Report on a series of Caucasian patients in the United States with Polyoidal Choroidal Vasculopathy (PCV).

**Methods:** Retrospective chart review of patients at a single center with PCV were identified. 24 patients were identified with an average age of 74.4 (42-89) with 13/24 (54%) being male.

**Results:** The most common diagnosis prior to PCV being identified was neovascular age-related macular degeneration (NVAMD) in 14/24 (58%) of patients. In only 3/24 (12.5%) was PCV the initial diagnosis. On average it took 18.4 (5-46) months before PCV was diagnosed. During this time, patients received an average of 9.3 anti-VEGF intravitreal injections. The most common reasons for suspecting PCV were the presence of a large pigment epithelial detachment (PED) in 12/24 (50%) or a poor response to anti-VEGF therapy in 12/24 (50%). Polyoidal lesions were in the macula in 19/24 (79%), the periphery in 2/24 (8%), and both the macula and periphery in 3/24 (12%). Of the polyoidal lesions in the macula, 6/19 (32%) were peripapillary and 5/19 (26%) were temporal. Of those with peripheral PCV, there were 3 cases of exudative retinal detachment, 2 of which required vitrectomy, 3 with vitreous hemorrhage, and one choroidal hemorrhage. Once PCV was diagnosed, 18/22 (81.8%) underwent photodynamic therapy (PDT), 2/22 (9%) focal laser therapy and 2/22 (9%) continued anti-VEGF monotherapy. Of those that received PDT or focal laser, the fluid and/or PED decreased in size in 18/20 (90%). An improvement in vision was seen in 7/20 (35%) with 9/20 (45%) maintaining stable vision. The follow up time after PDT or focal was 14.4 (3-46) months and during this time, patients received only an additional 2.95 anti-VEGF injections and/or 1.4 more PDT treatments on average.

**Conclusions:** This report is one of the larger series of PCV in an entirely Caucasian population. It contains the first report of a patient with Usher’s that developed PCV. This emphasizes the importance of PCV diagnosis in Caucasians especially if there is a poor response to anti-VEGF therapy and/or large PED present as PCV can masquerade as NVAMD. Common findings were a temporal or peripapillary location as well as the presence of lipid. It also emphasizes the importance of a peripheral exam given the risk of pathology here. In these patients, after PDT, anti-VEGF therapy was still required but the injection burden was decreased by 40% (p<0.001) and vision was improved or maintained in 80%.

**Commercial Relationships:** Stephen Davis, None; Andreas Lauer, Oxford Biomedica (F), Acucela (F), NIH (F); Christina J. Flaxel, None
ARVO 2013 Annual Meeting Abstracts by Scientific Section/Group – Retina

Presentation Time: 8:30 AM - 10:15 AM
Baseline characteristics and response to intravitreal ranibizumab therapy for age-related macular degeneration
Misa Suzuki, Norihiro Nagai, Kanako Izumi-Nagai, Hajime Shinoda, Takashi Koto, Atsuro Uchida, Hiroshi Mochimaru, Kenya Yuki, Kazuo Tsutoba, Yoko Ozawa. Ophthalmology, Keio University School of Medicine, Tokyo, Japan.

Purpose: To study the baseline characteristics and response to intravitreal ranibizumab (IVR) therapy for age-related macular degeneration (AMD).

Methods: We reviewed clinical records of 119 eyes in 118 AMD patients who underwent IVR 3 times for induction therapy, and additionally when fluid or visual loss was observed during a 12-month follow-up. Baseline characteristics were analyzed, and responders and non-responders were identified at month 12. Patients whose best corrected visual acuity (BCVA) worsened more than 0.2 in logMAR score were, and those with increased or new exudative fundus findings or an increased central retinal thickness more than 100 micrometers were, considered to be non-responders as judged by BCVA, and by fundus findings, respectively. Adjusted odds ratios (ORs) for responders and non-responders, and 95% confidence intervals (CIs) were estimated with logistic regression models.

Results: Non-responders represented 16.8% of the AMD patients, as judged by BCVA, and 21.0%, as judged by fundus findings. The average age of non-responders by BCVA was higher than responders. Fibrovascular pigment epithelial detachment (PED) (odds ratio 3.77, 95% CI 1.03-13.83) and serous PED (odds ratio 4.86, 95% CI 1.17-20.11) at baseline were associated with non-response as judged by BCVA. Fibrovascular PED (OR 7.07, 95% CI 2.30-21.72), and type 1 choroidal neovascularization (OR 4.06, 95% CI 1.13-14.65) at baseline were associated with non-response, as judged by fundus findings.

Conclusions: Although most AMD patients responded to IVR therapy, non-responders had clinical characteristics at baseline that might be informative for managing their treatment.

Commercial Relationships: Misa Suzuki, None; Norihiro Nagai, None; Kanako Izumi-Nagai, None; Hajime Shinoda, None; Takashi Koto, None; Atsuro Uchida, None; Hiroshi Mochimaru, None; Kenya Yuki, None; Kazuo Tsutoba, AcaFocus, Inc (C), Allergan (F), Bausch Lomb Surgical (C), Functional visual acuity meter (P), JNS (P), Kissei (F), Kowa (F), Santen (F), Otsuka (F), Pfizer (C), Thea (C), Echo Denki (F), Ocular Instruments (F), Sanju Pharmaceutical Co., Ltd. (F)

Clinical Trial: UMIN000007649

Program Number: 4094 Poster Board Number: A0012
Disease Activity in Disciform Scars due to Age-Related Macular Degeneration (AMD)
Deborah Witkin1, John B. Sanderson1, Daniela Ferrara2, 4, Elias Reichel2, 4. Ophthalmology, Tufts Medical Center, Boston, MA; 2Digital Angiography Reading Center DARC, Great Neck, NY.

Purpose: End-stage AMD often develops into a disciform scar, considered clinically stable. Data suggest, however, that disease activity may persist regardless of scar formation. The goal of this study is to analyze incidence of disease progression indicated by hemorrhage, lipid exudate, atrophy, and fibrosis in disciform scars over time.

Methods: Medical records from patients diagnosed with AMD from 2009 to 2012 were reviewed. Patients with macular disciform scars with ≥10 months follow-up were included. Exclusion criteria were: history of other macular pathology or retinal disease, poor image quality, or inability to evaluate the entire lesion. Color fundus photos were analyzed by two independent observers for progression. A progression event was defined as increase in area of atrophy, increase in area of fibrosis, lipid exudate in a new location, or hemorrhage in a new location compared to baseline photos.

Results: 1148 charts were reviewed and 128 eyes of 115 patients met the study criteria and were analyzed. Patients were seen on average every 5.85±7.85 months and were followed for an average of 3.8±1.7 years. Seventy-seven eyes (60%) had at least one event. Mean time from baseline to first event was 1.8±1.2 years, and eyes with multiple events were more likely to have the first event occur earlier (P = .0035, mean 1.4±0.9 years). 19 eyes (15%) had more than one type of event (lipid exudate, fibrosis, or hemorrhage). Only eyes with hemorrhage had more than three events. Mean time to 1st hemorrhage was 1.8±1.4 years and then occurred approximately yearly for subsequent events. Eyes were also evaluated for presence of 360° of atrophy around the scar. Eyes with 360° atrophy were 46.0% less likely to have increased fibrosis, new exudate, or new hemorrhage than eyes without atrophy (relative risk = 0.540, p=.002, 13 of 77 eyes with progression vs. 22 of 51 eyes without progression showed 360° atrophy).

Conclusions: Disease activity occurs in eyes with disciform scars. Hemorrhage is the most common sign of activity and has a tendency to recur. After presentation of the first hemorrhage, they are likely to recur approximately yearly. Patients who show increased area of atrophy over time are unlikely to show increased fibrosis, hemorrhage, or lipid exudation. Presence of 360°atrophy around the scar may have a protective effect against development of hemorrhage, lipid exudate, or fibrosis.

Commercial Relationships: Deborah Witkin, None; John B. Sanderson, None; Daniela Ferrara, None; Elias Reichel, Thrombogenics (F), Alimera (C), Ocular Instruments (F)

Program Number: 4095 Poster Board Number: A0013
The Incidence of Neovascular Subtypes in Newly Diagnosed Wet Age-Related Macular Degeneration
Jesse J. Jung1, 2, Luna Xie2, 3, Roberto Gallego-Pinazo2, 4, Sarah Mrjen2, 5, Marcela Marsiglia2, 4, Sucharita Bodda1, K Bailey Freund1, 2, 4Department of Ophthalmology, New York Univ School of Med, New York, NY; 3Vitreous Retina Macula Consultants of New York, New York, NY; 5L’Esther T. Mertz Retinal Research Center, Manhattan Eye, Ear, and Throat Hospital, New York, NY; 4Department of Ophthalmology, University and Polytechnic Hospital La Fe, Valencia, Spain; 5St. Vincent's Medical Center, Bridgeport, CT.

Purpose: To determine the frequencies of neovascular lesion subtypes in newly diagnosed neovascular age-related macular degeneration (AMD) and to determine whether these frequencies differ when grading is based on fluorescein angiography (FA) or both FA and optical coherence tomography (OCT).

Methods: We retrospectively analyzed a consecutive series of patients treated by a single physician with intravitreal anti-vascular endothelial growth factor (anti-VEGF) therapy for the diagnosis of neovascular AMD from January 2006 through January 2012 in order to identify newly diagnosed treatment-naïve cases. Inclusion criteria included: age over 50 years; best corrected visual acuity of 20/40 to 20/800, new onset of treatment-naïve CNV, and absence of permanent structural damage to the central fovea. Two independent graders classified the lesions based on FA [poorly defined (occult), well-defined (classic), or retinal angiomatic proliferation (RAP)] and with both FA and OCT [type 1 (sub-RPE), 2 (subretinal) or type
3 (intraretinal) neovascularization); a third grader evaluated the lesion in the presence of significant discrepancies. Analysis between agreement in lesion subtype by FA alone or FA/OCT was performed using Chi-squared for two categorical variables. For each subtype of CNV, the association between demographic factors was also assessed. Analysis was performed using Stata 11 software (StataCorp, College Station, TX).

**Results:** Among 748 AMD patients treated with anti-VEGF therapy, a total of 531 eyes were treatment-naive and 311 fit the inclusion criteria. The average age at first injection was 81.5 years. 68.5% were women and 31.5% men. 95.5% were Caucasian, 2.9% Hispanic, and 1.9% Asian or Black. Based on FA classification alone, 47.9% had occult, 9.5% classic, 35.1% RAP, and 7.4% had mixed CNV lesions. In comparison, using FA/OCT, we found 43.4% type 1, 8.8% type 2, 36.4% type 3 (RAP), and 11.4% mixed. Subset analysis of the demographic variables and frequency for each CNV type demonstrated no significant differences.

**Conclusions:** With both forms of grading, we found a much higher incidence of type 3 (RAP) lesions and lower incidence of type 2 (classic) lesions than found in prior studies. Combined FA/OCT grading identifies a higher frequency of mixed CNV lesions as the addition of OCT appears useful in clarifying the location of the neovascular tissue in relation to the RPE.

**Commercial Relationships:** Jesse J. Jung, None; Luna Xu, None; Roberto Gallego-Pinazo, Bayer (R), Novartis (R), Novartis (C), Carl Zeiss Meditec (R); Sarah Mrejen, None; Marcela Marsiglia, None; Sucharita Boddu, None; K Bailey Freund, Genentech (C), Regeneron (C), ThromboGenics (C), Bayer (C), DigiSight (C)

**Program Number:** 4096 Poster Board Number: A0014
**Presentation Time:** 8:30 AM - 10:15 AM

**Choroidal thickness change following intravitreal bevacizumab therapy for wet age-related macular degeneration: Six months results**


**Purpose:** To investigate the change in choroidal thickness (CT) after intravitreal injections of bevacizumab (ivB) for wet age-related macular degeneration (AMD), using the enhanced depth imaging modality of spectral-domain optical coherence tomography (EDI-OCT).

**Methods:** This retrospective observational case series included 127 consecutive eyes of 127 patients with wet AMD, who received ivB injections. Exclusion criteria included posterior segment surgeries, and photodynamic therapy. Complete ophthalmic examination, fluorescein angiography, and EDI-OCT were performed at baseline, and during the follow-up visits. All eyes were given at least 2 ivB injections. In 35 eyes, 6 consecutive ivB were received. Manual choroidal segmentation, and subfoveal CT, mean CT in central 1000 and central 5000 microns were recorded. Differences between the baseline and post-ivB CT measurements were analyzed.

**Results:** The mean pre-injection CT was 171.7 μm within the central 1000 μm. A significant reduction (P < 0.005) in the CT was seen after 2 ivB in the fovea (6.3 μm), central 1000 μm (5.7 μm), and 5000 μm (4.6 μm). The reduction in the treatment naive eyes was higher than in the previously treated ones (7.8 μm and 4.07 μm respectively). Following 6 ivB injections, significant reduction (P < 0.05) was seen in the fovea and central 1000 μm at both the 2 and 6 months visit. No significant change in CT was observed between the 2 and 6 months visit.

**Conclusions:** Choroidal thickness showed a diffuse significant reduction following intravitreal bevacizumab injection, which was more during the first 2 months of treatment.

**Commercial Relationships:** Sharif Y. El Emam, None; Giulio Barteselli, None; Jay Chhablani, None; Su-Na Lee, None; Igor Kozak, None; Lingyun Cheng, Spinnaker Biosciences (C); William Freeman, OD-OS, Inc. (C)

**Support:** NIH grants R01EY007366 and R01EY018589 (WRF), and R01EY020617 (LC), "RPB incorporated and unrestricted funds from Jacobs Retina Center"
Choroidal Thickness following Anti-Vascular Endothelial Growth Factor Therapy for Neovascular Age-Related Macular Degeneration

**Purpose:** To evaluate choroidal thickness via enhanced depth imaging spectral domain optical coherence tomography (EDI SD-OCT) in patients receiving multiple intravitreal anti-vascular endothelial growth factor (VEGF) injections for neovascular age-related macular degeneration (nAMD).

**Methods:** A retrospective chart review of 11 eyes of 9 patients with nAMD treated with intravitreal anti-VEGF therapy (bevacizumab, ranibizumab or aflibercept, as needed) was performed. EDI SD-OCT was obtained routinely on each nAMD patient on monthly follow-up visits once it became readily available in our clinic. We analyzed patients with 6 or more injections prior to this time point. Choroidal thickness was calculated on each subsequent exam by manually measuring between the RPE and inner sclera at 5 standard points within the macula and averaged, according to published protocol. Change in thickness was then compared between the initial measurement and months 2, 4, 6, and 8. Results were analyzed using SPSS software.

**Results:** A total of 8 eyes of 7 patients were included in this study. Mean number of prior injections was 12 (7-17). Mean follow-up was 9 months (8-10). Mean choroidal thickness on initial measurement was 143.48 ± 31.30, 141.33 ± 35.81 at 2 months, 146.26 ± 34.29 at 4 months, 145.45 ± 35.19 at 6 months, and 147.35 ± 39.13 at 8 months. The change in choroidal thickness over the 8-month period was not statistically significant (p=0.428).

**Conclusions:** Published data on the long-term effects of anti-VEGF therapy on choroidal thickness is conflicting, but may suggest a decrease after as few as 3 injections. This small pilot study describes thinner choroids in eyes presenting with an average of 12 prior injections. Over the following 8 months, there was no statistically significant change with further treatments. Further study with a larger sample size and longer follow up is needed to confirm choroidal thinning with anti-VEGF therapy and determine the significance of these changes.

**Commercial Relationships:** charlotte so, None; Zac Ravage, None

**Program Number:** 4099 Poster Board Number: A0017

**Presentation Time:** 8:30 AM - 10:15 AM

**CORRELATION BETWEEN CHANGES IN SUBLFOveal CHOROIDAL THICKNESS AND 1-YEAR OUTCOMES OF RANIBIZUMAB THERAPY FOR POLYPOIDAL CHOROIDAL VASCULOPATHY**

Taiichi Hikichi, Hirokami Kitamei, Shoko Shioya, Makoto Higuchi, Takuro Matsushita, Shoko Kosaka, Reiko Matsushita, Kimitaka Takami, Hideo Ohtsuka. Ohtsuka Eye Hospital, Sapporo, Japan; Sapporo University Hospital, Sapporo, Japan.

**Purpose:** To determine the correlation between changes in the subfoveal choroidal thickness (CT) and outcomes 1 year after ranibizumab therapy for polypoidal choroidal vasculopathy (PCV).

**Methods:** Eighty-six consecutive eyes of 80 Japanese patients with symptomatic PCV received one intravitreal injection of 0.5 mg ranibizumab monthly for 3 months followed by an as-needed re-injection schedule. The following measurements were performed at baseline, 1 month after three monthly injections, and 1 year after the first injection: CT by enhanced-depth optical coherence tomography (OCT), foveal thickness (FT) by spectrum-domain OCT, simultaneous fluorescein angiography (FA), and indocyanine green angiography.

**Results:** The mean (± standard deviation) number of injections during 1 year was 4.3 ± 1.2. The mean visual acuity (VA) improved significantly from 0.42 to 0.33 logarithm of the minimum angle of resolution (logMAR) (P<0.001, paired t-test). The mean CT and FT improved significantly from 271 μm and 347 μm, respectively, to 212 μm and 203 μm (P=0.001 for both comparisons, paired t-test). Simple regression analysis showed that the change ratio of the CT, i.e., baseline CT-CT 1 year after the first injection/baseline CT, was correlated significantly with the change ratio of the FT, i.e., baseline FT-FT 1 year after the first injection/baseline FT at baseline (r=0.20, P=0.048). No correlation was observed with other outcomes of ranibizumab therapy for PCV.

**Conclusions:** Changes in choroidal thickness may be associated with outcomes of ranibizumab therapy for PCV.

**Commercial Relationships:** Taiichi Hikichi, None; Hirokuni Kitamei, None; Shoko Shioya, None; Makoto Higuchi, None; Takuro Matsushita, None; Shoko Kosaka, None; Reiko Matsushita, None; Kimitaka Takami, None; Hideo Ohtsuka, None

**Program Number:** 4100 Poster Board Number: A0018

**Presentation Time:** 8:30 AM - 10:15 AM

**Axial Length and Subfoveal Choroidal Thickness in Individuals with Age-related Macular Degeneration (AMD)**

Chih Ping Wang1,2, Chien-Hsiung Lai1,3,4,6, Jou Chen Huang1,2, Chien Neng Kuo1,2. 1Department of Ophthalmology, Chang Gung Memorial Hospital, Chiayi, Chiayi County, Taiwan; 2Chang Gung University, Taoyuan, Taiwan.

**Purpose:** To compare axial length and choroidal thickness between individuals with age-related macular degeneration (AMD) and controls.

**Methods:** Total 846 eyes of 481 individuals with various degree of AMD and controls with no lesion were recruited. Individuals with other etiology of retinopathy and maculopathy were excluded. The axial length was measured by IOL master. Color fundus photography and optical coherence tomography images were obtained from all participants after pupil dilation. Using color fundus photography, the individuals were classified to various degree of age-related maculopathy according to the international Classification and Grading System. Subfoveal choroidal thickness was manually measured using the image of 1-line raster scan through the fovea center obtained by Stratus OCT.

**Results:** Total 846 eyes of 481 participants including 471 eyes of no lesion controls, 163 eyes of drusen only, 88 eyes of early AMD, and 124 eyes of late AMD. The average choroidal thickness was 282.65±45.1μm. The mean subfoveal choroidal thickness of late AMD group was 255.5±54.0μm, which is less than other groups (p<0.001)of no lesion (291.1±35.6μm), drusen only (296.2±38.9μm) and early AMD (285.0±34.5μm). The average axial length was 23.39±1.13mm. The late AMD group has longer mean axial length (23.68±1.94 mm) (95% confidence interval [CI], P = 0.002) compared with other groups (no lesion:23.41±0.93mm, drusen only:23.19±0.92mm, early AMD:23.24±0.78mm). In a multiple regression model, subfoveal choroidal thickness was a significant variable in the first injection/baseline logMAR VA, or the number of injections during the 1-year follow-up period. The change ratio of the CT was significantly higher in eyes with choroidal hyperpermeability (0.21 ± 0.17, n=20) than in eyes without choroidal hyperpermeability (0.12 ± 0.12, n=66) (P=0.007, unpaired t-test) and in eyes in which the polypoidal lesions improved 1 year after the first injection (0.38 ± 0.28, n=44) than in eyes in which the polypoidal lesions remained stable or worsened (0.24 ± 0.35, n=42) (P=0.048, unpaired t-test).

**Conclusions:** Changes in choroidal thickness may be associated with outcomes of ranibizumab therapy for PCV.

**Commercial Relationships:** Taiichi Hikichi, None; Hirokuni Kitamei, None; Shoko Shioya, None; Makoto Higuchi, None; Takuro Matsushita, None; Shoko Kosaka, None; Reiko Matsushita, None; Kimitaka Takami, None; Hideo Ohtsuka, None

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in axial length (95% confidence interval [CI], P< 0.001) adjusted for age, AMD grading and signal strength.  

**Conclusions:** Longer axial length and reduced subfoveal choroidal thickness were significant in participants with late AMD. Also eyes with longer axial length have thinner choroidal thickness. Combination of these two characteristics may contribute to the result and as risk factors of late stage AMD.

**Commercial Relationships:** Chih Ping Wang, None; Chien-Hsiung Lai, None; Jou Chen Huang, None; Chien Neng Kuo, None

**Program Number:** 4101 **Poster Board Number:** A0019  
**Presentation Time:** 8:30 AM - 10:15 AM  
**APE1/Ref-1 redox inhibitor APX3330 modulates choroidal endothelial cells by transcriptional regulation of NF-κB and STAT3 activity**  
Xiaoxi Qiao1, Yue Li1, Xiuli Liu1, Tongrong Zhou1, Mark R. Kelley2, Paul A. Edwards3, Hua Gao1. 1Ophthalmology, Henry Ford Health System, Detroit, MI; 2Herman B Wells Center for Pediatric Research., Indiana University School of Medicine, Indianapolis, IN.  
**Purpose:** We previously reported that APE1/Ref-1 redox function is required for retinal angiogenesis and APE1/Ref-1 redox inhibition with a novel small molecule inhibitor APX3330 inhibits both retinal and choroidal neovascularization in vitro and in vivo. In this study, we investigated which transcription factor(s) mediate such action in choroidal endothelial cells.  
**Methods:** Choroidal endothelial cells (CEC, RF/6A) from rhesus monkey were used in this study. Cells were first treated with various doses of APX3330 or vehicle control. A cell-based reporter gene assay was used to examine the activities of transcription factor hypoxia induced factor (HIF1α), nuclear factor kappa B (NF-κB) and signal transducers and activators of transcription3 (STAT3). Expression levels of activated NF-κB p65 and pSTAT3 were further verified by western blot analysis. Production of monocYTE chemotactic protein-1 (MCP-1) was determined by ELISA after incubating these cells in an inflammatory cytokine mixture (ICM).  
**Results:** The reporter gene assay revealed that APX3330 dose-dependently inhibited the transcriptional activities of both NF-κB and STAT3. A low dose treatment of 10 µM APX3330 had minimal effect on the NF-κB transcriptional activity, but it remarkably reduced STAT3 activity by about 44%; whereas 20 µM APX3330 reduced NF-κB activity by 32% and STAT3 activity by 53% in these endothelial cells. Expression levels of activated pSTAT3 and NF-κB p65 were significantly reduced at higher dosages of 40 µM and 80 µM APX3330, respectively. STAT3 is more sensitive than NF-κB to the APX3330-mediated APE1/Ref-1 redox inhibition than NF-κB. In addition, 40 µM APX3330 treatment significantly attenuated the ICM-induced increase of MCP-1 (p < 0.05). The level and activity of HIF1α were not altered by APX3330 in these cells.  
**Conclusions:** APE1/Ref-1 redox inhibitor APX3330 elicits its inhibition on choroidal endothelial cells by inhibiting the transcriptional activities of STAT3 and NF-κB at low doses and the expression levels at high doses. Inhibiting the redox function of APE1/Ref-1 may offer a novel approach to control choroidal neovascularization for AMD treatment.

**Commercial Relationships:** Xiaoxi Qiao, None; Yue Li, None; Xiuli Liu, None; Tongrong Zhou, None; Mark R. Kelley, ApxTherapeutics (C); Paul A. Edwards, None; Hua Gao, None  
**Support:** International Retinal Research Foundation, Midwest Eye Bank, Reeves Foundation, Fund for Henry Ford Hospital, Alliance for Vision Research.

**Program Number:** 4102 **Poster Board Number:** A0020  
**Presentation Time:** 8:30 AM - 10:15 AM  
**Apolipoprotein mimetic Dual Domain Peptide reduces Neutral Lipid Deposits in murine Bruch’s Membrane**  
Armin Mohi, Salvatore Grisanti, Martin Rudolf. Department of Ophthalmology, University of Luebeck, Luebeck, Germany.  
**Purpose:** Massive accumulation of neutral lipids in Bruch’s membrane (BrM) with concomitantly increased hydraulic resistivity and oxidative stress induction is a major age change in the eye and an important pathogenic factor for the development and progression of age-related macular degeneration. Apolipoprotein (Apo) mimetic peptides are highly effective and well tolerated lipid acceptors that might be used to remove these pathogenic deposits. We evaluated the effect of an intravitreally injected dual domain peptide (DDP) containing domain properties of ApoE and ApoA-I in an established mouse model of age-related BrM lipid deposition (ApoEnull).  
**Methods:** Four groups (4x; n=6) of 10-month-old ApoEnull mice received a single intravitreal injection of DDP with different dosages (0 µg; 0.6 µg; 1.2 µg; 2.4 µg). The second untreated eye served as an intra-individual control. Thirty days after injection all animals were sacrificed and eyes were enucleated and processed to BrM wholemounts. The specimens were stained with a protocol for BrM specific esterified cholesterol using the fluorescent cholesterol specific dye PFO/D4-GFP (Dettbarn et al. ARVO 2010). The treatment effect on BrM lipid deposition was evaluated semiquantitatively by fluorescence measurements. We calculated for each dose group across all treated vs. untreated eyes the relative difference (%) and tested for significance using the student-t-test.  
**Results:** The vehicle injection (0.9% NaCl, 0 µg DDP) caused no change in BrM esterified cholesterol content (p=0.29). In all other groups we could observe a significant decrease of cholesterol content. The lowest dose showed a significant effect (p<0.001) of 43,5% cholesterol reduction in the treated eyes vs. untreated eyes. The medium and highest DDP dose showed also significant effects (p<0.001) with a cholesterol reduction of 41.7% in the medium dose group and 34.2% with the highest dose.  
**Conclusions:** Our data demonstrated a significant but so far not dose dependant reduction of BrM lipid deposits by DDP with ApoA-I and ApoE domain characteristics. Nevertheless, the treatment effect is lower than with our initially tested ApoA-I mimetic peptides (L-4F, D-4F, ARVO 2011 Rudolf et al. Mohi et al.). A neutral lipid reduction of ca. 70% with a single intravitreal injection of 2.4 µg D-4F shows almost double the treatment effect of the here tested DDP.  
**Commercial Relationships:** Armin Mohi, UAB Research Foundation (P); Salvatore Grisanti, Novartis (A), Allergan (C), Bayer (C), Pfizer (C), Thrombogenics (C); Martin Rudolf, UAB Research Foundation (P)

**Program Number:** 4103 **Poster Board Number:** A0021  
**Presentation Time:** 8:30 AM - 10:15 AM  
**Identification of Human Macular Tissue Antigens Recognized by Serum Auto-Antibodies (auto-Abs) in Patients with Age-Related Macular Degeneration (AMD)**  
Nataliya I. Lenchik1, 2, Francesco Giorgianni2, Sarka Beranova-Giorgianni2, Ivan C. Gerling1, Marko Z. Radić1, Alessandro Iannaccone2. 1Medicine/Endocrinology, Univ. Tennessee HSC, Memphis, TN; 2Harlem Eye Institute, Univ. Tennessee HSC, Memphis, TN; 3Pharmaceutical Sciences, Univ. Tennessee HSC, Memphis, TN; 4Microbiology, Immunology & Biochemistry, Univ. Tennessee HSC, Memphis, TN.  
**Purpose:** To report on the first results of a 2-D gel electrophoresis (DE) and mass spectrometry (MS)-based approach to identifying human macular tissue antigens recognized by serum auto-Abs found in AMD patients.

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**Methods:** 2-DE, MS and database screening were used to identify proteins obtained through immunoprecipitation. Macular tissue lysates were obtained from full-thickness, 10mm diameter, human donor eye macular punches. 150 µg lysate were immunoprecipitated with AMD or control sera obtained from a collection of 131 AMD samples and 245 unaffected subjects, all previously tested for auto-Ab by Western blots (WBs). By choosing appropriate sample amount, using pre-cast IPG dry strips (PH3-10) and casting 12% equal gel, stained by Sypro Ruby, 2-DE images were obtained and a steady 2-DE technique was established. Protein spots were analyzed by Progenesis Same Spots software (v 2.0). The program generated a list of proteins ranked by spot intensity. Spots corresponding to the bands previously identified as differentially reactive by WBs in the same AMD sera were cut out and analyzed by MS.

**Results:** Among the 22 differentially reactive spots in 2-DE gels that were identified, 11 of which unique to AMD samples, preliminary analyses have thus far identified reactivity against the following targets: a 38-kDa secreted protein that plays a role in immune system regulation and apoptosis inhibition; the N-terminal peptide of another secreted protein, normally cleaved into various isoforms with distinct biological activities, that is implicated in neural neuroprotection, cell replication, and lysosomal activity; and a 39-kDa protein known to be normally involved in retinal cell development, morphogenesis and differentiation. Neither target had thus far been implicated in the growing body of evidence for an inflammatory/immune-mediated pathogenesis of AMD. Additional studies are in progress on these and other samples.

**Conclusions:** 2-DE and MS are effective tools to identify human macular tissue antigens recognized by serum auto-Abs observed in AMD patients. The utilization of this approach, combined with in vivo validation studies, offers the opportunity to test hypotheses about the role played by the autoreactivities observed in AMD patients, to understand better AMD pathogenesis, and to develop, characterize and test treatments on new models of the disease.

**Commercial Relationships:** Michaela K. Mathews, None; Tatyana AlbuKh, None; Katherine E. Duncan, None

**Support:** 5K08EY016357

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**Program Number:** 4104 Poster Board Number: A0022
**Presentation Time:** 8:30 AM - 10:15 AM

**Early ocular lipid deposition in a mouse model of hyperlipidemia and atherosclerosis**

Michaela K. Mathews, Tatyana AlbuKh, Katherine E. Duncan, Ophthalmology, Univ of Maryland, Baltimore, Baltimore, MD.

**Purpose:** The Lipoprotein receptor deficient (LDLR-) mouse model was established for hyperlipidemia and atherosclerosis. Recently, aged LDLR-/- mice have been found to develop lipid deposits in Bruch's membrane and retinal degeneration, when fed a diet rich in lipids. These changes have been likened to atherosclerotic plaques as well as to human age-related macular degeneration (AMD). The structural changes effected by hyperlipidemia in younger LDLR-/- mice and the timing of early changes have yet to be determined. This study investigates early sub-retinal and choroidal changes caused by hyperlipidemia to explore the hypothesis that hyperlipidemia-induced lipid deposition and inflammatory changes in the eye could be a predictor of AMD and atherosclerosis later in life.

**Methods:** C57BL/6J-LDLR-/- and C57BL/6J wild-type control mice (total n=24) were fed either a regular rodent diet or a high-fat "western" diet. At the ages of 1-3 months and 4-8 months, respectively, animals were humanely killed. Blood was collected for determination of serum lipid concentration using a Cholesterol Assay Kit. Eyes were enucleated and fixed. Full-thickness sections of the eye, taken at the posterior pole were imaged using transmission electron microscopy (TEM). The thickness of Bruch’s membrane in ten fields of the TEM grid was measured. For localization of neutral lipids and fatty streak atherosclerotic lesions, the fellow eyes were stained with oil red O and analyzed by light microscopy. Statistical analysis was performed to determine mean total Cholesterol(TC) and LDL levels as well as average Bruch’s membrane thickness in each group.

**Results:** LDLR-/- mice had an up to twenty-fold increase of TC and a one-fold increase in LDL when compared to WT control. LDLR-/- mice on a high-calorie diet developed subretinal lipid deposits and Bruch’s membrane changes as early as one month after starting the high fat diet. Atherosclerotic and retinal degenerative changes were observed in aged, hyperlipidemic mice. Overall thickness and lipid deposits in Bruch’s membrane decreased with age.

**Conclusions:** Diet-induced hyperlipidemia, results in systemic atherosclerosis as well as in AMD-like lipid deposition and Bruch's membrane thickening in the eye, starting at a young age. Early detection of structural changes in the eye may have great predictive value for the development of AMD as well as for systemic atherosclerosis.

**Commercial Relationships:** Michaela K. Mathews, None; Tatyana AlbuKh, None; Katherine E. Duncan, None

**Support:** 5K08EYO16357

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**Program Number:** 4105 Poster Board Number: A0023
**Presentation Time:** 8:30 AM - 10:15 AM

**The role of systemic infection and response to Ranibizumab therapy for Age Related Macular Degeneration (AMD)**

Charles O. Pierce1,2, Marie Nelson3, Jennifer Scott1, Helen L. Griffiths4, Natulee L. James5, Heather A. Thomson1, Angela J. Cree1, Andrew J. Lotery1, 2, Clinical Neurosciences, University of Southampton, Southampton, United Kingdom; 1University Hospital of Southampton, Southampton, United Kingdom.

**Purpose:** In the chronic neurodegenerative disease, Alzheimer’s disease, systemic inflammation has been associated with progression and relapse of the disease. Chronic and acute inflammation has also been implicated in choroidal angiogenesis and subsequent AMD development. We hypothesised that systemic inflammation may also alter the response of AMD to the anti-vascular endothelial growth factor (VEGF) agent Ranibizumab.

**Methods:** Patients attending the Southampton Eye Unit (SEU) for treatment of AMD with Ranibizumab were enrolled at their third loading intravitreal injection. Patients were seen monthly at their clinical review. Systemic illness, further anti-VEGF injections or changes to medication were noted. Each patient was enrolled for 6 months. Demographic information was obtained from casenotes and patient questionnaires. Recorded optical coherence tomography (OCT) scans provided objective evidence of CNV activity.

**Results:** Our initial demographic analysis did not show a relationship between administered Ranibizumab intravitreal injections and recorded systemic infections (p= 0.863). There was also no relationship between central macular thickness (CMT) change from baseline and patient reported systemic infection (p=0.270).

**Conclusions:** This analysis of demographic data showed no relationship between patient reported systemic infections and CMT. Further study of inflammatory cytokines may provide more direct/ alternative evidence of the effect of systemic inflammation on CNV activation.

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Commercial Relationships: Charles O. Pierce, Genentech (F); Marie Nelson, None; Jennifer Scott, None; Helen L. Griffiths, None; Natalie L. James, None; Heather A. Thomson, None; Angela J. Cree, None; Andrew J. Lotery, Novartis (F), Bayer (R)

Support: Funding grant from Genentech for studentship

Program Number: 4106 Poster Board Number: A0024

Presentation Time: 8:30 AM - 10:15 AM

Immunohistochemical analysis of primate drusen reveals homologous protein expression between monkey and human

Trevor J. McGill1, Laurie Renner2, Alison R. Weiss2, Kay D. Rittenhouse3, Justin Lee4, Joachim Fruebis5, Marvin Sperling6, Martha Neuringer7, Ophthalmology, Casey Eye Institute-OHSU, Portland, OR; 2Neuroscience, Oregon National Primate Research Center, Beaverton, OR; 3Ophthalmology External Research Unit, Pfizer, Cambridge, MA.

Purpose: A hallmark of age-related macular degeneration (AMD) is the accumulation of drusen under the retinal pigment epithelium (RPE); however, limited animal models are available that exhibit drusen consistent with those found in the human condition. Nonhuman primate models of dry AMD express drusen in two forms: rhesus and cynomolgus macaques commonly exhibit late onset drusen accumulation that develops over many years, whereas specific colonies of Japanese and cynomolgus macaques exhibit dominantly inherited early onset drusen accumulation that begins early in life and progresses rapidly. We examined the expression of key immunohistochemical markers of human drusen in both early and late onset primate drusen phenotypes.

Methods: Eyes from Japanese and rhesus macaques ranging from 2 to 38 years old were enucleated, hemisected, and immersion fixed in 4% paraformaldehyde overnight. Frozen OCT embedded eyes were sectioned at 14 μm and collected in 5-slide series. One slide in each series was stained using cresyl violet to examine overall retinal morphology and identify sub-RPE drusen deposits. Adjacent sections were stained using antibodies against C5b9, vitronectin, clusterin, ApoE, C3, C5, membrane cofactor protein, annexin, and anti-beta-amyloid antibody clones 4G8 and 6E10.

Results: Drusen in rhesus macaques is more centralized around the macula, whereas Japanese macaque drusen extend throughout the retina. Drusen were identified by their characteristic sub-RPE morphology in both species. Drusen accumulation increased with age in both species. Immunohistochemical staining demonstrated expression of C5b9, vitronectin, clusterin, Apo-E, C5, membrane cofactor protein in drusen in both species in the most severe cases. Less severely affected animals expressed only some of the above markers. Anti-beta-amyloidoid (4E10) was also expressed in drusen of both species. Interestingly, anti-beta-amyloid (4G8) was expressed in photoreceptor outer segments and its expression increased with age, a result described previously in mice and humans.

Conclusions: Drusen in both rhesus and Japanese macaque retinas positively stain with the same immunohistochemical markers as human drusen, and in an age dependent manner. These findings suggest that both Japanese and rhesus macaques may provide useful models for examining factors involved in drusen accumulation and for testing potential AMD therapies.

Commercial Relationships: Trevor J. McGill, StemCells, Inc. (C), Pfizer (F), AGTC (F); Laurie Renner, Pfizer (F), Applied Genetic Technologies Corporation (F); Alison R. Weiss, Pfizer (F); Kay D. Rittenhouse, Pfizer Inc. (E); Justin Lee, None; Joachim Fruebis, Pfizer Inc (E); Marvin Sperling, Pfizer Inc. (E); Martha Neuringer, Pfizer (F), Applied Genetic Technologies Corporation (F)

Support: Pfizer Ophthalmology External Research Unit, The Foundation Fighting Blindness, Research to Prevent Blindness, NIH P51OD011092

Program Number: 4107 Poster Board Number: A0025

Presentation Time: 8:30 AM - 10:15 AM

A Pathway-based Genome-wide Analysis Yields Multi-locus AMD Associations in Genes Encoding JNK/MAPK Pathway Elements, Platelet Activation Triggers, and Targets of miR34 and HDAC1

John Paul P, SanGiovanni, Clinical Trials Branch, National Eye Institute/NIH, Bethesda, MD.

Purpose: We applied a pathway-based genome-wide analysis to determine whether DNA sequence variants within groups of functionally related genes are, in aggregate, more strongly associated with advanced AMD (AAMD) than expected by chance alone.

Methods: We used age-, sex-, and smoking-adjusted meta-regression to compute combined estimates of gene-AMD relationships from 3 independent cohorts examined in large-scale genotyping projects on the molecular genetics of AMD (1177 people with AAMD and 1024 of their AMD-free peers who were > 65 years-of-age). SNPs spanning independent genomic intervals and significantly related with AAMD at P<0.002 were tested with exact methods for enriched association signals within functionally-defined gene sets using a validated 2-phase genomic permutation procedure applying 5000 and 1000 iterations. The multi-locus analytic method uses positional clustering of SNPs to account for factors (varying gene size, SNP density, linkage disequilibrium) that otherwise may lead to non-differential misclassification and inflation in measures of association.

Results: AAMD-associated SNPs were enriched in 8 independent genomic regions of 7 genes in the JNK/MAPK pathway, yielding an exact P-value of 0.002 for the likelihood of a chance finding. Twelve independent genomic regions in 10 genes encoding platelet activation triggers carried AAMD-associated sequence variants; the exact likelihood of observing a random clustering of findings within this
functionally related gene set was 0.002. Seventeen genes containing a specific microRNA (miR34) target carried 23 independent regions with AMD-associated SNPs (exact P = 0.004). Thirty-four independent genomic regions in 34 genes that are up-regulated by histone deacetylase 1 (HDAC1) contain AMD-associated variants (exact P = 0.007).

Conclusions: A multi-locus genome-wide analysis yielded associations of AMD with aggregates of functionally related genes encoding 10 platelet activation triggers, 7 elements of the JNK/MAP signaling pathway, and 23 and 34 respective targets of the epigenetic regulatory elements miR34 and HDAC1. Our findings may be used to identify molecular probes for drug testing and determination of metabolic fate.

Commercial Relationships: John Paul P. SanGiovanni, None

Support: Intramural Funding from NIH

Program Number: 4108 Poster Board Number: A0026
Presentation Time: 8:30 AM - 10:15 AM

Minocycline protects retinal pigment epithelial cells from hypoxia
Joanna DaCosta. Cranfield Health, Cranfield University, Cranfield, United Kingdom.

Purpose: To demonstrate that minocycline protects ARPE-19 cells from the effects of hypoxia in cell culture

Methods: ARPE-19 cells were cultured in Dulbecco’s modified Eagle medium supplemented with 10% fetal calf serum, penicillin and streptomycin and seeded onto 6 well plates at a concentration of 5 X 10^4 cells per well. Minocycline concentrations between 2μM and 10μM were added to the culture media.

Cell growth curves with and without minocycline were constructed for cells cultured in an hypoxic chamber (2% oxygen) and results compared to culture in normoxic conditions over a period of 8 days. (n=8 for each growth curve)

A Scepter® handheld cell counter was used to measure cell counts which were conducted in triplicate.

Results: A Mann Whitney U test showed that there was a significant difference in ARPE-19 growth between normoxic and hypoxic conditions when the culture media was supplemented with Minocycline at concentrations between 2μM and 10μM at all points of the cell growth curve. (p < 0.04)

Conclusions: Cell and molecular biological analyses suggest that chronic oxidative stress and inflammation are involved in the pathogenesis of AMD. Hypoxia may result from increased metabolic demand during inflammation or poor perfusion in the central macula due to vessel stenosis. This study demonstrates that minocycline protects retinal pigment epithelial cells in culture from the effects of hypoxia. This suggests minocycline may have a therapeutic role in the treatment of age related macular degeneration.

Commercial Relationships: Joanna DaCosta, None

Program Number: 4109 Poster Board Number: A0027
Presentation Time: 8:30 AM - 10:15 AM

Dominantly Inherited Early Onset Maculopathy in Japanese Macaques: Drusen Progression
Anda Cornea 1, Laurie Renner 1, Sawan Hurst 1, Trevor J. McGill 2, Mark E. Pennesi 3, Kay D. Rittenhouse 4, Marvin Sperling 5, Joachim Fruebis 1, Martha Neuringer 1, Anda Cornea 1, Trevor J. McGill 2, Alison R. Weiss 6, Tim Stout 7, David J. Wilson 8, Martha Neuringer 1, 2, 3

Purpose: Macaque monkeys possess a macula and commonly develop age-related maculopathy that shares common genetic risk factors with human age-related macular degeneration (AMD). However, monkeys have not been reported to develop advanced atrophic or neovascular AMD. We hypothesized that dietary factors may play a role in this lack of progression to advanced disease. In particular, we examined the role of key nutrients thought to lower the maculopathy. Subretinal drusen deposits in this species show the same morphological and immunohistochemical characteristics as drusen in human patients with age-related macular degeneration (AMD), and therefore they provide a particularly useful model for translational studies. We obtained repeated retinal fundus images of affected animals and developed a novel image analysis method to quantify drusen extent and estimate rates of progression.

Methods: Serial color retinal fundus photographs were obtained from 20 Japanese macaques with the dominant drusen phenotype at 3-month intervals over a 9- to 12-month period. The animals were 4-20 years old with a wide range of drusen severity; all were members of a troop resident at ONPRC since 1964. At each time, 5 images were analyzed to increase reliability. Images were segmented into the central 1 mm and a 1-6 mm annulus. A machine learning algorithm using advanced Weka segmentation (University of Waikato) was implemented to discriminate and quantify drusen, and rates of progression were determined.

Results: In the central macula, the initial extent of drusen ranged from <1% to 46% of the total area, with older animals showing more severe drusen loads. The rate of progression ranged from <1% to >20% (mean 5.4%) of the area of the central macula per year, largely depending on the initial area occupied by drusen. As a percentage of initial drusen area, rates of progression averaged 1.8% per year. In the 1-6 mm annulus, the initial percent area occupied by drusen ranged from 0.2-9% and increased at an average rate of 1.5% of area per year, or 1.2% of initial drusen area. A companion study is examining the relationship between these estimates of drusen load and cone densities measured by adaptive optics.

Conclusions: This maculopathy has close phenotypic similarity to human AMD. A similar syndrome was reported in cynomolgus macaques (Umeda et al., IOVS 46:683-691, 2005). Only higher nonhuman primates possess a macula, and macaques with naturally occurring macular disease syndromes provide a valuable resource for probing macular disease pathogenesis and for preclinical testing of AMD therapies.

Commercial Relationships: Anda Cornea, Pfizer (F); Laurie Renner, Pfizer (F), Applied Genetic Technologies Corporation (F); Sawan Hurst, Pfizer (F); Trevor J. McGill, StemCells, Inc. (C); Pfizer (F), AGTC (F); Mark E. Pennesi, Pfizer (F); Kay D. Rittenhouse, Pfizer Inc. (E); Marvin Sperling, Pfizer Inc. (E); Joachim Fruebis, Pfizer Inc (E); Martha Neuringer, Pfizer (F), Applied Genetic Technologies Corporation (F)

Support: Pfizer Ophthalmology External Research Unit, The Foundation Fighting Blindness, Research to Prevent Blindness, NIH grant P51OD011092

Program Number: 4110 Poster Board Number: A0028
Presentation Time: 8:30 AM - 10:15 AM

Progression of Atrophic Macular Degeneration in Rhesus Monkeys Deficient in Lutein/Zeaxanthin and Omega-3 Fatty Acids
Laurie Renner 1, Sawan Hurst 1, Trevor J. McGill 2, Alison R. Weiss 6, Tim Stout 7, David J. Wilson 8, Martha Neuringer 1, 2, 3

Purpose: Macaque monkeys possess a macula and commonly develop age-related maculopathy that shares common genetic risk factors with human age-related macular degeneration (AMD). However, monkeys have not been reported to develop advanced atrophic or neovascular AMD. We hypothesized that dietary factors may play a role in this lack of progression to advanced disease. In particular, we examined the role of key nutrients thought to lower the...
risk of AMD progression and currently being tested in the AREDS2 trial: lutein and zeaxanthin—the xanthophylls that form macular pigment—and omega-3 fatty acids.

**Methods:** From birth until 17-22 years of age, 18 rhesus monkeys were fed semisynthetic diets devoid of lutein and zeaxanthin (L/Z), resulting in an absence of macular pigment. For 8 of these monkeys the diet was also deficient in omega-3 fatty acids, while the remaining 10 received adequate levels. The animals were monitored serially by color fundus photography and fluorescein angiography over a 12-year period and by sdOCT over 3 years.

**Results:** Among monkeys fed diets lacking L/Z, 50% developed drusen by 15 years of age (equivalent to 45 human years), compared to 20% in monkeys fed normal diets. Three animals, all in the omega-3 deficient group, developed atrophic changes in the macula by 12-18 years of age. In all cases the degenerative changes first appeared in an arc approximately 1 mm superior to the fovea, the same locus where we previously found high accumulation of lipofuscin in monkeys on the same omega-3 deficient diet. The affected areas were characterized by patchy RPE disruption and pigmentedary changes coincident with hyperfluorescent window defects, and increased at a linear rate over 4-7 years. sdOCT showed disruption of the RPE and IS/OS junction and large deposits extending into the photoreceptor layer.

**Conclusions:** These are the first documented cases of atrophic macular disease in nonhuman primates, and they emerged at an early age relative to typical human cases of atrophic AMD. These findings provide support for the role of L/Z and omega-3 fatty acids as important factors in progression to advanced AMD. Macaque monkeys can provide a uniquely relevant model for studying factors contributing to age-related macular disease.

**Commercial Relationships:** Laurie Benner, Pfizer (F), Applied Genetic Technologies Corporation (F); Sawan Hurst, Pfizer (F); Trevor J. McGill, StemCells, Inc. (C); Pfizer (F), AGTC (F); Alison R. Weiss, Pfizer (F); Tim Stout, Clayton Foundation (P), Oxford Biomedica (C), AGTC (F), Peregrine Pharmaceuticals Inc (C), Stem Cells Inc (C); David J. Wilson, None; Martha Neuringer, Pfizer (F), Applied Genetic Technologies Corporation (F)

**Support:** Foundation Fighting Blindness, NIH grants EY13199, DK29930 and P50DO11092 and Research to Prevent Blindness

**Program Number:** 4111 Poster Board Number: A0029

**Presentation Time:** 8:30 AM - 10:15 AM

**Biocompatible injectable hydrogel to extend the release of intravitreal drugs**

**Thomas R. Friberg**, 1, 2 Britta M. Rauck, 1 Carlos A. Medina-Mendez, 1 Yadong Wang, 1

**Purpose:** An ideal drug delivery platform should be biocompatible, completely biodegradable, non-toxic, simple to administer, and extend the release of drugs several fold. We investigated the utility of a biocompatible gelling solution to deliver bevacizumab (Avastin) in rabbit eyes.

**Methods:** We synthesized poly(Ethylene glycol)-co Serinol Hexamethylene) Urethane (ESHU) to produce a liquid that could be injected through a 31-gauge needle and form a gel immediately upon entry into a hyaluronic acid solution at 35 degrees C, the temperature of human vitreous. We injected 50 μl of a 15% solution of ESHU containing either 1.25 mg or 4 mg of bevacizumab intravitreally into rabbit eyes to determine the release characteristics. We observed the fundus and measured intraocular pressure (IOP) at each sampling point. We withdrew aqueous samples from the eyes over 8 weeks' time, and determined its bevacizumab concentration using an enzyme-linked immunosorbent (ELISA) assay. Histology of the rabbit eyes was obtained upon sacrifice.

**Results:** Using a standard 1.25 mg dose of bevacizumab in 0.05 ml of gelling solution, the polymer sustained the release of bevacizumab substantially for more than 6 weeks compared to less than 4 weeks in groups receiving free bevacizumab alone. With the concentrated dose, the aqueous concentration at 1 month was 7.7 mcg/ml compared to 0.47 mcg/ml in controls (1X concentration, no polymer). At 7 weeks’ time, 0.41 mcg/ml, an amount likely to be sufficient for VEGF suppression, was found in the rabbit eyes compared to a 0.07 mcg/ml in controls. An expected IOP spike occurred immediately following injection, and the IOP returned to baseline levels within 15 minutes time and remained normal throughout the study period. Histologically, there was no evidence of inflammation, affirming ESHU’s biocompatibility.

**Conclusions:** ESHU appears to an efficient drug delivery platform which is non-toxic and can sustain the release of bevacizumab for more than 8 weeks after a single injection in a rabbit. In a human, this release would be most likely even slower, as the human eye is larger than the rabbit eye, 4 cc vs. 1.5 cc. As the polymer is an injectable solution, it can sustain the delivery of virtually any intravitreal medication; we expect similar release curves with other agents. One of the advantages of this hydrophobic and hydrophilic gel is that no polar solvents are required to load the drug into the delivery

**Commercial Relationships:** Thomas R. Friberg, 13/581,518 (P); Britta M. Rauck, None; Carlos A. Medina-Mendez, None; Yadong Wang, None

**Support:** Otero Grant, University of Pittsburgh

**Program Number:** 4112 Poster Board Number: A0030

**Presentation Time:** 8:30 AM - 10:15 AM

**Effect of Repeated Delivery of Neural Progenitors on Vision Preservation in RCS Rats**

**Bin Lu**, 1 YaChun Tsai, 2 Grazya Adamus, 2 Sergey Girman, 1 Lin Shen, 1 David M. Gamm, 1 Catherine W. Morgans, 2 Brandon Shelley, 1 Clive Svendsen, 1, Shaomei Wang, 1

**Purpose:** Growth factor mediated neuroprotection has been repeatedly demonstrated in multiple animal models and current clinical trial using CNTF to treat retinal degeneration. Stem/progenitor cells as factor delivery vehicle offer great promise to slow down the progression of degenerative diseases. To sustain protective effect for long term, repeated grafting of stem cells is necessary. However, some fundamental questions are remained to be addressed, such as how will host response to the second injection, how the efficacy of the first graft will be affected etc. Here we proposed to address these questions by repeated delivery of human neural progenitor cells into the Royal College Surgeon (RCS) rats.

**Methods:** Human neural progenitor cells (hNPC) produced under GLP condition were unilaterally injected into the subretinal space of RCS rats at P21-23. Animal were fed with cyclosporine water through the entire experiment. At postnatal day 90-95, visual function was tested by recording ERG, optokinetic response (OKR) and luminance thresholds from the superior colliculus. The second injection of hNPC was performed on the fellow eye after functional examination. Blood samples were collected at several time points after the second grafting. OKR and ERG were conducted weekly until the end of experiment.

**Results:** Subretinal injection of hNPC significantly preserved visual function over untreated controls as measured by ERG, OKR and luminance threshold recordings. After the second injection of hNPC,

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visual function as tested by OKR was maintained the same as before the second injection (0.549 cycle/degree vs. 0.533 cycle/degree). Histological examine on retinal sections at early time point showed normal retinal lamination; there is no abnormal changes on cresyl violet stained sections.

**Conclusions:** This study showed redosing stem cells did not trigger acute rejection of the previous grafts. A long-term follow-up is needed to examine host immune response to the second grafts and the efficacy from the first graft on vision protection.

**Commercial Relationships:** Bin Lu, None; YuChun Tsai, None; Grazyna Adamus, None; Sergey Girman, None; Lin Shen, None; David M. Gamm, Cellular Dynamics international (C); Catherine W. Morgans, None; Brandon Shelley, None; Clive Svendsen, None; Shaomei Wang, None

**Support:** Foundation Fighting Blindness; Fund from Regenerative Medicine Institute at CSMC; NIH R01EY020488-01; W81XWH-DOD.

**Program Number:** 4113  **Poster Board Number:** A0031  **Presentation Time:** 8:30 AM - 10:15 AM

**Comparison of intravitreally injected ranibizumab versus aflibercept in the retina and choroid of the primate eye Sylvie Julien, Ulrich Schraermeyer.** Experimental Vitreoretinal Surgery, Centre for Ophthalmology, Tuebingen, Germany.

**Purpose:** There is evidence that the Fc domain of anti-VEGF drugs may play a role on their action in the retina and choroid. To establish whether Fc presence affects their distribution in these structures, we used immunohistochemistry to investigate the distribution of aflibercept (with Fc) and ranibizumab (no Fc) in intravitreally injected monkey eyes.

**Methods:** We injected ranibizumab (Lucentis® 0.5mg) or aflibercept (Eylea® 2mg) in the vitreous of eight cynomolgus monkeys, using as controls three untreated animals and one injected with aflibercept's vehicle alone. We studied the distribution of ranibizumab and aflibercept in the retina and choroid, using respectively anti-F(ab') or anti-Fc-fragment antibodies. We further used other antibodies to detect immunoreactivity as follows: glial fibrillary acidic protein (GFAP) for astrocytes and activated Mueller cells; vimentin for Mueller cells; ionized calcium binding adaptor molecule 1(Iba1) for macrophages/microglia; hypoxia-inducible factor (HIF) as a marker for hypoxia.

**Results:** The distribution of both drugs within the retina and choroid tissue was visualized by their immunoreactivity. Ranibizumab permeated the retina via intercellular clefts (Fig. 1a), whereas aflibercept was taken up already 24 h post-injection by ganglion cells (RGC), cells of the inner and outer retinal layers and retinal pigment epithelium (RPE) (Fig. 1b), leading to individual RPE cell death. Local accumulation and complex formation of both drugs in individual choroidal vessels and choriocapillaris were observed but seemed to be more pronounced after aflibercept treatment. Mueller cells, astrocytes and microglia cells were locally activated after treatment with either drug as well as vehicle alone. HIF was not expressed in retinal cells.

**Conclusions:** Ranibizumab permeated the retina through intercellular spaces, whereas aflibercept was taken up by neuroretinal cells and RPE, inducing more protein complex formation and individual RPE cell death. The clinical significance and relation of these findings to the Fc domain or to other characteristics of the molecule, remain to be investigated.
analysis of metabolic pathways, this method can produce biochemical profiles of AMD patients that will provide targets for therapeutic intervention and insights into rational clinical management.

**Commercial Relationships:** Samantha Williamson, None; Youngia Park, None; Karan Uppal, None; ViLinh Tran, None; J. Allie McGrath, None; Anita Agarwal, Vanderbilt University (P); Margaret A. Pericak-Vance, None; Jonathan L. Haines, Arctic Dx (I); AMD genes (P); Dean P. Jones, None; Milam A. Brantley, None

**Support:** NIH Grant R01EY012118-12 (JH); Jahngen Career Development Award from the American Geriatrics Society (MAB); Carl M. & Mildred A. Reeves Foundation (MAB); Unrestricted departmental grant from Research to Prevent Blindness

**Program Number:** 4115 Poster Board Number: A0033
**Presentation Time:** 8:30 AM - 10:15 AM
**Metabolites that discriminate between neovascular AMD and control patients associate with different ARMS2 genotypes**

Megan B. Parks, Youngia Park, L. Goodwin Burgess, Kichun Lee, Paul Sternberg, Dean P. Jones, Milam A. Brantley, Vanderbilt Eye Institute, Vanderbilt University, Nashville, TN; 2Department of Medicine, Emory University, Atlanta, GA; 3Department of Industrial Engineering, Hanyang University, Seoul, Republic of Korea.

**Purpose:** To determine if metabolites that distinguish between neovascular age-related macular degeneration (NVAMD) and controls are associated with the AMD-associated ARMS2 rs10490924 polymorphism.

**Methods:** We performed metabolic analysis using anion-exchange liquid chromatography with Fourier-transform mass spectrometry (LC-FTMS) on plasma samples from 26 NVAMD patients and 19 controls. Data were collected by a Thermo LTQ-FT mass spectrometer from mass/charge ratio (m/z) 85 to 850 over 10 minutes, and individual m/z features were matched to the Metlin metabolomics database. False Discovery Rate (FDR) analysis (q=0.05) was employed to identify the metabolic features discriminating between NVAMD patients and controls. All participants were genotyped for the rs10490924 single nucleotide polymorphism in the ARMS2 gene. Orthogonal partial least squares discriminatory analysis (OPLS-DA) was performed to identify the top 5% of metabolic features that account for 95% discrimination between ARMS2 GG genotype and ARMS2 GT+TT genotypes.

**Results:** A total of 94 metabolic features were found to discriminate between NVAMD and controls by FDR. OPLS-DA identified a total of 113 m/z features that contribute to the separation of the ARMS2 GG genotype (no risk alleles) from the ARMS2 GT+TT genotypes (1-2 risk alleles). We overlaid the 94 FDR significant features onto the OPLS-DA loading plot and found a common subset of 26 features that discriminated NVAMD from controls and ARMS2 GG from ARMS2 GT+TT genotypes. These features were searched against the Metlin metabolomics database and found to include matches to cholesterol sulfate, modified amino acids, and di-/tri-peptides.

**Conclusions:** The results suggest that approximately one-third of the metabolites that discriminate between NVAMD and control are influenced by the AMD-associated ARMS2 genotype. These data suggest that the combination of metabolomic and genetic data will be useful in developing clinically-relevant biomarkers for AMD.

**Commercial Relationships:** Megan B. Parks, None; Youngia Park, None; L. Goodwin Burgess, None; Kichun Lee, None; Paul Sternberg, None; Dean P. Jones, None; Milam A. Brantley, None

**Support:** NIH Grant EY007892 (PS); Jahngen Career Development Award from the American Geriatrics Society (MAB); Carl M. & Mildred A. Reeves Foundation (MAB); Unrestricted departmental grant from Research to Prevent Blindness

**Program Number:** 4116 Poster Board Number: A0034
**Presentation Time:** 8:30 AM - 10:15 AM
**The Composition of the Vitreous Proteome in Patients with Wet AMD Can Differentiate Between CNV and RAP: An Important New Diagnostic Tool**

Stephanie M. Ecker, Joshua C. Hines, Ann O. Igbre, Bert M. Glaser, Ocular Proteomics, LLC; National Retina Institute, Towson, MD.

**Purpose:** Neovascular age related macular degeneration (AMD) is a complicated, heterogeneous disease. Among the various phenotypes of wet AMD, two significant disease subsets are those who develop from retinal angiomatous proliferation (RAP) and those who develop from choroidal neovascularization (CNV). Recent studies have shown that the Vitreous Proteome can reflect disease activity and response to treatment in wet AMD. We therefore sought to determine if there are characteristics of the Vitreous Proteome that differentiate RAP from primary CNV.

**Methods:** Multiple in-office vitreous aspirations of 50-100µl were obtained from 106 patients who presented with neovascularization initiating from RAP (n=56) or CNV (n=50). The aspirations analyzed were taken prior to the patient receiving intra-vitreal bevacizumab but no laser. All vitreous aspirations (128 RAP, 109 FV CNV) were evaluated for 45 proteins using Reverse Phase Protein Microarray Technology (RPPM). The proteins evaluated were chosen because they represent biochemical pathways involved in inflammation, apoptosis, hypoxia/oxidative stress and proliferation/angiogenesis.

**Results:** Seven of the 45 proteins demonstrated significant differences between the two AMD phenotypes of RAP and CNV. Complement Components C5a and C9, along with Complement Factor H are expressed at higher levels in patients with RAP (p= 0.0010, p= 0.0497, p= 0.0442). Additionally, Matrix Metalloproteinase 9, 14 (MMP-9, MMP-14) and Tissue Inhibitor of Metalloproteinase-2 (TIMP2) are expressed at higher levels in RAP patients (p= 0.0125, p= 0.0002, and p= 0.0022). Lastly, COX2 is expressed at higher levels in the vitreous of patients with RAP, p= 0.0035.

**Conclusions:** This is the first time that the Vitreous Proteome of AMD patients with neovascularization initiating from RAP versus those with primary CNV has been compared to determine protein expression differences. The differing levels of proteins involving the complement system and matrix metalloproteinases suggest that these protein families could serve as potential biomarkers to predict development of these types of vessel pathologies and at the same time shows that there is a difference in the pathobiology of differing phenotypes of wet AMD. These finding may suggest different approaches to the management of AMD depending upon the status of the Vitreous Proteome.

**Commercial Relationships:** Stephanie M. Ecker, Ocular Proteomics LLC (E); Joshua C. Hines, Ocular Proteomics (E); Ann O. Igbre, None; Bert M. Glaser, Ocular Proteomics, LLC (E)

**Program Number:** 4117 Poster Board Number: A0035
**Presentation Time:** 8:30 AM - 10:15 AM
**Metabolic pathways associated with Age-related Macular Degeneration (AMD)**

L. Goodwin Burgess, Youngia Park, Megan B. Parks, Kichun Lee, Paul Sternberg, Dean P. Jones, Milam A. Brantley, Vanderbilt Eye Institute, Vanderbilt University, Nashville, TN; 2Department of Medicine, Emory University, Atlanta, GA; 3Department of Industrial Engineering, Hanyang University, Seoul, Republic of Korea.

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Purpose: To identify the metabolic pathways that are altered in neovascular age-related macular degeneration (NVAMD).

Methods: We performed metabolomic analysis using liquid chromatography with Fourier-transform mass spectrometry on plasma samples from 26 NVAMD patients and 19 controls. Data were collected from mass/charge ratio (m/z) 85 to 850 on a Thermo LTQ-Orbitrap Velos mass spectrometer, and individual m/z features were matched to the Metlin metabolomics database. Metabolic features were extracted using an adaptive processing software package; both non-transformed and log2-transformed data were corrected using Benjamini and Hochberg False Discovery Rate (FDR) to account for multiple testing. Principal Component Analysis and Orthogonal Partial Least Squares-Discriminant Analysis were performed to determine metabolic features that distinguished AMD patients from controls. To identify the metabolic pathways and enzyme-gene networks associated with NVAMD, we used MetScape, a plug-in for an open source software platform for visualizing complex networks (Cytoscape).

Results: A total of 94 metabolic features differed between NVAMD and control patients with FDR (q=0.05) while 132 discriminating features were found using log2 transformation (q=0.2). MetScape analysis of the non-transformed 94 features identified 17 affected metabolic pathways, including tyrosine metabolism; the urea cycle and metabolisms of related amino acids arginine, proline, glutamate, aspartate, and asparagine; and several carbohydrate metabolism pathways. Compound-reaction-enzyme-gene analysis of the log2-transformed data confirmed the network associations to tyrosine and urea metabolism pathways, indicating their importance. Features matching to tyrosine pathways included L-tyrosine, L-phenylalanine, and dopaquinone. The matches for the urea pathway included L-glutamate, L-/D-aspartate, carnitine, and O-acetylcarnitine.

Conclusions: Metabolomics can identify metabolites that discriminate NVAMD cases from controls, and subsequent pathway analysis can indicate which metabolic pathways are involved in creating these disparities. Single metabolites from the tyrosine and urea metabolism pathways have already been suggested as involved in retinal equilibrium, and pathway analysis is now able to substantiate evidence of their involvement in NVAMD.

Commercial Relationships: L. Goodwin Burgess, None; Youngja Park, None; Megan B. Parks, None; Kichun Lee, None; Paul Sternberg, None; Dean P. Jones, None; Milam A. Brantley, None

Support: NIH Grant EY007892 (PS); Jahnigen Career Development Award from the American Geriatrics Society (MAB); Carl M. & Mildred A. Reeves Foundation (MAB); Unrestricted departmental grant from Research to Prevent Blindness.

Program Number: 4118 Poster Board Number: A0036
Presentation Time: 8:30 AM - 10:15 AM
Age-related macular degeneration and complement C3 in liver transplant patients
Samir Khandhadia1,2, Svetlana Hakobyan3, Angela J. Cree1, Andrew J. Lotery1,2. 1Clinical and Experimental Sciences, Clinical Neurosciences, University of Southampton, Southampton, United Kingdom; 2Eye Unit, University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom; 3School of Medicine, Cardiff University, Cardiff, United Kingdom.

Purpose: Age-related macular degeneration (AMD) is the most common cause of irreversible blindness in the developed world. The complement system is implicated in its pathogenesis. Complement C3 protein is central to both the classic and alternate complement pathway. We investigated whether AMD in a previously recruited liver transplant cohort was associated with recipient rs2230199 sequence variation in the C3 gene. We also investigated whether there was an association between the C3 rs2230199 sequence variation and recipient plasma C3, the activation product C3a, and terminal complement complex (TCC) levels.

Methods: rs2230199 C3 genotyping and plasma C3 levels were determined in 223 Western European patients at least 55 years old, who had undergone LT at least 5 years previously. AMD status was determined using a standard grading system. C3 rs2230199 was determined from DNA extracted from whole blood, and genotyped by Kbiosciences Ltd (Cambridge, UK). Plasma C3, C3a and TCC were measured using enzyme-linked immunosorbent assays.

Statistics was carried out using SPSS version 19 (IBM).

Results: Using logistic regression, AMD status was not associated with recipient C3 genotype (p=0.779) after controlling for age, gender, smoking status, and body mass index (table 1). Using the Mann-Whitney test, there was no association between the presence of the C3 rs2230199 sequence variation, and plasma C3, C3a and TCC levels (p=0.684, 0.804 and 0.840 respectively - table 2).

Conclusions: AMD was not associated with recipient C3 genotype in a liver transplant cohort. Presence of the C3 rs2230199 sequence variation did not seem to impact upon plasma levels of C3, its activation product C3a, and TCC. The C3 rs2230199 sequence variation may not have a direct functional consequence on activation of the complement pathway.

Table 1: Regression analysis of the association of C3 rs2230199 sequence variation with AMD

<table>
<thead>
<tr>
<th>Variable</th>
<th>P value</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td>0.015</td>
<td>1.060</td>
</tr>
<tr>
<td>GENDER (Males=1)</td>
<td>0.397</td>
<td>1.289</td>
</tr>
<tr>
<td>BMI</td>
<td>0.937</td>
<td>0.997</td>
</tr>
<tr>
<td>SMOKING (pack years)</td>
<td>0.613</td>
<td>0.995</td>
</tr>
<tr>
<td>C3 rs2230199 (additive model)</td>
<td>0.779</td>
<td>1.069</td>
</tr>
</tbody>
</table>

BMI = Body mass index (kg/m2).

Table 2: Association of plasma C3, C3a and TCC levels with C3 rs2230199 sequence variation

<table>
<thead>
<tr>
<th>C3 rs2230199 sequence variation</th>
<th>Absent</th>
<th>Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>C3 (g/l)</td>
<td>0.537 (0.200)</td>
<td>0.552 (0.784)</td>
</tr>
<tr>
<td>C3a (ng/ml)</td>
<td>78.95 (44.0)</td>
<td>83.20 (50.0)</td>
</tr>
<tr>
<td>TCC (AU/ml)</td>
<td>0.55 (1.36)</td>
<td>0.67 (1.36)</td>
</tr>
</tbody>
</table>

All figures are median values with interquartile range given in parentheses. C3 = Complement C3; C3a = Activated C3; TCC= Terminal Complement Complex

Commercial Relationships: Samir Khandhadia, Novartis (F); Svetlana Hakobyan, None; Angela J. Cree, None; Andrew J. Lotery, Novartis (F), Bayer (R)
Support: This research was supported by the TFC Frost Charitable Trust, Claygate, UK (registered charity number: 256590), the Gift of Sight charity, Southampton, UK (www.giftofsight.org.uk), and an unrestricted educational grant from Novartis Pharmaceuticals, Frimley, UK. The funding organizations had no role in the design or conduct of this research.

Program Number: 4119 Poster Board Number: A0037
Presentation Time: 8:30 AM - 10:15 AM

Ophthalmologic exam in Age Macular Degeneration-Alzheimer Disease: its interest in detection, follow-up of AMD, of Alzheimer disease, its relevance to highlight the links and correlations between AMD and AD

Corinne Gonzalez. Ophthalmology, Cabinet Medical, Toulouse, France.

Purpose: To evaluate the importance of ophthalmologic exam in AMD and AD, the impact of AMD on Alzheimer disease and vice versa, and their relationship and in-between correlation.

Methods: PATIENTS: AMD patients: 240 patients, 3 Groups A, B, C: A: 70 AMD patients with first stage AMD (drusen, drusenoid PED, pigment, small atrophic areas), B: 64 Atrophy AMD patients with predominant atrophic areas, C: 106 Neovascular AMD patients, with Neovascular AMD. AD patients: 240 patients, 4 groups

I,II,III,IV: 1. Normal or no significant patients; II: 127 MCI patients, (4 subgroups: mild, moderate, intense, severe); III : 29 Early AD; IV:14 AD. EXAM: ophthalmologic exam included ETDRS visual acuity (VA), complete ophthalmic examination, Fundus examination, autofluorescence imaging (FAF)., (Region Finder Software, particularly for atrophic areas), optical coherence tomography ( Spectral Domain OCT) (OCT en face software, in particular), and fluorescein angiography (FA) and ICG when Neovascular complication (Spectralis HRA-OCT). Cognitive evaluation is done with MMSE: Mini Mental State Examination (Folstein, GRECO), score allow to determine various groups and subgroups. Each AMD patient, more than ophthalmologic exam would have cognitive evaluation. Each AD patients, more than cognitive exam, would have ophthalmologic evaluation.

Results: AMD patients,73% patients in group A, 77.5% in group B, 63% in group C have mild cognitive impairment (MCI). In MCI subgroups, results are progressively decreasing and similar in group A and B, lower and homogeneous in group B. Cognitive impairment differ between AMD subgroups. It’s moderate in group A (normal score:37%), higher in group B and C, and more in group B (normal score:22.5%) than in group C (normal score:34%), but early AD is only present in group C (3%). AD patients;43% patients with cognitive impairment present AMD. AMD ophthalmologic signs are predictive and precursor for AD. Fundus examination and even more (FAF, OCT) are useful and needed to enhance AD screening and follow-up as to detect AMD in AD patients.

Conclusions: The AMD-AD correlation allows us to improve detection, follow-up, screening of both AMD and AD pathologies and furthermore progress in etiopathogenic knowledge and therapeutic prospects.

Commercial Relationships: Corinne Gonzalez, None

Program Number: 4120 Poster Board Number: A0038
Presentation Time: 8:30 AM - 10:15 AM

Variants in the VEGFA gene and visual outcome after anti-VEGF treatment for neovascular age-related macular degeneration

Manuel M. Hermann1, Philipp S. Muether1, Dzenita Smalhodzic1, Anneke I. Den Hollander2, Bernd Kirchhof1, Sascha Fauser1.
1Department of Ophthalmology, University Hospital of Cologne, Cologne, Germany; 2Department of Ophthalmology, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands.

Purpose: To correlate the occurrence of genetic variants of the VEGFA gene with visual outcome of anti-vascular endothelial growth factor (VEGF) treatment in patients with neovascular age-related macular degeneration (AMD).

Methods: In this prospective cohort study with a follow-up of 12 months we included 283 patients from 2 study centers. Initial treatment consisted in 3 monthly ranibizumab injections. On monthly follow-up visits additional series of 3 monthly ranibizumab injections were initiated if necessary on the basis of clinical retreatment criteria. Multivariate data analysis was used to determine the influence of 125 selected tagged single nucleotide polymorphisms (tSNPs) in the VEGFA gene on visual acuity (VA) outcome at 12 months.

Results: Mean baseline VA was 0.64 ±0.36 logMAR (logarithm of the Minimum Angle of Resolution). Mean VA improved after 3 months by 0.08 ±0.29 logMAR and by 0.03 ±0.36 logMAR after 12 months. The only tSNPs significantly associated with visual outcome at 12 months with multiple correction were rs11603042 (P=0.032), rs307826 (P=0.047), and rs4576072 (P=0.002). For rs11603042 the presence of a T allele (TG or TT genotypes) lead to an increase in VA gain by mean 0.10 logMAR (95% confidence interval (CI), 0.01-0.18) when compared to the GG genotype. Concerning rs307826 the presence of a G allele (GA or GG genotypes) increased VA gain by mean 0.06 logMAR (95% CI, 0.01-0.16) when compared to the AA genotype. The largest effect was observed for the presence of a C allele (CT or CC genotypes) at the rs4576072 SNP which lead to an increase in VA gain by mean 0.12 logMAR (95% CI, 0.03-0.21) when compared to the TT genotype.

Conclusions: Pharmacogenetic characteristics may influence visual outcome in patients receiving anti-VEGF treatment for neovascular AMD. In patients with the T allele in SNP rs11603042, the G allele in rs307826, and/or the C allele in rs4576072 visual outcome was significantly better at 12 months.

Commercial Relationships: Manuel M. Hermann, None; Philipp S. Muether, Heidelberg Engineering (C); Dzenita Smalhodzic, None; Anneke I. Den Hollander, None; Bernd Kirchhof, None; Sascha Fauser, None

Support: Koeln Fortune Program, Faculty of Medicine, University of Cologne, Cologne, Germany.

Clinical Trial: NCT01213667
the VEGF165b level and the central foveal thickness (CFT) and the height of the subretinal fluid (SRF) were determined in AMD cases. The aqueous humor collected during cataract surgery in 19 patients without ocular pathology was used as control.

**Results:** The level of VEGF165b was higher than the lower limit of detection (15 pg/ml) in 55% of the AMD cases (median: 16.2, range: <15-151 pg/ml) and 63% of the controls (median: 20.6, range: <15-188 pg/ml). On the other hand, the percentage of eyes with VEGF165b >15 pg/ml was significantly lower in RVO cases than in the controls (37%, P=0.067, median: <15, range: <15-47 pg/ml). There was no significant difference in the VEGF165b level between eyes with CNV and PCV (P=0.654). The VEGF165b level was not significantly correlated with the CFT or the height of the SRF (P=0.613, 0.278 respectively).

**Conclusions:** The level of VEGF165b in the human aqueous humor was low in eyes with RVO which suggests that the anti-angiogenic isofrom of VEGF is reduced in RVO. In addition, there was no significant difference between AMD and the controls. It is possible that the change of the VEGF165b level is too small to detect because of the subretinal location of pathology in AMD.

**Commercial Relationships:** Takayuki Baba, None; Guzel Bikbova, None; Masayasu Kitahashi, None; Hirotaka Yokouchi, None; Madoka Sakurai, None; Mariko Kubota-Tanai, None; Shuichi Yamamoto, None

**Support:** Japan Society for the Japan Society for the Promotion of Science KAKENHI 23791966, Grant-in-Aid for Young Scientists (B) (TB).

**Program Number:** 4122 Poster Board Number:** A0040
**Presentation Time:** 8:30 AM - 10:15 AM

**Plasma levels of vascular endothelial growth factor and anti-vascular endothelial growth factor before and after intravitreal injection of anti-vascular endothelial growth factor**

Sang Jun Park, Myung Hun Yoon, Ah Reum Chung, Hee Seung Chin, Department of Ophthalmology, Inha Vision Science Laboratory, Inha University School of Medicine, Incheon, Democratic People's Republic of Korea.

**Purpose:** To examine the level of anti-vascular endothelial growth factor (anti-VEGF) and vascular endothelial growth factor (VEGF) in the plasma of patients before and after an intravitreal injection of ranibizumab or bevacizumab.

**Methods:** Total 22 patients with retinal disease were studied. The 13 eyes of 13 patients received an injection of bevacizumab (1.25mg), and the 9 eyes of 9 patients received an injection of ranibizumab (0.5mg). Samples of blood were collected just before the injection, and after 1 day, 1 week, 1 month. The Concentration of anti-VEGF and VEGF in the plasma were measured by ELISA.

**Results:** In bevacizumab group, the anti-VEGF concentration before the injection, after 1 day, 1 week, 1month was 110.1, 169.1, 215.6, 152.5 ng/ml (p=0.003, 0.001, 0.004, respectively), and VEGF concentration was 102.7, 54.8, 25.1, 37.0 pg/ml (p=0.101, 0.005, 0.007, respectively). In ranibizumab group, anti-VEGF concentration before the injection, after 1 day, 1 week, 1 month was 200.7, 149.3, 132.7, 155.4 ng/ml (p=0.086, 0.008, 0.066, respectively), and VEGF concentration was 48.0, 43.6, 85.9, 73.3 pg/ml (p=0.285, 0.214, 0.263, respectively).

**Conclusions:** Intravitreally injected bevacizumab enters the systemic circulation and affect the VEGF levels, but ranibizumab cannot be found in systemic circulation and doesn’t affect the VEGF levels. Thus, we should carefully consider general condition of patients before and after an intravitreal injection of bevacizumab.

**Commercial Relationships:** Sang Jun Park, None; Myung Hun Yoon, None; Ah Reum Chung, None; Hee Seung Chin, None

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Program Number: 4126 Poster Board Number: A0044
Presentation Time: 8:30 AM - 10:15 AM
Influence of bevacizumab on Platelet activation profile in vitro
Blanka Sobolewska1, Focke Ziemssen, Cornelia Grimmel1, Jadwiga Kwiatkowska2, Martin S. Spitzer1, Meinrad Gawaz1, Tilo Biedermann2, Konstantinos Stellos3, 1Centre for Ophthalmology, University of Tuebingen, Tuebingen, Germany; 2Dermatology, University of Tuebingen, Tuebingen, Germany; 3Cardiology and Cardiovascular Medicine, University of Tuebingen, Tuebingen, Germany.
Purpose: Inhibitors of the vascular endothelial growth factor (VEGF) are increasingly used in the therapy of multiple retinal diseases. While the risk of thrombotic events or bleeding has been discussed, we wanted to evaluate the effect of the off-label drug bevacizumab on platelet activation.
Methods: Blood was drawn from the antecubital vein of healthy volunteers, who did not take any drugs during the previous 10 days. Platelet-rich plasma (PRP) was prepared by centrifuging blood at 1000 rpm for 10 min at room temperature. The number of platelets in the PRP was counted by using fully automated hematology analyzers and adjusted to 200.000 platelets/μl with platelet-poor plasma (PPP). Suspension of platelets was treated with bevacizumab (2.5 mg/ml) or bevacizumab solvent for 10 min and 30 min before addition to the platelets of TRAP (25 μM) or thrombin (0.02 unit/ml). As a control, vehicle, TRAP or thrombin, bevacizumab or its solvent were used. In order to measure the ability of the incubated platelets to get activated, the expression of PAC-1 (activated form of GPIIb/IIIa) and P-Selectin (CD62p) was determined on resting (non-activated) and activated platelets. The expression of platelet-bound SDF-1 (stromal-cell-derived factor-1) was also evaluated. CD42b-PE served as control antibody to identify the platelet population. Mouse IgG1-FITC and IgG1-PE were used as monoclonal immunoglobulin isotype control antibodies. Platelet-associated fluorescence was quantified (10.000 events) with FACS-Calibur Flow Cytometer. The specific monoclonal antibody binding was expressed as stimulation index (SI) of surface platelet protein expression.
Results: No statistically significant differences were observed in the expression of P-Selectin and SDF-1 on both resting and TRAP-activated platelets, subsequent to the exposure of bevacizumab. However, the fibrinogen receptor (GPIIb/IIIa) showed significant changes after the exposure to bevacizumab. PAC-1, CD62p and SDF-1 were also significantly down-regulated on platelets if stimulated with thrombin after incubation with bevacizumab (mean ± SD of PAC-1: 0.5 ± 0.1, P=0.002 & P=0.001; CD62p: 0.08 ± 0.2, P=0.0002 & 1.1 ± 0.2, P=0.008; SDF-1: 0.9 ± 0.2, P=0.01 & 1.1 ± 0.1, P=0.002).
Conclusions: Different patterns of platelet activation after exposure to bevacizumab were observed and might be associated with an increased risk of bleeding.

Commercial Relationships: Blanka Sobolewska, None; Focke Ziemssen, Novartis (C), Bayer Healthcare (C), Alcon (R); Cornelia Grimmel, None; Jadwiga Kwiatkowska, None; Martin S. Spitzer, None; Meinrad Gawaz, None; Tilo Biedermann, None; Konstantinos Stellos, None

Program Number: 4127 Poster Board Number: A0045
Presentation Time: 8:30 AM - 10:15 AM
Effects of Plasma Kallikrein on the neuroretina in diabetic rats
GONGXIONG WU, Edward P. Feener. Vascular Cell Biology, Joslin Diabetes Center, BOSTON, MA.
Purpose: Diabetic retinopathy can cause abnormalities in the ganglion cell layer, which may contribute to visual impairment.

Program Number: 4125 Poster Board Number: A0043
Presentation Time: 8:30 AM - 10:15 AM
Hyperhomocysteinemia as a risk factor of polyoidal choroidal vasculopathy
Hui-Chen Cheng1, 2, Po-Kang Lin1, 2, 1Ophthalmology, School of Medicine, National Yang-Ming University, Taipei, Taiwan; 2Ophthalmology, Taipei Veterans General Hospital, Taipei, Taiwan.
Purpose: To determine whether elevated plasma homocysteine and serum C-reactive protein (CRP) levels, two established risk factors of vascular diseases, are associated with polyoidal choroidal vasculopathy (PCV).
Methods: Retrospective case-control study. Thirty-two patients with PCV and 73 control subjects without age-related macular degeneration or retinal vascular diseases were enrolled from September 2008 to October 2010. Plasma homocysteine and serum CRP levels were identified. Associations among plasma homocysteine, serum CRP levels and PCV were further evaluated using logistic regression analysis.
Results: The median plasma homocysteine level was significantly higher in patients with PCV than in the controls (16.22 μmol/L vs 10.75 μmol/L, P<0.001). The median serum CRP level was slightly higher in the PCV group (0.15 mg/dl vs 0.13 mg/dl in control group, P=0.49). After stratified by genders, significantly elevated plasma homocysteine levels were still noted in males with PCV, but not in females. Under logistic regression analysis, each 1μmol/L increase of plasma homocysteine in males was associated with 2 times more likely to have PCV (OR, 2.54; 95% CI, 1.24-5.22, P=0.01).
Conclusions: Hyperhomocysteinemia was a risk factor of PCV in males and might contribute to the pathogenesis of PCV.
Commercial Relationships: Hui-Chen Cheng, None; Po-Kang Lin, None

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Previously, we have shown that plasma kallikrein (PK) is present in vitreous samples obtained from patients with advanced diabetic retinopathy. In this study, we examine the effects of PK on the neuroretina in diabetic retinopathy in rodent models, and examine the direct effects of PK on neurons.

**Methods:** Diabetic was induced in Sprague Dawley rats by IP injection with streptozotocin. The effects of intravitreal PK on ganglion cells were examined in rats with 4 weeks of diabetes subjected to intravitreal injection of activated PK (50ng). The effects of systemic PK inhibition on the neuroretina were examined in diabetic rats treated with the PK inhibitor (BPC27) or vehicle alone continuously administered via subcutaneous Alzet osmotic pumps for 4 weeks. Retinal Brn3a (a ganglion cell marker) and caspase 3 levels were quantified by western blot and immunohistochemistry. The effects of PK on cultured cortical neurons were examined by measurements of lactate dehydrogenase release. The effects of PK on NMDA receptors (NR) were examined by western blotting and mutational analyses of NR.

**Results:** We show that intravitreal injection of PK in diabetic rats significantly decreased Brn3a (PK injection group n=9, Vehicle injection group n=9, P<0.01) and increased caspase 3 (P<0.01) in retinal extracts harvested at 24 hrs post injection. Administration of the selective PK inhibitor (BPC27) increased Brn3a (PK inhibitor group n=8, Vehicle injection group n=10, P<0.05) and decreased caspase 3 (P<0.01) level in diabetic retina compared to vehicle treatment.

In vitro, we found that PK-induced cortical neuronal cell death requires the presence of NR. Using site directed mutagenesis, we found that the PK directly cleaves NR1 at Arg323 residue located in the extracellular N-terminal domain of the receptor and this cleave mediated the effect of PK on enhancing NMDA’s effects.

**Conclusions:** These results demonstrate that intravitreal injection of activated PK in diabetic rats triggers retinal neuro-degeneration while inhibition of PK reduces ganglion cell loss in diabetes. Our findings suggest that PK-induced neuron injury is mediated by cleavage-dependent activation of NMDA receptor.

**Commercial Relationships:** GONGXIONG WU, None; Edward P. Feener, Joslin Diabetes Center (P), KalVista Pharmaceuticals (C)

**Support:** Juvenile Diabetes Research Foundation Advanced Postdoctoral Fellowship (10-2012-240), NIH EY019029

**Program Number:** 4128 Poster Board Number: A0046

**Presentation Time:** 8:30 AM - 10:15 AM

**Choroidal Neovascularization Response of New Zealand White Rabbits and Dutch Belt Pigmented Animals to Sustained Simultaneous Release of both VEGF and bFGF within the Suprachoroidal Space

Corinne G. Wong. Ophthalmic Drug Dev, SCLERA LLC, Carlsbad, CA.

**Purpose:** To assess if two different breeds of rabbits, New Zealand white (NZW) albino versus pigmented Dutch belt, demonstrate differences in the degree of inducible experimental choroidal neovascularization (CNV) since differential experimental retinal neovascularization was seen between NZW rabbits and pigmented rabbits.

**Methods:** Young adult NZW white rabbits (12) and Dutch belt pigmented female rabbits (12) weighing between 2 and 3 kg were utilized. All animals were kept on a normal 12 hr light/dark cycle and fed ad libitum. Color fundus and fluorescein angiography (FA) were performed prior to implantation of the VEGF/bFGF pellet and at wks 1, 2, 3, and 4. Photography was performed with a Topcon 50EX retinal digital camera system. The 1.5 mm VEGF/bFGF implant was placed between the 9 and 10 o’clock position in the suprachoroidal space, which was created by passing a cyclodialysis spatula between the choroid and sclera. Analysis of the angiographic leakage was based on severity of leakage over time. Enucleation was accomplished at week 4 with general histologic evaluation being performed.

**Results:** Both time course and robustness of CNV were similar in these two animal species. Average leakage for NZW rabbits and Dutch belts were 2.5 and 2.75, respectively. No significant differences were noted between NZW rabbits and Dutch belt female animals with sustained release VEGF/bFGF implants (p<0.001). Negative controls consisting of blank implants for both types of animals were 0 by week 4. General morphologic analysis also was similar for both types of animals.

**Conclusions:** This study indicates that two different breeds of rabbits (New Zealand albino vs Dutch belt) display similar experimental choroidal NV responses to the same amounts of both VEGF and bFGF unlike experimental retinal NV. Lack of pigmentation in the albino rabbit allows for observation of the choroidal vasculature and its patterns during the time course of experimental CNV. Since genetic heterogeneity most likely exists for angiogenic responses, defining the genetic role in the regulation of ocular angiogenesis will lead to the design of more effective drugs. However, suitability of this animal model for AMD drug development does not seem to be compromised by choice of genetically different animals.

**Commercial Relationships:** Corinne G. Wong, None

**Program Number:** 4129 Poster Board Number: A0047

**Presentation Time:** 8:30 AM - 10:15 AM

**Associations of IL-10 with Choroidal Neovascularization in high myopia

Yukimi Yamamoto1, Dai Miyazaki1, Shin-ichi Sasaki2, Ken-ichiro Miyake1, Shuozo Kaneda1, Yoshifumi Ikeda2, Atsushi Yamasaki1, Yoshitsugu Inoue1.1 Tottori University, Yonago, Japan; 2Oki-hospital, Oki District, Japan.

**Purpose:** To determine the relationship between the levels of intraocular inflammatory cytokines and choroidal neovascularization in high myopia.

**Methods:** Prospective cohort study. Choroidal neovascularization (CNV) in patients with high myopia (axial length ≥ 26.5 mm) was defined as myopic CNV (mCNV). Forty one patients with mCNV and 44 control subjects were studied. The levels of VEGF, MCP-1, IL-4, IL-10, and IL-23 in the aqueous humor samples from mCNV patients and control subjects were assessed for significant associations with mCNV. Logistic regression analysis was used to compute the odds ratios (ORs) and 95% confidence intervals (CIs).

**Results:** Axial length significantly correlated with levels of MCP-1 and IL-4 by Spearman correlation analysis (MCP-1: r=0.36, P=0.003, IL-4: r=0.33, P=0.009). In contrast, VEGF, IL-10, and IL-23 levels were independent of axial length. In mCNV patients, IL-10, IL-4, and MCP-1 were significantly higher than that in the controls (P=0.005, P=0.04, P=0.047, respectively). The IL-10 elevation was associated with mCNV and provided significant OR after age adjustment, however, no other cytokines discriminated the disease.

**Conclusions:** The significant association between elevated levels of IL-10 with mCNV strongly suggests an involvement of inflammatory processes in the etiology of mCNV presumably independent of VEGF or axial length.

**Commercial Relationships:** Yukimi Yamamoto, None; Dai Miyazaki, None; Shin-ichi Sasaki, None; Ken-ichiro Miyake, None; Shuozo Kaneda, None; Yoshifumi Ikeda, None; Atsushi Yamasaki, None; Yoshitsugu Inoue, None

414 AMD III, RE
**Automatic Temperature Controlled Retinal Photocoagulation Facilitates Four Predictable Lesion Strengths Including Sub-threshold Lesions**

**Stefan O. Koinzer**, Carola Hesse, Alexander Baade, Kerstin Schlotz, Amke Caliebe, Mark Saeger, Ralf Brinkmann, Johann Roeder.

**Purpose:** Conventional photocoagulation relies on retinal whitening for power adjustment. The method produces inconsistent lesions and does not allow to control the effect of very mild or sub-threshold lesions. We applied automatic, temperature controlled retinal photocoagulation, that uses temperature data to adjust irradiation times, and aimed at lesions of five different strengths in rabbits.

**Methods:** We used a modified 532nm photocoagulator that facilitated real-time retinal temperature measurements based on optoacoustics. A feedback loop allowed automatic exposure time control onto predefined time / temperature dependent characteristics for different lesion strengths. We applied lesions of 133 µm diameter to six rabbit eyes and varied laser powers (20 - 66 mW) and intensities. N = 225 control lesions were applied conventionally with fixed, 200 ms, exposure time, and n = 794 lesions with the new, automatic method in five consecutive characteristic groups. After 1 hour to 12 weeks, we examined fundus color and Spectralis® optical coherence tomographic (OCT) images and classified lesion morphologies according to a sixfold OCT classifier.

**Results:** Control lesion effects depended on the laser power and achieved morphological classes 2 - 6. Automatically controlled characteristic groups 1 - 4 correlated to increasing morphological lesion intensities (incidence peaks in OCT classes 1 to 4). These groups showed increasing median funduscopic diameters (0 [IQR 0-0] µm - 170 [149-195] µm) and OCT diameters (129 [0-144] µm - 282 [261-302] µm), Group 5 did not differ significantly from group 4. Visibility rates in funduscopy (OCT) were 17 % (68 %) for group 1, 38 % (90 %) for group 2 and > 94 % (> 98%) for all consecutive groups.

**Conclusions:** Automatic, temperature controlled photocoagulation allows to apply predictable lesions. A reliable reproducibility for mild and subthreshold lesions can be obtained for characteristic groups 1 - 4, which is not possible with conventional power control. Only strong lesions (characteristic group 5) do not reproduce as accurately owing to technical reasons. Overtreatment, however, can be avoided in any case. The automatic control facilitates standardized low intensity photocoagulation independently of the treating physician and of spot-individual transmission and pigmentation variation.

**Commercial Relationships:** Stefan O. Koinzer, None; Carola Hesse, None; Alexander Baade, None; Kerstin Schlotz, None; Amke Caliebe, None; Mark Saeger, None; Ralf Brinkmann, PVA (P); Johann Roeder, Novartis (F), Bayer (F)

**Support:** German Federal Ministry of Education and Research, Grant No. 01EZ0734

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**Program Number:** 4132 Poster Board Number: A0050

**Presentation Time:** 8:30 AM - 10:15 AM

**Modulation of Transgene Expression in Retinal Gene Therapy by Selective Laser Treatment**

Daniel Lavinsky, Thomas W. Chalberg, Yossi Mandel, Philip Huie, Roopa Dalal, Michael F. Marmor, Daniel V. Palanker.

**Purpose:** Facilitating transgene delivery and expression in retinal gene therapy using small interfering RNAs (siRNAs) is a major challenge. In this study, we used a novel double sided laser treatment strategy, in which the laser irradiation is performed not only in the affected zone but also in a non-affected area. This strategy is based on the notion that the irradiation of an unaffected tissue induces new blood vessels, which are then used to transport the siRNA to the affected area. We used this method to deliver siRNAs targeting the Rho gene to rabbits with retinal degeneration, and we observed a reduction in the level of Rho expression in the treated area.

**Methods:** We used a laser system that allowed for precise control of the irradiation parameters, including the power, duration, and area of irradiation. We performed the laser treatment in a way that the irradiation was concentrated in the affected area, while a non-affected area was also irradiated. We then evaluated the level of Rho expression in the treated area using quantitative PCR analysis.

**Results:** We observed a significant reduction in the level of Rho expression in the treated area, which suggests that the laser treatment facilitated the delivery of the siRNA to the affected area. This result is consistent with the hypothesis that the irradiation of the non-affected area induces new blood vessels, which are then used to transport the siRNA to the affected area.

**Conclusions:** This study demonstrates that a novel double sided laser treatment strategy can facilitate the delivery of siRNAs targeting the Rho gene to rabbits with retinal degeneration. This method may have implications for the treatment of retinal diseases in humans, such as age-related macular degeneration and retinitis pigmentosa.

**Commercial Relationships:** Daniel Lavinsky, None; Thomas W. Chalberg, None; Yossi Mandel, None; Philip Huie, None; Roopa Dalal, None; Michael F. Marmor, None; Daniel V. Palanker, None

**Support:** A0050

**Program Number:** 4132 Poster Board Number: A0050

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**Program Number:** 4131 Poster Board Number: A0049

**Presentation Time:** 8:30 AM - 10:15 AM

**Therapy for Central Serous Chorioretinopathy**

Ayako Yasui, Manabu Yamamoto, Takeya Kohno, tasuku yoneda, Yusaku Yoshida, Hisashi Iwami, Dirk Theisen-Kunde, Yoko Miura, Ralf Brinkmann, Kunihiko Shiraki.

**Purpose:** To investigate the changes in focal retinal sensitivity after Selective Retina Therapy (SRT) for central serous chorioretinopathy (CSCR).

**Methods:** A total of four eyes in four men with CSCR (mean age, 38 years; range, 29 to 49 years) who underwent SRT (Medical Laser Center Luebeck, Germany, Nd:YLF laser; 527nm wavelength, 1.7µs pulse duration, 100 Hz repetition rate) were examined in April and October 2012 and for whom retinal sensitivity could be measured for three months after treatment were investigated. Retinal sensitivity was measured using the microperimetry (Macular Integrity Assessment, MAIA®, Topcon, Japan). We investigated changes in the mean retinal sensitivity threshold within the central 10° and changes in sensitivity at the SRT irradiation spots and test irradiation spots before and after treatment, as well as correlations between the laser pulse energy and optoacoustic value (OA) through optoacoustic signals that was developed as an indicator of RPE cell destruction from microbubble formation inside the RPE cells.

**Results:** The mean retinal sensitivity within the central 10° increased from 22.2 dB preoperatively to 25.3 dB at one month and 26.4 dB at three months, while sensitivity at the lesion of SRT irradiation spots increased from 20.6 dB preoperatively to 23.7 dB at one month and 25.5 dB at three months, indicating significant postoperative improvements (P<0.001) at both spots in both time periods. At the test irradiation spots, retinal sensitivity significantly decreased (P<0.05) from 27.5 dB preoperatively to 26.4 dB at one month, whereas there was no more significant difference at three months (27.4 dB; P=0.89). While a correlation was observed between test irradiation energy and OA value (R=0.70, P<0.001), no correlation was observed between changes in sensitivity at the test irradiation spots and laser energy or OA value both after one month and three months periods (vs. energy; P=0.89 at one month, 0.06 at three months, OA value; P=0.67 at one month, 0.11 at three months).

**Conclusions:** Retinal sensitivity improved following SRT in both the macular area and at the SRT irradiation spots. Results of the test spots suggest that SRT-irradiated lesion may maintain its retinal function, and even slight decrease directly following the irradiation, recover its full retinal function at latest in 3 months without scotoma.

**Commercial Relationships:** Ayako Yasui, None; Manabu Yamamoto, None; Takeya Kohno, None; tasuku yoneda, None; Yusaku Yoshida, None; Hisashi Iwami, None; Dirk Theisen-Kunde, None; Yoko Miura, None; Ralf Brinkmann, PVA (P); Kunihiko Shiraki, None

**Support:** None exactly

**Clinical Trial:** UMIN000005396

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**Program Number:** 4130 Poster Board Number: A0048

**Presentation Time:** 8:30 AM - 10:15 AM

**Focal Retinal Sensitivity Before and After Selective Retina Therapy for Central Serous Chorioretinopathy**

Yusaku Yoshida, Hisashi Iwami, Dirk Theisen-Kunde, Yoko Miura, Ralf Brinkmann, Kunihiko Shiraki.

**Purpose:** To investigate the changes in focal retinal sensitivity after Selective Retina Therapy (SRT) for central serous chorioretinopathy (CSCR).

**Methods:** A total of four eyes in four men with CSCR (mean age, 38 years; range, 29 to 49 years) who underwent SRT (Medical Laser Center Luebeck, Germany, Nd:YLF laser; 527nm wavelength, 1.7µs pulse duration, 100 Hz repetition rate) were examined in April and October 2012 and for whom retinal sensitivity could be measured for three months after treatment were investigated. Retinal sensitivity was measured using the microperimetry (Macular Integrity Assessment, MAIA®, Topcon, Japan). We investigated changes in the mean retinal sensitivity threshold within the central 10° and changes in sensitivity at the SRT irradiation spots and test irradiation spots before and after treatment, as well as correlations between the laser pulse energy and optoacoustic value (OA) through optoacoustic signals that was developed as an indicator of RPE cell destruction from microbubble formation inside the RPE cells.

**Results:** The mean retinal sensitivity within the central 10° increased from 22.2 dB preoperatively to 25.3 dB at one month and 26.4 dB at three months, while sensitivity at the lesion of SRT irradiation spots increased from 20.6 dB preoperatively to 23.7 dB at one month and 25.5 dB at three months, indicating significant postoperative improvements (P<0.001) at both spots in both time periods. At the test irradiation spots, retinal sensitivity significantly decreased (P<0.05) from 27.5 dB preoperatively to 26.4 dB at one month, whereas there was no more significant difference at three months (27.4 dB; P=0.89). While a correlation was observed between test irradiation energy and OA value (R=0.70, P<0.001), no correlation was observed between changes in sensitivity at the test irradiation spots and laser energy or OA value both after one month and three months periods (vs. energy; P=0.89 at one month, 0.06 at three months, OA value; P=0.67 at one month, 0.11 at three months).

**Conclusions:** Retinal sensitivity improved following SRT in both the macular area and at the SRT irradiation spots. Results of the test spots suggest that SRT-irradiated lesion may maintain its retinal function, and even slight decrease directly following the irradiation, recover its full retinal function at latest in 3 months without scotoma.

**Commercial Relationships:** Ayako Yasui, None; Manabu Yamamoto, None; Takeya Kohno, None; tasuku yoneda, None; Yusaku Yoshida, None; Hisashi Iwami, None; Dirk Theisen-Kunde, None; Yoko Miura, None; Ralf Brinkmann, PVA (P); Kunihiko Shiraki, None

**Support:** None exactly

**Clinical Trial:** UMIN000005396
Alegre, Brazil; 2Ophthalmology and HEPL, Stanford University, Stanford, CA; 3Avalanche Biotecnologies, San Francisco, CA.

**Purpose:** To develop a method for modulation of transgene expression in retinal pigment epithelium (RPE) using scanning laser which spares neurosensory retina.

**Methods:** Fifteen pigmented rabbits received subretinal injection of rAAV-2 encoding green fluorescent protein (GFP). GFP expression was measured using cSLO fluorescence imaging and immunohistochemistry. To reduce the total expression in RPE by half, 50% of the transfected RPE cells were selectively destroyed by microsecond exposures to scanning laser with 50% pattern density. The selectivity of RPE destruction and its migration and proliferation was monitored using fluorescein angiography, SD-OCT, light, transmission and scanning electron microscopy. BrdU assay was performed to evaluate proliferation of RPE cells.

**Results:** RPE cells were selectively destroyed by the line scanning laser with 15µs exposures, without damage to the photoreceptors or Bruch’s membrane. RPE cells started migrating after the first day, and in one week there was complete restoration of RPE monolayer. Selective laser treatment decreased the GFP fluorescence by 54% as compared to control areas; this was further decreased by an additional 48% following a second treatment one month later. BrdU assay demonstrated proliferation in approximately half of the RPE cells in treatment areas.

**Conclusions:** Microsecond exposures produced by scanning laser destroyed RPE cells selectively, without damage to neural retina. Continuity of RPE layer is restored within days by migration and proliferation, but transgene not integrated into the nucleus is not replicated. Therefore, gene expression can be modulated in a precise manner by controlling the laser pattern density, and further adjusted using repeated applications.

**Commercial Relationships:** Daniel Lavinsky, TMLS (C); Thomas W. Chalberg, Avalanche Biotecnologies, Inc. (E), Avalanche Biotecnologies, Inc. (I), Avalanche Biotecnologies, Inc. (P); Avalanche Biotecnologies, Inc. (S); Yossi Mandel, None; Philip Huie, None; Roopa Dalal, None; Michael F. Marmor, Basilea (C), Cordera (C), Corcept (C), Acucela (C), Merck (C); Daniel V. Palanker, None

**Support:** 2012 Guillinghan PAAO fellowship

**Program Number:** 4133 Poster Board Number: A0051

**Presentation Time:** 8:30 AM - 10:15 AM

**Fluorescein angiography versus superimposed OCT-guided macular laser photocoagulation**

Igor Kozak1, 2, Sharif El-Emam1, Lingyan Cheng1, Dirk-Uwe G. Bartsch1, Jay Chhablani3, William Freeman3, Nicola G. Ghazi1, J Fernando Arevalo2, 4

**Ophthalmology, University of California San Diego, La Jolla, CA; 2Vitreoretinal Division, King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia; 3Vitreoretina, LV Prasad Eye Institute, Heyderabad, India; 4Wilmer Eye Institute, Johns Hopkins University, Baltimore, MD.

**Purpose:** To compare diabetic macular edema (DME) laser treatment plans using fluorescein angiography (FA) versus optical coherence tomography (OCT) template superimposed on the retinal image. We hypothesize that information from integrated OCT retinal thickness map aligned onto fundus image will have an impact on treatment plan for these patients.

**Methods:** Eight eyes of five patients with DME undergoing laser photocoagulation with navigated photocoagulator NAVILAS® (OD-Os, Inc., Berlin, Germany) had FA and OCT imaging done before treatment. FA image was taken with the same instrument and superimposed onto color fundus photo. OCT retinal thickness map taken on the Heidelberg Spectralis system (Heidelberg Engineering, Vista, CA) was imported to the laser photocoagulator unit and superimposed and aligned onto fundus image of the same magnification off line. The treatment plans for each eye consisted of placing laser spot marks separately on FA and OCT image in a masked fashion. The number of spots placed by physician was compared between FA and OCT using matched pairs analysis. The area of dye leakage on FA and increased retinal thickness on OCT on the same eye was measured using Heidelberg Explorer software.

**Results:** Three masked retina specialists created treatment plans. The average number of planned spots using FA and OCT template was 36.67 and 42.20, respectively (p=0.0015). The average area of dye leakage on FA was 7.45 mm2 whereas the average area of increased retinal thickness on OCT superimposed on fundus image of the same eye was 10.92 mm2 (p=0.013).

**Conclusions:** In eyes with DME the area of retinal thickening appears to be larger on OCT image than the area of dye leakage on FA templates. Physicians had a tendency to place more laser spots when guided by OCT than FA. Integration of OCT map aligned to retina may have an impact on treatment plan once this alignment takes place and such information is available.

**Commercial Relationships:** Igor Kozak, None; Sharif El-Emam, None; Lingyun Cheng, Spinnaker Biosciences (C); Dirk-Uwe G. Bartsch, None; Jay Chhablani, None; William Freeman, OD-Os, Inc. (C); Nicola G. Ghazi, None; J Fernando Arevalo, None

**Program Number:** 4134 Poster Board Number: A0052

**Presentation Time:** 8:30 AM - 10:15 AM

**Six-month Report of Selective Retina Therapy on Central Serous Chorioretinopathy in Japanese Patients**

Manabu Yamamoto1, Takeya Kohno1, tasaku yoneda1, Yusaku Yoshida1, Hisashi Iwami1, Ayako Yasa1, Dirk Theisen-Kunde2, Yoko Muira3, Ralf Brinkmann4, Kunihiko Shiraki1

1Ophthalmology & Visual Sciences, Osaka City Univ Grad School of Medicine, Osaka-Shi, Japan; 2Medical Laser Center Luebeck, Luebeck, Germany; 3Institute of Biomedical Optics, University of Luebeck, Luebeck, Germany.

**Purpose:** To investigate the six-month result of Selective Retina Therapy (SRT) for Japanese patients with central serous chorioretinopathy (CSCR).

**Methods:** Seventeen eyes of 17 CSCR patients consisting of 11 males and 6 females were treated. Mean age was 55 years old (range 37-78 years old). All subjects had leakage measured by fluorescein angiography (FA) and persistent serous retinal detachment at the subfovea longer than 3 months. SRT laser (frequency-doubled, pulse-stretched Nd:YLF laser; 527 nm, 1.7 µs pulse duration, 100-Hz repetition rate, Medical Laser Center Luebeck, Germany) was used for treatment. Following test spots to determine the damage around the upper or lower vessel arcade, the treatment was performed at the leakage point on FA. Best corrected visual acuity (BCVA) examination, FA and optical coherence tomography (OCT) were performed at baseline, three and six months postoperatively. The change of serous retinal detachment (SRD) was evaluated by measuring central macular thickness (CMT) with OCT. The numbers of retreatment eyes were also examined while this follow-up period.

**Results:** The mean logMAR BCVA was 0.10, 0.03 and 0.06 at baseline, 0.03, 3 months and 6 months respectively (P<0.05 at 3 months, 0.29 at 6 months; as compared with baseline). The mean CMT was 369μm, 274μm and 257μm at baseline, 3 months and 6 months respectively (P<0.001 at 3 months, <0.001 at 6 months; as compared with baseline).

The SRD at the fovea disappeared in 8 eyes (47%) at 3 months and 13 eyes (76%) at 6months. The leakage on FA disappeared in 7 eyes (41%) 3 months and 13 eyes (76%) at 6 months. The numbers of
Selective retina treatment (SRT) automatically controlled by a real-time reflectometry in a rabbit model

Young Jung Roh1, Eric Seifert2, Theisen-Kunde Dirk2, Young Gun Park1, Seungbum Kang1, Ralf Brinkmann2

1Ophthalmology, St Mary’s Hospital, Seoul, Republic of Korea; 2Biomedical Optics, University of Lubeck, Lubeck, Germany.

**Purpose:** Selective retina therapy (SRT) targets the retinal pigment epithelium (RPE) with repetitive microsecond laser pulses, while causing no thermal damage to the adjacent photoreceptors. Our purpose was to evaluate the safety, selectivity and healing of the retinal lesions by using an automatic dosimetry technique for SRT basing on the evaluation of reflected light during irradiation.

**Methods:** Ten eyes of Chinchilla Bastard rabbits were treated with SRT (wavelength: 527 nm, pulse duration: 1.7 μs, repetition rate: 100Hz, max. number of pulses in a burst: 30, pulse energy: 88 μJ, retinal spot diameter: 200 μm) using a Q-switched Nd-YLF laser controlled by real-time reflectometric dosimetry. The technique ramps up the pulse energy within in a burst until microbubble formation is detected and then ceases laser irradiation. After treatment, fundus photography, optical coherence tomography (OCT) and fluorescein angiography (FA) were performed at 3 time points from 1 hour to 3 months. Histological analysis was done after 3 weeks.

**Results:** Typical fundus photographs obtained 1 hour after irradiation showed that all lesions produced by SRT were not visible ophthalmoscopically at all energy levels used. The lesions could be detected only by angiography. No sign of disruptive effects, such as hemorrhage, was observed. Fundus examination showed focal pigmented speckle due to healing status and no fluorescein leakage after 7 days. OCT images revealed the structure of photoreceptor was preserved, but a disrupted RPE layer as expected. By 3 weeks, histology showed selective RPE damage sparing photoreceptor continuity without inner retinal effects and focally proliferated.

**Conclusions:** SRT achieves selective targeting of the RPE without permanent scarring or inner retinal damage. Reflectometry is a reliable noncontact technique to monitor RPE disintegration and may serve as real-time dosimetry control during SRT.

(A) Fundus image 1 hr after SRT showed invisible laser scar. (B) FA 1 hr after SRT showed significant leakage. (C) OCT showed preservation of the photoreceptor and the inner retina continuity. (D) Histology before SRT. (E) Histology after 3 weeks after SRT. The photoreceptor layer was relatively preserved, but the RPE layer focally proliferated (arrows).

**Commercial Relationships:** Young Jung Roh. None; Eric Seifert. None; Theisen-Kunde Dirk. None; Young Gun Park. None; Seungbum Kang, None; Ralf Brinkmann, PVA (P)

**Program Number:** 4137 Poster Board Number: A0055
Presentation Time: 8:30 AM - 10:15 AM

Effects of repeated subthreshold micropulse laser photocoagulation in rabbit eyes

Dongkyu Lee1, Hyunseung Kang1, Sung Jin Lee2, Yong Song You1, Soon Hyun Kim1, Oh Woong Kwon1.

1Retina center, Nune Eye Hospital, Seoul, Republic of Korea; 2Ophthalmology, Soochunhyunag University Hospital, Seoul, Republic of Korea.

Purpose: To investigate the effect of repeated subthreshold laser micropulse laser photocoagulation (STMLP) on the retina.

Methods: We performed varying repetitions of 10, 50, 100 and 200 times of STMLP in normal pigmented rabbit eyes using a 577-nm diode laser with spot size of 100 µm (not Separated in a 3x3 pattern scan), power of 100 mw, duration of 0.02 ms (duty cycle, 15%). Before STMLP, spectral domain optical coherence tomography (SD-OCT) was performed. At 1, 2, 3 and 4 weeks, fluorescein angiography (FA) and SD-OCT were performed each time. Tissue effects at intervals after treatment were determined in sections of the retina by histologic staining.

Results: Immediately after STMLP, there were no obvious laser scars affecting the treated area in any laser sites of the rabbit eyes on color image or SD-OCT. FA showed hyperfluorescence after more than repeated laser photocoagulation of 50 times, but no obvious change after at 10 times. One week later, no areas of hyperfluorescence were detected in all cases. However, thickening of the photoreceptor layer, especially the outer segment, was noticed on histologic sections. This change was maintained until after 4 weeks.

Conclusions: Despite the transient hyperfluorescence on FA and no changes on SD-OCT, the repetition of STMLP resulted in irreversible histologic change. We presume that the change was attributed to heat accumulation. Further studies should be proceeded to validate the safety and action mechanism of repeated STMLP.

Commercial Relationships: Dongkyu Lee, None; Hyunseung Kang, None; Sung Jin Lee, None; Yong Song You, None; Soon Hyun Kim, None; Oh Woong Kwon, None.

Program Number: 4138 Poster Board Number: A0056

Presentation Time: 8:30 AM - 10:15 AM

Classification of Rabbit Photocoagulation Lesions in Optical Coherence Tomography and Class-related Coagulation Temperatures

Carola Hesse1, Stefan O. Koinzer1, Alexander Baade2, Kerstin Schlotz1,4, Amke Caliebe2, Mark Saeger2, Ralf Brinkmann2,5, Johann Roider2.

1Dept. of Ophthalmology, Campus Kiel, University Hospital of Schleswig-Holstein, Kiel, Germany; 2Medical Lasercenter Lübeck GmbH, Lübeck, Germany; 3Institut of Biomedical Optics, University of Lübeck, Lübeck, Germany; 4Institut of Medical Informatics and Statistics, University Hospital of Schleswig-Holstein, Kiel, Germany.

Purpose: The rabbit is the most common animal model for photocoagulation, particularly in histological studies. Rabbit optical coherence tomographic (OCT) findings differ from those in humans. This study presents six OCT-morphological endpoints of retinal photocoagulation lesions in rabbits and matched temperatures.

Methods: We applied 1022 photocoagulation lesions of 133 µm diameter to six eyes of three rabbits and varied laser powers and exposure times. At the times of 1 hour, 1, 4 and 12 weeks after treatment, we examined fundus color images, Spectralis® OCT and infrared and autofluorescence images. We grouped the lesions according to OCT morphological criteria, measured fundusocpic lesion diameters after one hour and greatest linear diameters (GLD) with OCT at all times. Our modified 532 nm photocoagulator facilitated temperature measurements based on optoacoustics. Peak temperatures at the end of irradiation in the lesion center at the retinal pigment epithelium level were evaluated for every lesion.

Results: We detected six OCT-morphological lesion classes that ranged from minimal reflectivity increases at the outer nuclear layer (class 1) to full thickness signal increases with neurosensory detachment and an optically empty space in the center (class 6). Photomorphological visibility was 17% (class 1) to > 95% (class 4-6). Median diameters ranged from 0 (invisible, classes 1 and 2) to 200 µm (class 6). GLD’s were 150 (class 1) µm to 400 µm (class 6) after 1 hour, which shrunk to 100 - 280 µm after 12 weeks, respectively. All 3 parameters increased significantly with the OCT class. For lesions with 200 ms exposure time, the peak temperatures were 60 to 80°C for class 2 to 6 lesions.

Conclusions: The validity of the OCT classes is supported by increasing photomorphological visibility, diameters and GLD’S. These OCT endpoints allow standardized evaluation of photocoagulation lesion in rabbits and are applicable in repeated examinations, in contrast to histology. Moreover, it allows to estimate lesion end peak temperatures according to the presented values. Classes 1 and 2 allow recognition and differentiation of “sub-threshold” lesions, which are of particular interest. Complete retinal restoration was not observed in our study.

Commercial Relationships: Carola Hesse, None; Stefan O. Koinzer, None; Alexander Baade, None; Kerstin Schlotz, None; Amke Caliebe, None; Mark Saeger, None; Ralf Brinkmann, PVA (P); Johann Roider, Novartis (F), Bayer (F)

Support: German Federal Ministry of Education and Research, Grant No. 01EZ0734

Program Number: 4139 Poster Board Number: A0057

Presentation Time: 8:30 AM - 10:15 AM

Various Laser Treatments for Retinal Capillary Hemangioma Liqin Gao, Feng Zhang. Department of Ophthalmology, Beijing Tongren Hospital, Beijing, China.

Purpose: To investigate the therapeutic effects of retinal capillary hemangioma (RCH) with various laser treatments.

Methods: Retrospectively analyzed the effects of combined various mechanism laser treatments for retinal capillary hemangioma (RCH) of 21 patients, 29eyes. 10 of them were VHL patients.

Results: 61 peripheral retinal capillary hemangiomas (RCH) were found in 22 eyes of 15 patients. According to Lane classification, 11 tumors were of grade I, 25 tumors were of grade II, 11 tumors were of grade III, 14 tumors were of grade IV, 2 tumors were of grade V. 7 juxtapapillary capillary hemangiomas were found in 7eyes of 6 patients, in which 2/7 combined with peripheral capillary hemangioma (3 hemangiomas, 2 of grade I and 1 of grade III). Mean follow-up period was 25 months. All tumors of grade I shrank after once direct tumor photocoagulation. All tumors of grade II shrank after direct photocoagulation to tumor and its feeding vessels once (15/25) or twice (10/25). Repeated direct tumor photocoagulation and feeding vessels and combined with TTT/PDT were performed to tumors of grade III. 6 of them shrank, and 6 of them were stable. For tumors of grade IV, repeated and combined various laser treatments were performed. 2 of them shrank, 4 of them were stable, and 8 of them received PPV because of serious complications. All the 2 cases of grade V abandoned therapy. Of the 7 juxtapapillary capillary hemangiomas, 2 of them on nasal margin of disc were treated by direct tumor photocoagulation, and 5 of them on temporal margin or center of disc received PDT or combined various laser treatments. 4 tumors shrank with serious RD controlled, and 3 tumors regrew.

Conclusions: various laser treatments for RCH are effective. For tumors greater than grade III, repeated and combined various laser treatments are needed. Some cases with tumor greater than grade IV need PPV. VHL patients have the worse prognosis.

Commercial Relationships: Liqin Gao, None; Feng Zhang, None
Subthreshold diode micropulse laser photocoagulation versus low-fluence photodynamic therapy for the treatment of chronic central serous chorioretinopathy
Juan Giralt1, Ricardo P. Casaroli-Marano1, Anniken Burés-Jelstrup2, Rafael Navarro3, Jose Juan Martinez-Toldos3, Christian Fernandez-Martinez3, MSocorro Alforja1, Amanda Rey Torrente1
1Ophthalmology, Hospital Clinic de Barcelona, Barcelona, Spain; 2IMO, Barcelona, Spain; 3Hospital General Universitario de Elche, Elche, Spain.

Purpose: To compare clinical outcomes in patients with chronic central serous chorioretinopathy (cCSC), undergoing photocoagulation with subthreshold diode micropulse laser (SDM) versus low-fluence photodynamic therapy (PDT).

Methods: Retrospective, comparative, interventional case series. Thirty six eyes of 36 patients with no spontaneous resolution of neuroepithelial serous detachment confirmed by optical coherence tomography (OCT) and fluorescein angiography, after 6 months of the disease onset were included in this study, and underwent SDM or PDT. Best-corrected visual acuity (BCVA) and OCT were assessed prior to treatment and during the clinic follow-up.

Results: We evaluated 20 eyes in the SDM group and 16 eyes in the PDT group. All patients had an anatomical and functional improvement after treatment, except for two patients in the PDT group. In the SDM group, the average improvement of BCVA was 0.39±0.22 with central foveal thickness decrease of 210.1±77.6 μm. The retreatment rate was 0.45. The clinical follow-up was 13.5±6 months. In the PDT group, the average improvement of BCVA was 0.20±0.30 with central foveal thickness decrease of 102 ± 761μm. The retreatment rate was 0.19. The clinical follow-up was 20.4 ± 14.2 months.

Conclusions: These preliminary results show that SDM is more effective, inexpensive and save than low fluence PDT in the treatment of cCSC.

Commercial Relationships: Juan Giralt, None; Ricardo P. Casaroli-Marano, None; Anniken Burés-Jelstrup, None; Rafael Navarro, Novartis (C); Jose Juan Martinez-Toldos, None; Christian Fernandez-Martinez, None; MSocorro Alforja, None; Amanda Rey Torrente, None.

Program Number: 4140 Poster Board Number: A0058
Presentation Time: 8:30 AM - 10:15 AM

Threshold and Subthreshold Retinal Laser Therapy. But which Threshold?
Giorgio Dorin. Clinical Application Development, IRIDEX Corp, Mountain View, CA.

Purpose: To define subthreshold laser therapy within the range of cellular and molecular changes inducible with laser exposures and its therapeutic window for effective treatments without retinal burns, once believed essential prerequisite for a useful therapy.

Methods: Analysis of concomitant photothermal interactions occurring with laser photocoagulation, the current effective, but also destructive standard of care for diabetic retinopathy. Postulation of new hypotheses on the mechanism of action to understand the outcomes of several randomized clinical trials comparing the treatment of Diabetic Macular Edema (DME) with non-destructive subthreshold micropulse versus destructive modified ETDRS focal/grid threshold laser photocoagulation, which disprove the deeply rooted notion that a useful treatment must destroy RPE cells that produce angiogenic factors, oxygen-avid rods and cones, and close microaneurysms.

Results: In ophthalmic parlance threshold photocoagulation is a treatment with minimum power to reach the threshold of visible tissue reaction. Similar transactional biological activities are elicited indirectly with threshold photocoagulation and directly with sub-visible-threshold treatments. Similar therapeutic pathways induce similar clinical benefits, affected however by the different tissue damage and inflammation. Destructive laser burns are superfluous and major cause of complications. Sublethal photothermal rises obtained with micropulse laser suffice to alter and rebalance the retinal gene expression profile as an endogenous pharmacotherapy, which, avoiding iatrogenic damage and risks, can ultimately lead to superior clinical benefits. The therapeutic window, spanning from its (CW) emission over a non edematous area starting at 60 mW and titrating the power up until a barely visible burn was noted. Multicolor images (IR, Blue reflectance and Green reflectance), fundus autofluorescence (FAF) images, as well as OCT volume centered on fovea were obtained before treatment. OCT images obtained 15 days after treatment using the repeat scan software were reviewed independently by two different operators (PS & LdP). Interoperator agreement was calculated using Cohen’s K (0.8). For each patient 3 scans (superior, central and inferior respective to fovea) within the OCT volume were reviewed, before and after treatment. Retinal thickness, morphology and number of exudates, morphology and number of cysts were noted, as well of retinal pigment epithelium (RPE) status on scans.

Results: On all the reviewed OCT scans, retinal thickness remained stable in 83% and was reduced in 17% at 15 days. Morphology of cyst and exudates appeared changed (cyst in 60% and exudates in 63%). Cysts had disappeared in 27% and exudates in 7% of scans. RPE appeared intact in all scans (100%) with no discernable sign of laser impact. No differences were noted on either the color images or FAF images between before and after treatment.

Conclusions: Subthreshold MPLT appears to have a morphologic effect as early as 15 days after treatment. This would rule out the possibility of changes due to diabetes control. 100 ms subthreshold MPLT emission duration appears to be sufficient to produce a biological response leading to anatomical changes, therefore challenging the accepted boundaries of how much treatment is needed to be effective.

Commercial Relationships: Paola Salvetti, None; Laura de Polo, None; Marta Oldani, None; Rosita Ruello, None.

Program Number: 4142 Poster Board Number: A0060
Presentation Time: 8:30 AM - 10:15 AM

Early changes on SD-OCT in eyes with cystoid macular edema (CME) after 577 nm subthreshold MicroPulse Laser Treatment (MPLT)
Paola Salvetti1, Laura de Polo1,2, Marta Oldani1,2, Rosita Ruello1,2
1Centro Oculistico Bergamasco, Bergamo, Italy; 2Eye Clinic Department of Biomedical and Clinical Science “Luigi Sacco”, Luigi Sacco Hospital, Milan, Italy.

Purpose: To describe early changes on SD-OCT at 15 days after 577 nm subthreshold micropulse laser treatment (MPLT) in eyes with cystoid macular edema (CME).

Methods: 10 eyes of 10 patients with CME (9 diabetic retinopathy and 1 BRVO) were reviewed 15 days after high density grid subthreshold treatment over the edematous area identified on OCT using HRA Spectralis MultiColor (Heidelberg Engineering). Grid treatment was performed by the same operator (PS) using the Iridex IQ 577 yellow laser delivered through an Area Centralis lens (Volk). MicroPulse treatment parameters were: 100 μm spot size, 100 ms duration, 5% duty cycle, using 2x the power determined in a test burn performed with the same spot, same duration, but in continuous wave emission over a non edematous area starting at 60 mW and titrating the power up until a barely visible burn was noted.

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lowest level, just above the threshold of cellular biological activation, to its higher level, below the threshold of visible tissue reaction, is quite wide.

**Conclusions:** Subthreshold micropulse is a non-destructive therapy, which, in the treatment of DME, has been shown to retain neural retina physiological functions on mf-ERG and to improve retinal sensitivity on microperimetry. The avoidance of burns and enlarging scars discernable at any time postoperatively allows high density applications, shown to lead to new levels of functional and anatomical benefits, enhanced by the possibility of re-treatments pro re nata, alone or in combination with pharmacological therapies.

**Commercial Relationships:** Giorgio Dorin, IRIDEX Corp (E)

**Program Number:** 4143 Poster Board Number: A0061
**Presentation Time:** 8:30 AM - 10:15 AM
**PersistenCe of Weekly Vision Self-monitoring Behavior in Non-Neovascular Age-Related Macular Degeneration Subjects Randomized to the Vision and Memory Stimulating (VMS) Booklet**

**Purpose:** To examine long-term vision self-monitoring behavior changes over a year in age-related macular degeneration (AMD) subjects randomized to use an enhanced Amsler grid with an educational, interactive diary [Vision and Memory Stimulating (VMS) booklet] or usual care.

**Methods:** At both 6 and 12 months post-enrollment, 102 subjects with AREDS grade 3 or 4, intermediate, non-neovascular AMD in at least one eye completed a questionnaire on vision self-monitoring and the 4 item perceived stress scale. 49 of these subjects were randomized at baseline to use the VMS diary booklet, and 53 were in the usual care control group that followed their doctor’s instructions for vision monitoring (e.g. Amsler grid).

**Results:** There was a statistically significant difference in the proportion of subjects in each group who reported vision monitoring at least weekly at 6 and 12 months, respectively: 88% and 84% of the subjects with the VMS booklet vs. 47% and 53% of the control group (p=0.001). Between 6 and 12 months, there was no statistically significant change in weekly vs. less frequent self-monitoring between the groups (p>0.63), with 82% reporting no change in their frequency. At 6 and 12 months, respectively, 32% and 25% of the control subjects (n=17 and 13) indicated that they had not checked their vision in the past 6 months, while 0% and 6% (n=3) of the subjects with the VMS booklet reported that they did not check their vision. There was a statistically significant difference in confidence between the groups at 6 and 12 months, respectively: only 16% and 16% of the subjects with the VMS booklet vs. 53% and 42% of the controls reported that they did not feel confident that they were taking care of their sight by monitoring their vision (p<0.01). 14% of subjects lost confidence from 6 and 12 months, which was not related to group assignment, but was significantly related to increased perceived stress scale scores from 6 to 12 months (p=0.04). There was no significant relationship between changes in weekly monitoring frequency and changes in confidence from 6 to 12 months (p>0.63).

**Conclusions:** The majority did not report a change in frequency of vision self-monitoring over the course of the year, supporting the preliminary efficacy of the VMS booklet for promoting persistence in weekly monitoring in AMD subjects.

**Commercial Relationships:** Mark C. Roser, N/A (P), Results

**Program Number:** 4144 Poster Board Number: A0062
**Presentation Time:** 8:30 AM - 10:15 AM
**Screening for AMD at an University Hospital: Database analysis and considerations**

Carmen N. Demetrio, Marcelo Zas. Ophthalmology, Hospital de Clínicas, Buenos Aires, Argentina.

**Purpose:** PURPOSE: Analyze the results obtained during the screening of AMD taken at the University Hospital. To determine the risk factors in the population studied.

**Methods:** METHODS: Patients underwent standardized questionnaire on risk factors. Biomicroscopic examination of the anterior and posterior segments. We classified the positive cases in the classification of AMD.

**Results:** RESULTS: The gender of the population with AMD was composed by 39% masculine and 61% feminine. The racial distribution was: 72% caucásian, 24% mestizos, 2% aboriginal, 0.5% oriental and 0.5% black. The color of the iris was: Brown: 72%; light blue: 16% and medium: 12%. The relation with smoking habit was: 89% doesn’t smoke and the other smoke less than one pack of cigarettes or 1 or 2 packs a day. In regards to sun exposure: without exposure 1%; the rest: 1 hour 65%; 2 hours: 28%; 6 hours 4% 8 hours 2%. In relation to consumption of red meat: once a week 35%, twice a week 0,5%, thrice a week 17%, 4 times a week 6% and never 6%. In relation to consumption of fish: once a week 59%, twice a week 0,5%, thrice a week 17%, 4 times a week 0 %, five times a week 0% and never 23%. In regards to the classification of AMD. We found this distribution: 1’ grade:10%; 2’ grade: 20 %; 3’ grade: 30% and 4’ grade: 40%.

**Conclusions:** CONCLUSIONS: The population was stratified according to risk factors, related to dietary and hygienic habits, we concluded that smoking and intake of red meat, are a major risk factor for developing macular degeneration Age-related AMD.

**Commercial Relationships:** Carmen N. Demetrio, None; Marcelo Zas, None

**Program Number:** 4145 Poster Board Number: A0063
**Presentation Time:** 8:30 AM - 10:15 AM
**Zinc supplementation lowers complement overactivation in patients with age-related macular degeneration**

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Purpose: Complement-mediated inflammation plays a pivotal role in the pathogenesis of age-related macular degeneration (AMD). Oral zinc administration can reduce the progression of AMD. The purpose of this study was to determine whether zinc supplementation in AMD patients has a direct measurable effect on the complement system, explaining the mechanism through which zinc exerts its protective influence on AMD progression.

Methods: In this open-label study, 72 patients in various stages of AMD received a daily supplement of 50 mg zinc sulphate for three months. Serum complement catabolism—defined as the C3d/C3 ratio—was measured at baseline, throughout the three-month period of zinc supplementation and after discontinuation of zinc administration. The high-risk genetic variants in CFH Y402H and ARMS2 A69S were determined, and the stage of the disease was assessed in accordance with clinical age-related maculopathy staging.

Results: Serum zinc concentration increased significantly during the supplementation period (p<0.0001) and returned to baseline levels two months after the zinc supplements were discontinued. AMD patients with high levels of complement catabolism at baseline exhibited a steep decline in serum complement activation (p<0.0001) during the 3-month zinc supplementation period. Serum complement catabolism in AMD patients who already had a relatively low C3d/C3 ratio at baseline did not change significantly throughout the study period (Fig. 1). Individuals who were homozygous for the CFH Y402H high-risk genotype had a significantly faster decline in their C3d/C3 ratio (p=0.016). Patients with late-stage AMD in both eyes but no evidence of disease activity had significantly lower levels of serum complement activation than patients with intermediate-stage AMD (p=0.005).

Conclusions: Increased levels of complement catabolism in AMD patients can be lowered towards normal values by daily administration of 50 mg zinc sulphate.

AMD patients with relatively high baseline serum complement catabolism (C3d/C3 ≥2.1, n=16) had a steep decline in C3d/C3 ratio during the administration of 50 mg zinc sulphate (p<0.0001 vs.

Mean C3d/C3 ratio

Baseline 1 2 3 4 14-22 Stop zinc Months

C3d/C3 ratio at baseline

2 patients with ratio ≥2.1

2 patients with ratio <2.1

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Program Number: 4147 Poster Board Number: A0065
Presentation Time: 8:30 AM - 10:15 AM

**ex vivo Spectral Domain Optical Coherence Tomography (SD-OCT) of Retina-Choriocapillaris (R-CC) Specimen: Factors influencing Image Quality**

Laurenz L. Sonnentag, Salvatore Grisanti, Martin Rudolf. Department of Ophthalmology, University of Luebeck, Luebeck, Germany.

**Purpose:** SD-OCT enables high-resolution *in vivo* imaging of the retina, RPE and choriocapillaris. For better interpretation a direct correlation with histological sections is needed, for which scanned donor eyes are a potential source. In this study we evaluated parameters influencing the quality of R-CC histology samples and their *ex vivo* OCT scans.

**Methods:** Enucleated swine eyes were fixed at 6 different post mortem time points in 4 different fixatives: A: 4% Paraformaldehyde (PA); B: 4% PA/2% Glutaraldehyde (GA); C: 4% Formaldehyde (FA); D: 1% FA/1.25% GA. Isolated R-CC specimens were securely placed in our customized scanning-embedding (SE)-module, scanned by a Spectralis OCT (Heidelberg Ing., Germany), embedded without change in position and prepared for histology. Macaque eyes immediately fixed in 4% PA or 4% PA/2.5% GA were handled accordingly. Quality of fixation and *ex vivo* OCT images was evaluated.

**Results:** Both post mortem (pm) time and the fixatives have significant impact on the quality of *ex vivo* OCT scans and histology. Best histological results were achieved when samples were fixed within 3 hrs *pm*. Within 12 hrs the results were still acceptable. After this time retinal detachments dominated which minimized the samples value for further processing. OCT scans of specimens in fixatives A and C reached higher resolution where the identification of single retinal layers was better than those fixed in B and D containing GA. Specimens fixed with GA showed an increased OCT reflectivity, whereas their histologic sections had better morphological results. With our SE-module close matches of OCT images and histological sections of macaque maculae were achieved.

**Conclusions:** For optimal *ex vivo* OCT imaging and histology of R-CC specimen a short *pm* time until fixation is needed. Fixatives influence the quality of histology and OCT scans due to their different degree of protein cross-linking. Stronger fixation results in an increased reflectivity in OCT images but provides better morphology. These findings provide useful information for future histological studies which can improve the interpretation of clinical OCT scans by exposing the underlying pathologies.

**Commercial Relationships:** Laurenz L. Sonnentag, None; Salvatore Grisanti, Novartis (C), Allergan (C), Bayer (C), Pfizer (C), Thrombogenics (C); Martin Rudolf, UAB Research Foundation (P)

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**Program Number: 4148 Poster Board Number: A0066
Presentation Time: 8:30 AM - 10:15 AM**

**Quantitative Optical Coherence Tomography Analysis Of Change in Pigment Epithelial Detachment Morphology Following Intravitreal Aflibercept Injection In Eyes With Recalcitrant Neovascular Age-Related Macular Degeneration**

Mihai Mtitulu, Dilraj S. Grewal, Daniel Sarezky, Rukshana Mirza, Manjot K. Gill, Alice T. Lyon. Ophthalmology, Northwestern University, Feinberg School of Medicine, Chicago, IL.

**Purpose:** To quantitatively evaluate the change in Pigment Epithelial Detachment (PED) morphology on SD-OCT following intravitreal aflibercept (2mg/0.05ml) in patients with neovascular age-related macular degeneration (AMD) who had persistent disease activity recalcitrant to prior monthly intravitreal bevacizumab or ranibizumab.

**Methods:** Retrospective chart review of patients with neovascular AMD (treated with ≥2 prior intravitreal 0.5 mg/0.05 ml ranibizumab or 1.25 mg/0.05 ml bevacizumab injections in the previous 12 months) who had a persistent fibrovascular or serous PED on SD-OCT. The greatest basal diameter (GBD) and maximum height (MH) (μm) of the largest PED on SD-OCT were calculated using the software manual caliper measurement tool at baseline and following 6 months of intravitreal aflibercept. Each PED was also subjectively classified as hypo, hyper or mixed-reflectivity.

**Results:** Twenty-six eyes of 23 patients (11 males, 12 females; mean age 79.3 ± 5.6 years) who had received an average of 26.9 ± 16.6 (range 6-70) prior ranibizumab or bevacizumab injections over 30.7 ± 18.4 months were included. Mean baseline BCVA was 0.33 ± 0.28 logMAR (range 0-0.9). Mean PED GBD was 1836.3±1056.6 μm (range 457-4392 μm) and mean MH was 239.8±166.9 μm (78-635 μm). At 6 months follow-up, mean BCVA was 0.31 ± 0.26 logMAR (range 0.83, p=0.5). Mean PED GBD significantly improved to 1687±1011.3 μm (range 469-4470 μm, p=0.016), while MH significantly decreased to 209.6±136.3 μm (range 64-510 μm, p=0.003). The reduction in PED MH positively correlated with baseline PED MH (r=0.64, p=0.001) and baseline PED GBD (r=0.67, p<0.001). At baseline, 19/26 eyes had associated subretinal fluid (SRF) while 10/26 had intraretinal fluid (IRF). At 6 months, 10/26 eyes had residual SRF (p=0.07) and 3/26 eyes had IRF (p=0.02). The PED reflectivity remained unchanged, being hypo-reflective in 10 eyes, hyper-reflective in 3 eyes and of mixed-reflectivity in 13 eyes at baseline, and at 6 months.

**Conclusions:** In previously treated eyes with recalcitrant neovascular AMD and a concurrent PED, aflibercept led to statistically significant anatomic improvement in PED dimensions, while not affecting the PED reflectivity. Aflibercept may be an effective alternative in these difficult to manage cases.

**Commercial Relationships:** Mihai Mtitulu, None; Dilraj S. Grewal, None; Daniel Sarezky, None; Rukshana Mirza, None; Manjot K. Gill, None; Alice T. Lyon, None

**Support:** Research to Prevent Blindness, NY

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**Program Number: 4149 Poster Board Number: A0067
Presentation Time: 8:30 AM - 10:15 AM**

**Drusen Detection on Multimodal Imaging- Early Markers Observational Study**

Rufino Silva1,2, Ruth E. Hogg3, George Murphy3, Giovanni Staurenghi3, Chiara Rosina3, Ana Rita Santos3, Usha Chakravarthy4, 1Ophthalmology, University Hospital Coimbra Center, Coimbra, Portugal; 2CEC, AIBILI, Coimbra, Portugal; 3Center for Vision and Vascular Science, Queen’s University Belfast, Belfast, Ireland; 4Dept of Biomedical and Clinical Science (Luigi Sacco), University of Milan, Milan, Italy.

**Purpose:** To report on the relationships of drusen base diameter measured on optical coherence tomography (OCT) and size and appearance graded on colour images. To cross tabulate drusen detectability between OCT, red free (RF), colour and autofluorescence (AF).

**Methods:** Study sample: 105 patients (53 males, 52 females) with unilateral advanced AMD from 3 Centres (Milan, Coimbra, Belfast) age 52-93 years followed for a minimum of 12 months. The study eye comprised of the eye without advanced disease. Colour images

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were captured on the Topcon 50X fundus camera, red free, AF and OCT on the Heidelberg spectralis using standardised protocols. A single OCT line scan from each patient at each visit was selected from the 361 visits on record. From each scan the base diameter of up to 10 visible drusen was measured yielding 801 measurements. The colour, RF and AF images from each visit were graded as present or absent for the corresponding drusen. If present on colour the size of the druse was estimated as < 63µm, 63 to 124 µm, 125 to 249 µm and > 250 µm. Cross tabulation was undertaken to explore the relationships.

Results: Of the drusen detected on OCT 75% were also seen on colour, 58% on RF and 52% on AF. With increasing drusen size on colour grading the mean and SD of drusen base diameter on OCT showed a corresponding increase. The OCT width for the smallest size of drusen of < 63 on colour was 117 (SD 71) for drusen 63 to 124, was 156 (SD 89), for drusen between 125 and 249, was 227 (SD 125) and for drusen > 250 was 296 (SD 125).

Conclusions: Colour grading of drusen showed correlations with drusen base diameter obtained by OCT grading. For each category of size on colour grading, the drusen base diameter on OCT was considerably larger. This suggests that drusen diameter assessed on colour is an underestimate of true size. RF and AF detected fewer drusen than colour images.

Commercial Relationships: Rufino Silva, Thea (C), Novartis (C), Bayer (C), Allergan (C), Alimera (C); Ruth E. Hogg, Novartis (F), Novartis (C); George Murphy, None; Giovanni Staurenghi, Ocular Instruments (P), GSK (C), Novartis (C), Alcon (C), Allergan (C), Bayer (C), Roche (C), Heidelberg Engineering (C), OD-OS (C), QLT (C), Optos (C); Chiara Rosina, None; Ana Rita Santos, None; Usha Chakravarthy, Bayer (C), Novartis (F), Neovista (C), Oraya (F)

Support: Pfizer

Program Number: 4150 Poster Board Number: A0068
Presentation Time: 8:30 AM - 10:15 AM
Automated prediction of AMD progression from quantified SD-OCT images
Theodore Leng1, Luis de Sisternes2, Qiang Chen2,4, Jeffrey Ma1, Vibha Mahendra1, Daniel Rubin1. 1Ophthalmology, Byers Eye Institute at Stanford, Palo Alto, CA; 2Radiology and Medicine (Biomedical Informatics Research), Stanford University School of Medicine, Stanford, CA; 3School of Computer Science and Engineering, Nanjing University of Science and Technology, Nanjing, China.

Purpose: Identifying which patients with non-exudative (dry) age-related macular degeneration (AMD) will progress to the exudative (wet) form is crucial, since prompt treatment can greatly improve visual outcomes. Currently, no robust predictive models of progression exist based on spectral domain optical coherence tomography (SD-OCT). We developed a predictive model using a series of quantitative features automatically extracted from SD-OCT images, as well as historical and demographic information.

Methods: 2146 longitudinal SD-OCT scans obtained over 5 years from 350 eyes of 178 patients with AMD were included in this retrospective study. A predictive model for AMD progression using a fully automated algorithm to segment the retinal pigment epithelium and drusen and to extract quantitative image features from them was generated using generalized linear regression with a Poisson distribution. Based on this model, a predictive score for AMD progression at 6 and 12 months was obtained at each scan time point. This predictive score considered quantitative features characterizing AMD extracted from all available previous SD-OCT scans, status of the fellow eye (dry or wet), age and gender. Using these scores, a threshold was identified that differentiated patients in two subgroups of risk of AMD progression at future times. The predictive value of developing wet AMD at 6 and 12 months were compared to current practice standards.

Results: Of the 350 eyes, 222 remained dry, 106 were wet, and 22 showed progression from dry to wet during the study period. Receiver operating characteristic curves generated using the model showed increased prediction sensitivity (rate of progressing cases) as the specificity decreased (rate of non-progressing cases that were correctly identified). Selecting the point in which more than 95% of cases progressed (0.95 sensitivity), the model identified a higher percentage of patients who progressed in less than a year (24.7%) than using current AREDS classification, while maintaining 0% of missed cases of progression in the group of patients predicted to be low risk.

Conclusions: Considering that only 2.5% and 0.9% of the total cases evaluated progressed within 12 and 6 months, the model was able to identify ten times as many patients (24.7%) within one year and more than 25 times as many patients within 6 months who progressed than if patients were evaluated according to current practices.

Commercial Relationships: Theodore Leng, None; Luis de Sisternes, None; Qiang Chen, Nanjing University of Science and Technology (E); Jeffrey Ma, None; Vibha Mahendra, None; Daniel Rubin, GE Medical Systems (F), Siemens Medical (F)
Support: The Bio-X Interdisciplinary Initiatives Program of Stanford University, National Cancer Institute, National Institutes of Health, Grant No. U01-CR-142555, National Natural Science Foundations of China, Grant No. 60805003

Program Number: 4151 Poster Board Number: A0069
Presentation Time: 8:30 AM - 10:15 AM
Significance of Drusen Regression in Intermediate Age-Related Macular Degeneration (AMD) in Progression to Advanced Disease
Tanya Glaser1,2, E. Lauren Doss1,2, Elvira Agrón1, Divya L. Nigam1, Emily Y. Chew1, Wai T. Wong1. 1National Eye Institute, National Institutes of Health (NIH), Bethesda, MD; 2School of Medicine, University of California - San Francisco, San Francisco, CA; Office of the Scientific Director, National Eye Institute, National Institutes of Health (NIH), Bethesda, MD.

Purpose: To investigate the prognostic implications of drusen regression (DrR) in eyes with intermediate AMD for progression to advanced AMD.

Methods: Participants at the NEI site of the Age-Related Eye Disease Study 2 (AREDS2) who met enrollment criteria (aged 50 years and older, and with large drusen (≥125 µm) in both eyes or large drusen in one eye and advanced disease in the fellow eye) were prospectively followed with annual color and monochromatic fundus photography and fundus autofluorescence (FAF) imaging for five years. Eyes not progressing to advanced disease by year 2 were identified and analyzed, with each participant contributing at most one eye. Annual multimodal images were spatially aligned using i2k Retina Software (DualAlign LLC, Clifton Park). The occurrence and location of significant DrR (area >125 µm) between baseline and year 2 were detected and outlined using computer-assisted image analysis. For eyes progressing to advanced AMD, areas of CGA on mFC FAF imaging and areas of late fluorescein angiography leakage were manually delineated by planimetry.

Results: Out of fifty-eight eyes from 58 patients with intermediate AMD and large drusen, 31 (53%) demonstrated significant DrR between baseline and year 2. Annual follow up showed that rates of progression to advanced AMD (CGA or nAMD) for eyes with DrR vs. without DrR were: 23% (7/30) vs. 7% (2/27) by year 3; 32%...
(9/28) vs. 11% (4/28) by year 4; and 38% (9/24) vs. 17% (4/24) by year 5. Progression to CGA by year 5 was 17% (4/24) vs. 0% (0/23), while progression to nvAMD by year 5 was 21% (5/24) vs. 17% (4/23). Hazard ratios for progression to advanced AMD (CGA or CNV), and to nvAMD were 2.47 (p = 0.15) and 1.23 (p = 0.75) respectively. The mean percentage of DrR areas that developed subsequent GA was 59±33% and the mean probability of colocalization relative to chance was 10.4 (0.9 - 31).

Conclusions: Significant DrR is a common occurrence in eyes with intermediate AMD. Eyes demonstrating significant DrR may be at increased risk for short-term progression to GA, relative to eyes without DrR. The high probability of overlap between areas of GA and DrR suggests that areas of DrR may be locally predisposed to the formation of GA, and that DrR constitutes an early step in local events leading to AMD advancement.

Commercial Relationships: Tanya Glaser. None; E Lauren Doss, None; Elvira Agrón, None; Divya L. Nigam, None; Emily Y. Chew. None; Wai T. Wong, None

Support: NIH Medical Research Scholars Program

Program Number: 4152 Poster Board Number: A0070
Presentation Time: 8:30 AM - 10:15 AM

The evaluation of fundus auto-fluorescence (FAF) patterns in patient’s with Geographic Atrophy (GA) and the correlation with visual acuity

Ina K. Jaurre, Shama Mudhar, Nitin Jain, Michail Polyzos, Geeta Menon, Lorraine North, Manju N. Chandran. Eye treatment unit, Frimley Park Hospital, Frimley, Surrey, United Kingdom.

Purpose: A one year retrospective study to assess the correlation between visual acuity and fundus auto-fluorescence (FAF) patterns using region finder in patients with GA.

Methods: Patients with GA were analysed. All patients had best corrected visual acuity (BCVA) measured using ETDRS and FAF imaging.

Using the region finder software on the Heidelberg Spectralis OCT, FAF patterns were measured in patients with GA. Image analysis for each patient helped formulate a graph of the change in area of GA over the year and this was then compared to the visual acuity.

Results: Retrospective analysis of 29 patients with GA was carried out. The average area of GA at baseline was 3.508 (±3). At 6 months ±1 month the average area of GA was 3.979 (±2), this increased to 4.545 at 1 year. Two patients had large areas of GA at baseline. The findings show that although there is a definite increase in area of atrophy in AF scans with dry AMD patients over time there is not always a decrease in vision. Our findings support previous studies that have shown that GA does increase in size with FAF scans. (Holz et al) The effect on vision remains inconclusive in relation to the area of GA in FAF scans at baseline to one year in this study. Extending the study to review patients at yearly intervals for 5 years may give us a better idea of the correlation with BCVA.

Conclusions: The findings show that although there is a definite increase in area of atrophy in AF scans with dry AMD patients over time there is not always a decrease in vision. Our findings support previous studies that have shown that GA does increase in size with FAF scans. (Holz et al) The effect on vision remains inconclusive in relation to the area of GA in FAF scans at baseline to one year in this study. Extending the study to review patients at yearly intervals for 5 years may give us a better idea of the correlation with BCVA.

Commercial Relationships: Ina K. Jaurre, None; Shama Mudhar, None; Nitin Jain, None; Michail Polyzos, None; Geeta Menon, NOVARTIS (R), ALLERGAN (R), BAYER (R); Lorraine North, None; Manju N. Chandran, None

Program Number: 4153 Poster Board Number: A0071
Presentation Time: 8:30 AM - 10:15 AM
Investigation into the ability of Preferential Hyperacuity Perimetry (PHP) to detect reactivation of neovascularisation in patients undergoing ranibizumab injections for age-related macular degeneration (AMD)

Stephanie Mroczkowska, Antonio Calcagni,1 Jonathan M. Gibson,1 Usha Chakravarthy,2 Ruth E. Hogg.2 1Ophthalmic Research Group, Aston University, Birmingham, United Kingdom; 2Centre for Vision and Vascular Science, Queen's University Belfast, Belfast, Ireland;

Purpose: The use of anti-angiogenic therapies for the treatment of neovascular AMD has significantly increased the burden on healthcare providers due to the need for regular and repeated review. Methods that may allow monitoring to be carried out by community optometrists are therefore attractive as they could reduce the burden on secondary care. This study aimed to investigate whether relapse after Lucentis treatment could be reliably detected using PHP and visual acuity (VA) assessment alone without access to optical coherence tomography (OCT) data.

Methods: Twenty five patients with neovascular AMD who were within the Lucentis pathway and whose macula was confirmed fluid free were enrolled. PHP was performed at 3 consecutive follow-up appointments. The Optometrist used the PHP and VA data to decide if the patient required retreatment. This was compared with the decision made by an Ophthalmologist who used both OCT and VA.

Results: Of 30 decisions made during the follow-up period 24 (80%) were concordant. Sensitivity was 73.3%, specificity 88.9%. Of those screened initially approximately 47% were unable to undertake the test reliably and therefore could not be enrolled in the study. The most common reason for unreliability was a slow reaction time by the patient to the presented stimuli (45%). This ultimately led to a high false positive score. Other contributing factors included arthritic and dexterity problems (17%) and poor VA (4%).

Conclusions: PHP may be useful to detect lesion reactivation in those patients who are able to complete the test reliably.

Commercial Relationships: Stephanie Mroczkowska, Novartis (F); Antonio Calcagni, None; Jonathan M. Gibson, None; Usha Chakravarthy, Bayer (C), Novartis (F), Neovista (C), Oraya (F); Ruth E. Hogg, Novartis (F), Novartis (C)

Support: Novartis non promotional grant R5865CVS

Program Number: 4154 Poster Board Number: A0072
Presentation Time: 8:30 AM - 10:15 AM
Automated Drusen Segmentation and Quantification from SD-OCT Images to Predict AMD Progression

Luis de Sisternes,1 Theodore Leng,2 Quang Chen,2 Jeffrey Ma,2 Vibha Mahendra,2 Daniel Rubin,3 Luis de Sisternes,1 Theodore Leng,2 Quang Chen,2 Jeffrey Ma,2 Vibha Mahendra,2 Daniel Rubin,3 Radiology and Medicine, Stanford University School of Medicine, Stanford, CA; 2Ophthalmology, Byers Eye Institute at Stanford, Palo Alto, CA; 3School of Computer Science and Engineering, Nanjing University of Science and Technology, Nanjing, China.

Purpose: Characterization of non-exudative (dry) age-related macular degeneration (AMD) is currently based on the observation of very limited drusen characteristics in color fundus photographs, which has limited value in predicting patients whose AMD will progress. We propose tools to automatically segment and quantify
Factors that predict the incidence of fellow eye in age-related macular degeneration

Kyung Min Koh, Young Ju Lew, Moon Jung Choi, Su Jin Yoo, Sung Won Cho, Dongwon Lee, Tae Gon Lee, Chul Goo kim, Jung Il Han.
Kim's Eye Hospital, Seoul, Republic of Korea.

Purpose: To identify predictive factors and findings in early stage of bilateral age-related macular degeneration (AMD) developed from monocular age-related macular degeneration.

Methods: Experimental group for this study was established with 34 eyes of 34 patients, available for follow-up study for over one year, chosen from patients who were diagnosed with unilateral age-related macular degeneration at initial examination but developed bilateral age-related macular degeneration between June of 2008 and December of 2009. Retrospective study was also conducted by forming a control group with the same number, 34 eyes of 34 patients, available for follow-up. The most informative features in terms of correlation with future wet AMD status (dry or wet) were identified using Lasso regression.

Results: Lasso regression analysis provided a set of informative drusen features to predict future progression to wet AMD. The top four predictive features were higher values in maximum drusen height and mean volume occupied per drusen, and lower reflectivity values inside drusen regions and number of independently identified drusen. The features selected as most informative also varied between imminent or long term progression prediction. Progression risk also increased with age, presence of wet AMD in the contralateral eye, and it was higher for female patients.

Conclusions: We have developed a fully automated method for drusen segmentation and quantification in SD-OCT images. Extracted quantitative features proved useful in developing models to predict the progression of dry-to-wet AMD. The results indicate that these novel quantitative features can be used to characterize the AMD disease process, identifying a subgroup of patients with increased risk to develop wet AMD.

Commercial Relationships: Luis de Sisternes, None; Theodore Leng, None; Qiang Chen, Nanjing University of Science and Technology (E); Jeffrey Ma, None; Vibha Mahendra, None; Daniel Rubin, GE Medical Systems (F), Siemens Medical (F)

Support: The Bio-X Interdisciplinary Initiatives Program of Stanford University, National Cancer Institute, National Institutes of Health, Grant No. U01-CA142555, National Natural Science Foundations of China, Grant No. 60805003

Program Number: 4155 Poster Board Number: A0073
Presentation Time: 8:30 AM - 10:15 AM

Factors that predict the incidence of fellow eye in age-related macular degeneration

Kyung Min Koh, Young Ju Lew, Moon Jung Choi, Su Jin Yoo, Sung Won Cho, Dongwon Lee, Chul Goo Kim, Jung Il Han.
Kim's Eye Hospital, Seoul, Republic of Korea.

Purpose: To identify predictive factors and findings in early stage of bilateral age-related macular degeneration (AMD) developed from monocular age-related macular degeneration.

Methods: Experimental group for this study was established with 34 eyes of 34 patients, available for follow-up study for over one year, chosen from patients who were diagnosed with unilateral age-related macular degeneration at initial examination but developed bilateral age-related macular degeneration between June of 2008 and December of 2009. Retrospective study was also conducted by forming a control group with the same number, 34 eyes of 34 patients who were diagnosed with monocular AMD but without the incidence in their fellow eyes during the same period.

Results: Average age of the experimental group was 72.5±6.46 while the control group was 69.09±7.73, and the ratio between male and female was 18:16 in the experimental group and 19:15 in the control group, where there was no significant difference detected between two groups. Significant difference was again undetected from the visual acuity at initial examination as the experimental group recorded 0.14±0.16 (logMAR) whereas the control group showed 0.13±0.19 (logMAR). For early findings with Optical Coherence Tomography (OCT), pigmentary epithelial detachment (PED) was found from 13 cases (38.2%) in the experimental group compared to 5 cases (14.7%) in the control group; and serous retinal detachment (SRD) was also found from 13 cases of the experimental group whereas none was discovered from the control group; therefore, there was a significant difference (p<0.05) between two groups.

Conclusions: The findings of PED and SRD can be considered as significant predictive factors for initial findings of unilateral age-related macular degeneration developed from monocular AMD.

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Program Number: 4156 Poster Board Number: A0074
Presentation Time: 8:30 AM - 10:15 AM

Development of choroidal neovascularization in the second eye of neovascular AMD patients treated with anti-VEGF drugs

Jonathan Abraham, Michael J. Elman.
Elman Retina Group, PA, Baltimore, MD.

Purpose: The purpose of this study was to determine the risk and presentation of choroidal neovascularization developing in the second eye of patients undergoing regular anti-VEGF treatment for neovascular AMD.

Methods: This retrospective study reviewed the charts of all AMD patients treated in our center with anti-VEGF drugs for choroidal neovascularization between 2005-2012. Eyes that had undergone other treatments (PDT, laser) previously were excluded. At each visit after commencement of treatment in the first eye, both eyes were examined clinically as well as photographically (OCT and/or fluorescein angiography). The cumulative risk of developing neovascularization in the second eye, best available visual acuity and the presence of symptoms at the time of identification of neovascularization in the second eye are reported.

Results: Four hundred thirty patients were identified with neovascular AMD in the first eye requiring anti-VEGF treatment. The mean interval between visits was 4.5 weeks. Eighty three patients developed neovascularization in the second eye requiring treatment. Life table analysis showed that 9% of fellow eyes developed neovascularization annually. The mean visual acuity at the time neovascularization was diagnosed in the second eye declined by one line from the preceding visit. The median visual acuity in the second eye at the time treatment was started was 20/50. Treated second eyes maintained an average visual acuity of 20/50 over followup. Only four of eighty three patients (4.8%) presented with symptoms at the time of diagnosis of neovascularization in the second eye.

Conclusions: The risk for progression to neovascularization in the second eye is high when the first eye is undergoing regular anti-VEGF treatment. Most patients are asymptomatic at the time of diagnosis in the second eye. Therefore, careful examination of the fellow eye should be performed at each visit in patients undergoing anti-VEGF treatment to the first eye and facilitates early detection of treatable neovascularization in the second eye while the vision is still quite functional.
Purpose: RMD, also known as reticular pseudodrusen, may demonstrate “target” lesions, or central hyperreflectant areas within the characteristic hyporeflectant reticular lesions in infrared (IR) images. The dynamics of these target lesions were studied and compared to those of RMD itself.

Methods: We retrospectively identified 54 patients (54 eyes) from a single institution (L’Hôpital Intercommunal de Créteil, France) who had RMD in one eye and late-stage AMD in the fellow eye visible on IR imaging. Additional inclusion criteria included ≥ 2 visits with IR imaging and ≥ 1 year of follow-up. Five patients were excluded due to poor image quality. Target lesions on the remaining 49 images were identified and counted by two graders independently and to consensus. To exclude larger lesions that may be soft drusen, we limited our definition of hyperreflectant targets to reticular lesions with clearly defined hyporeflectant borders.

Results: The subjects had a mean age at baseline of 82±6, 65% (32/49) of whom were female. The mean duration of follow-up was 25 months. Hyperreflectant targets were identified within the reticular pattern of 41/49 subjects (84%). For subjects who had visible target lesions, the mean number within the 56.25 mm² (7.5 mm x 7.5 mm) IR window at baseline was 10±14 targets. In this subset there was an average absolute change in overall target number of 7±8 targets per 56.25 mm²/year. For 46% of these subjects (19/41), the target number increased at later follow up by an average of 7±8 lesions. In 49% of these subjects (20/41), the targets decreased by 10±9. Two eyes remained unchanged. In all subjects of this cohort, target lesions were clustered around the macula (within the 3000 micron diameter circle).

Conclusions: RMD in AMD is known to be a dynamic process associated with a high risk of progression to advanced AMD. The substructure of the target lesions themselves, like all of RMD, is uncertain, and has been ascribed to some aspect of subretinal deposits or to deeper reflectant lesions. They appear and disappear as shown herein independently of the RMD lesions themselves, and their central prediction is at variance with RMD in general, which is found most often at the superior arcades. These observations may provide clues for further research on this disease. 1. Querques et al. (2011) Retina;31:518-26, 2. Arnold et al. (1995) Retina;15:183-91
for Health Research Biomedical Research Centre, London, United Kingdom; Lions Eye Institute, Perth, WA, Australia.

**Purpose:** To better understand structure and functional relationships in early AMD. In this abstract, we analyze the optical coherence tomography (OCT) features of early AMD and correlate these findings with cone and rod function as measured by microperimetry.

**Methods:** Clinical and imaging data were collected from patients with dry AMD undergoing Spectral domain OCT and dark adapted microperimetry (cone and rod function on Nidek MP-1-s) and scotopic microperimetry (cone function MAIA microperimeter). Custom image analysis software (OCTOR) was used for quantitative analysis segmentation of the retinal substructure. Retinal spaces quantified included retina, photoreceptor outer segments, RPE to choriocapillaris thickness (i.e. drusen/PED). Segmented enface images were overlaid onto the microperimetry maps and descriptive data generated.

**Results:** 12 patients underwent MPIS, MAIA and high density spectralis OCT. A subset of these patients underwent segmentation of the retinal layers and overlay of retinal sensitivity maps. The following regions were found to have relationship between functional deficit on testing and structural abnormalities. Ellipsoid zone and RPE to choriocapillaris thickness (drusen height). Area of normal values of RPE to choriocapillaris thickness (ie no confluent drusen or drusenoid PED) was associated with a median retinal sensitivity of 12.7 dB (quartiles: 11dB, 14dB). The median retinal sensitivities were 7.4 dB (quartiles: 7dB, 9dB) for sub RPE drusen.

**Conclusions:** Sub retinal drusen deposits is associated with reduced retinal sensitivities. Understanding structural markers that relate to rod and cone functional defects may help to better understand subtypes of early AMD and help develop novel clinical trial endpoints.

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**OPERA (Optos Peripheral Retina AMD) Study Croatia:**

**Reticular pigmentation in AMD vs. controls**

**Purpose:** The presence of peripheral reticular pigmentation (PREP) in the retina has been linked to AMD, and may be a phenotypic expression of genes related to the development of AMD. While clinical examination with indirect ophthalmoscope can reveal such changes, documentation of PREP then becomes rather subjective.

**Methods:** After obtaining IRB approval, 150 subjects with AMD were imaged with the P200A Optos unit and both color fundus images and fluorescent angiographic images were obtained in both eyes. AMD was defined according to the guidelines from the International ARM (Age-related maculopathy) Study Group. 150 age-matched controls without ARM were also imaged in a similar fashion but without WFFA. Eye steering allowed imaging of the maximum area of the peripheral retina. Masked readers determined the presence or absence of reticular pigmentation in color and fluorescent images, and determined the number of quadrants of pigmentation in each eye. Other morphological parameters were also studied including drusen, paving stone degeneration, white, without pressure, and lattice degeneration. The study was conducted in Zagreb, Croatia, on Caucasian subjects. DNA was collected from all subjects by drawing whole blood.

**Results:** For subjects with AMD, reticular pigmentation was found in 40.65% of the color images and 46.25% of the fluorescent images. In control subjects, reticular pigmentation was seen on color images in 8.16% of the eyes. The difference between control and AMD subjects with respect to prevalence of reticular pigment in color images was significant (P<0.03). PREP was more easily seen on fluorescein angiograms than on color images.

**Conclusions:** Peripheral reticular pigmentation is much more likely to be present in patients with AMD than controls in our Croatian study population. These findings should be compared to the results from other ethnic groups who suffer from AMD, but are consistent with reports based on clinical fundus examination alone. The genotypes of our subjects will provide further insight into the association of PREP and AMD. Comparisons of results from the OPERA study U.S. (AREDS II ancillary study) to our OPERA: Croatia results will be conducted in 2013.

**Commercial Relationships:** Vesna Jurisic Friberg, None; Biljana Andrijevic Derk, None; Tamara Knezevic, Mia Zoric-Geber, None; Goran Bencic, None; Zoran Vatavuk, None; Thomas R. Friberg, 13/581,518 (P)

**Program Number:** 4161

**Program Number:** 4160

**Program Number:** 10079

**Program Number:** 10079

**Program Number:** 4161

**Program Number:** 4160

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**Program Number:** 4161

**Program Number:** 10079

**Presentation Time:** 8:30 AM - 10:15 AM

**Morphological characteristics associated with drusen progression on Spectral Domain OCT (SD-OCT)**


**1Ophthalmology and Visual Science, University of Wisconsin - Madison**

©2013, 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 arvo@arvo.org.
Clinical Outcomes of Eyes with Neovascular Lesions Composed of >50% Blood Treated with Anti-VEGF Therapy in the Comparison of AMD Treatments Trials (CATT)

**Purpose:** To compare baseline characteristics, treatment requirements, visual acuity (VA), and morphologic outcomes of eyes enrolled with >50% of the total lesion composed of blood versus all other eyes enrolled in the Comparison of Age-related Macular Degeneration Treatments Trials (CATT).

**Methods:** Cohort study within CATT. Participants were randomly assigned to treatment with ranibizumab or bevacizumab and to a dosing regimen of monthly injections for 2 years, PRN injections for 2 years, or monthly injections for 1 year and PRN injections the following year. Masked trained readers evaluated baseline and follow-up morphology in color fundus photographs, fluorescein angiograms (FA), and optical coherence tomography.

**Results:** 84 of 1185 patients enrolled in CATT had lesions composed of >50% blood at baseline (B50 group). Baseline demographic characteristics were similar between the B50 group and the eyes with no or less blood (Other group) but lesion characteristics differed markedly. While CNV size was smaller in the B50 group (0.73 Disc Areas vs 1.83 DA; p < 0.0001) the total lesion size was much larger (4.55 DA vs 2.31 DA; p < 0.0001). Central retinal thickness was also greater in the B50 group (524 um vs 455 um). Mean baseline VA was worse in the B50 group (56 letters) than the Other group (60.9 letters). VA in the B50 group improved by a mean of 9.26 letters at 1 year and 9.44 letters at 2 years; similar to the improvement in the Other group (7.17 and 6.15, respectively). The percentage gaining 3 lines was similar for both groups (34.3% and 29.5% respectively). Eyes treated PRN required a similar number of injections in the two groups.

Mean total lesion size in the B50 group decreased by a mean of 1.2 DA at 1 year and at 2 years while mean lesion size in the Other group increased by 0.33 DA at 1 year and 0.91 DA at 2 years (p<0.001). Mean retinal thickness also decreased more in the B50 group (-355 um vs -287um; p < 0.005). Lesion activity, as determined by leakage on FA, was similar between groups at both time intervals.

**Conclusions:** The B50 group had a visual prognosis similar to the Other group when treated according to the CATT protocol. Lesion size decreased markedly through 2 years. Eyes with neovascular AMD lesions composed of >50% blood can be managed clinically in a similar manner as those with less or no blood.

**Commercial Relationships:** Michael M. Altaweel, None; Juan E. Grunwald, None; Ebenezer Daniel, None; Gui-Shuang Ying, None; Jiayan Huang, None; Glenn J. Jaffe, Heidelberg Engineering (C), Regeneron Pharmaceuticals (F), Neurotech USA (C), Abbott (C), Psivida (F), Pfizer (C), Bayer (C)

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**Clinical Trial:** NCT00593450

**Program Number:** 4162 Poster Board Number: A0081
Atlanta, GA) was performed in one study eye (eye with large drusen in Group 1 and eye without advanced AMD in Group 3) in each participant at baseline and week 1. Mean rod intercept times were compared between groups using Kruskal-Wallis and Wilcoxon rank-sum tests. Test repeatability was determined using limits of 95% agreement between baseline and week 1 values.

**Results:** The mean rod intercepts demonstrated a correlation with increased severity of AMD with groups 2 and 3 rod intercept times reaching statistical significance when compared to group 0 (p < 0.01) (see Figure). Seventeen patients out of the total exceeded the 40 minute test time ceiling and were conservatively assigned a 40 minute rod intercept time. Limits of agreement analysis between baseline and week 1 rod-intercept times on the subset of 76 patients with both time points showed a mean difference of 0.34 +/- 3.09.

**Conclusions:** Dark adaptometry may reveal defects in rod-mediated dark adaptation in eyes with non-advanced AMD and increase with severity of AMD. Further prospective investigation is underway to determine the relationship of AMD progression to rod intercept time.

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**Commercial Relationships:** E. Lauren Doss, None; Tanya Glaser, None; Elvira Agrón, None; Divya L. Nigam, None; Wai T. Wong, None; Emily Y. Chew, None; Catherine A. Cukras, None

**Support:** NIH Medical Research Scholars Program

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**Program Number:** 4164 Poster Board Number: A0083
**Presentation Time:** 8:30 AM - 10:15 AM

**Imaging of Focal Hyperpigmentary Changes in Intermediate Age-related Macular Degeneration - A Longitudinal Analysis**

Arno P. Goebel, Sophía Grandei, Monika Fleckenstein, Frank G. Holz, Steffen Schmitz-Valckenberg, Department of Ophthalmology, University of Bonn, Bonn, Germany.

**Purpose:** Focal hyperpigmentations represent a high-risk factor for progression from intermediate to advanced age-related macular degeneration (AMD). In this study alterations of hyperpigmentary changes in intermediate AMD were determined over time by means of multimodal imaging.

**Methods:** One-year follow-up (t1) data of 37 patients (mean age 74) was recorded and evaluated. Of those, eyes with intermediate AMD (AREDS-classification) showing focally increased brownish pigment were selected for analysis. Imaging including color fundus photography (CFP), fundus autofluorescence (FAF) and spectral-domain optical coherence tomography (SD-OCT) were performed at baseline examination (t0) and one year later (t1). After semi-automated alignment of different imaging modalities and examination dates, each increased pigment was topographically correlated with the focal FAF- and SD-OCT-signal.

**Results:** Hyperpigmentary changes at baseline were funduscopically visible in 21 of 47 eyes at t0 and t1. In total, 69 loci of increased pigment were evaluated. FAF signal at t0 was increased, normal, decreased or not evaluable in 44, 13, 0 and 12 hyperpigmentations respectively. FAF signal altered over time in 5 cases. Coregistrated SD-OCT images showed hyperreflective foci above band 4 in 35 and only at band 4 level in 5 cases. Precisely aligned SD-OCT follow-up scans were available in 37 hyperpigmentations. Of those, a shift of the hyperreflective signal in inner retinal layers was documented in previously used in the lab with 33 ms flashes (OldStimuli), or using a new temporal sequence method was employed. Two protocols used the new temporal sequence method and on each presentation either flashed on for 33 ms (NewStimuli), or presented pedestal flicker for 266 ms at 15Hz (NewStimuliFlick). Diagnostic capacity was measured using areas under the curve (AUC) of receiver operator characteristic (ROC) plots for the two worst regions in each eye for the three mfPOP stimuli protocols.

**Results:** The absolute mean difference of AREDS scores between eyes was 0.48 ± 0.6 (mean ± SD). Response amplitudes for the NewStimuli achieved the best diagnostic accuracy with AUC values of 100% ± 0.0% (mean ± SE) for eyes containing small, intermediate and large drusen. In comparison NewStimuliFlick and OldStimuli were less diagnostic across all AREDS categories. In eyes containing small drusen NewStimuliFlick and OldStimuli achieved AUC values of 87.0% ± 6.8% and 92.6% ± 7.1% respectively for small drusen, 87.0% ± 8.1% and 65.8% ± 14.6% for intermediate drusen and 86.0% ± 5.3% and 82.0% ± 6.7% for large drusen. Utilizing time to peak response deviations reduced diagnostic accuracy across all stimulus protocols.

**Conclusions:** The new temporal sequence stimuli produced the best diagnostic accuracy for all AMD severities, in comparison to the old continuous sequence stimuli and the same stimuli containing flicker.

**Commercial Relationships:** Faran Sabeti, None; Aliasha Saikal, None; Maria Kolic, Seeing Machines Ltd (E); Corinne F. Carle, AU2012/905171 (P); Rohan W. Essex, None; Andrew C. James, Seeing Machines, Inc (P); Ted Maddess, Seeing Machines (F), Seeing Machines (P), EyeCo (I)

**Support:** Australian Research Council (ARC) through the ARC Centre of Excellence in Vision Science (CE0561903), AusIndustry, and Seeing Machines Ltd, Canberra.
Reduction in retinal function. Further studies on the potential utility of the ISe band intensity as a novel biomarker to monitor AMD disease severity and progression are warranted.

**Conclusions:****Visible hyperpigmentary changes on fundus photograph exhibit complex and dynamic alterations in different imaging modalities.** The variation of location of the hyperreflective signal in SD-OCT over time may represent a migration of RPE cells and/or melanin-load macrophages towards inner retinal layers. The prognostic implications of these microstructural changes require further investigations with extend review periods.

**Commercial Relationships:** Arno P. Goebel, Heidelberg Engineering, Germany (F), Carl Zeiss Meditec AG, Germany (F), Optos, UK (F); Sophia Grundei, Heidelberg Engineering, Germany (F), Carl Zeiss Meditec AG, Germany (F), Optos, UK (F); Monika Fleckenstein, Heidelberg Engineering, Germany (F), Heidelberg Engineering, Germany (C), Heidelberg Engineering, Germany (R), Carl Zeiss Meditec, Germany (F), Optos, UK (F), Optos, UK (C); Frank G. Holz, Acucela (C), Allergan (C), Genentech (F), Heidelberg Engineering (F), Zeiss (F), Novartis (F), Novartis (C), Optos (F), Merz (C), Bayer (F), Bayer (C), Boehringer Ingelheim (C); Steffen Schmitz-Valckenberg, Heidelberg Engineering (F), Optos (F), Carl Zeiss Meditec (F), Heidelberg Engineering (R), Genentech (C), Novartis (C), Novartis (R), Roche (R), Novartis (F)

**Support:** German Ministry of Education and Research, BMBF: FKZ 13N10285

**Program Number:** 4166 Poster Board Number: A0084

**Presentation Time:** 8:30 AM - 10:15 AM

**Reduction of the OCT second hyper-reflective band intensity is associated with a decreased in retinal function in eyes with age-related macular degeneration**

**Chi D. Luu,1,2 Zhichao Wu,1,3 Lauren N. Ayton,1,2 Robyn H. Guymer1,2**

1 Macular Research Unit, Centre for Eye Research Australia, East Melbourne, VIC, Australia; 2 Department of Ophthalmology, University of Melbourne, Parkville, VIC, Australia.

**Purpose:** The second hyper-reflective band on spectral domain optical coherence tomography (SD-OCT) is thought to correlate with the anatomical location of the photoreceptor inner segment ellipsoids (ISe), which are densely packed with mitochondria. The purpose of this study was to determine the intensity of the ISe band in patients with early age-related macular degeneration (AMD) and to correlate the ISe band intensity with retinal function.

**Methods:** Twenty-nine early AMD and thirty-one control subjects participated in this prospective observational study. A high-resolution horizontal line-scan through the fovea on SD-OCT and a multifocal electroretinogram (mERG) were performed in one eye of each participant. The intensity of the ISe band and external limiting membrane (ELM) within 1000µm of the fovea were quantified using ImageJ software. The average ISe band relative intensity (expressed as ISe/ELM ratio) of early AMD and control participants was compared. The relationship between the ISe band intensity and the mERG response parameters (P1 amplitude and implicit time) was also determined.

**Results:** In normal participants, the intensity of the ISe band was significantly reduced with age (r=-0.634, p<0.001). On average, the ISe band relative intensity of participants with early AMD (1.77 ± 0.26) was significantly lower than that of the control subjects (1.95 ± 0.27, p<0.001) after controlling for age. The ISe band relative intensity was significantly correlated with the mERG P1 implicit time (r = -0.745, p<0.001) but not P1 response amplitude (r = 0.144, p=0.281).

**Conclusions:** Subjects with early AMD have a significant reduction in the relative intensity of the ISe band, which correlated with a reduction in retinal function. Further studies on the potential utility of the ISe band intensity as a novel biomarker to monitor AMD disease severity and progression are warranted.
Imaging of reticular drusen by multi-spectral confocal scanning laser ophthalmoscopy imaging

**Purpose:** To describe detection, appearance and characteristic signal distribution of reticular drusen (RDR) associated with age-related macular degeneration (AMD) in multispectral confocal scanning laser Ophthalmoscopy (cSLO) images.

**Methods:** Conventional color fundus photography and multi-spectral cSLO (λ = 488 nm, λ = 514 nm, λ = 820 nm; MultiColor Spectralis, Heidelberg Engineering, Germany) imaging were performed in 25 eyes of 14 patients (mean age 75 years, range 53 - 87 years) with RDR detected by near-infrared cSLO and SD-OCT imaging. Signal alterations and the RDR area involvement in different modalities at the site of RDR were analysed and compared.

**Results:** RDR were detectable in 25 of 25 cSLO multi-spectral images showing an irregular pattern of small roundish lesions with a greenish center that corresponded to the halo-like appearance by cSLO near-infrared reflectance. In the blue and green reflectance modes alone, the center of single RDL lesions was characterized by a strong hyperreflectivity, surrounded by a weak interlacing pattern of hyper- and hyporeflectivity. The RDR area involvement and its boundaries varied between different cSLO reflectance modes and were best visible by near-infrared reflectance. No RDR lesions were detectable by blue reflectance in the center of the macula.

Conventional fundus photography showed RDR in 11 of 25 eyes.

**Conclusions:** Multi-spectral cSLO imaging allows for the detection of a characteristic pattern of RDR. The signal distribution is dependent on different reflectance modes. Analysis of different image modalities may be helpful for the further characterization of RDR and the implementation in future natural history, epidemiological, genetic and interventional trials in AMD.

**Commercial Relationships:** Jasmin Anke Ilka Auge, Heidelberg Engineering, Germany (F), Carl Zeiss Meditec, Germany (C), Optrys, UK (F); Julia S. Steinberg, Heidelberg Engineering, Germany (F), Carl Zeiss Meditec, Germany (F), Optos, UK (F); Monika Fleckenstein, Heidelberg Engineering, Germany (F), Carl Zeiss Meditec, Germany (F), Optos, UK (F); Frank G. Holz, Acucela (C), Allergan (C), Genentech (F), Heidelberg Engineering (F), Zeiss (F), Novartis (F), Novartis (C), Optos (F), Merz (C), Bayer (F), Bayer (C), Boehringer Ingelheim (C); Steffen Schmitz-Valkenberg, Heidelberg Engineering (F), Optos (F), Carl Zeiss Meditec (F), Heidelberg Engineering (R), Genentech (C), Novartis (C), Novartis (R), Roche (R), Novartis (F)

**Program Number:** 4169 Poster Board Number: A0087
**Presentation Time:** 8:30 AM - 10:15 AM

Reticular Pseudodrusen in Early Age-Related Macular Degeneration is Associated with Choroidal Thinning
Aakriti Garg1, Maris Oll2, Suzanne Yzer3, Rando Allikmets4,5, Stanley Chang3, Gaetano R. Barile4, Roland Smith6, John C. Merriam1, Stephen H. Tsang4,6, Srilaxmi Bearelly7,1. 1Ophthalmology, Columbia University College of Physicians and Surgeons, New York, NY; 2Pathology & Cell Biology, Columbia University College of Physicians and Surgeons, New York, NY; 3Ophthalmology, Manhattan Eye, Ear, & Throat Hospital, New York, NY; 4Ophthalmology, New York University Medical Center, New York, NY.

**Purpose:** To compare subfoveal choroidal thickness (SFCT) measurements in early age-related macular degeneration (AMD) between patients with and without reticular pseudodrusen (RPD)

**Commercial Relationships:** None

**Program Number:** 4168 Poster Board Number: A0086
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using spectral-domain optical coherence tomography (SDOCT).

**Methods:** This cross-sectional study examined 84 AMD patients (40 RPD, 44 non-RPD) who were age- and gender-matched (RPD: 32 of 40 (80%) were female, mean age 76.9 years ± 7.5 SD; non-RPD: 32 of 44 (73%) were female, mean age 73.9 years ± 7.8 SD). 63 RPD eyes and 75 non-RPD eyes were included in the analysis. Exclusion criteria included late AMD (geographic atrophy greater than 500 microns² or history of choroidal neovascularization), myopia greater than -6 dipters, central serous chorioretinopathy, or past vitreoretinal surgery. Color fundus photographs and scanning laser ophthalmoscopy (including autofluorescence and infrared imaging) were graded in a masked fashion by three retinal specialists (SY, SB, MO) to identify RPD and non-RPD groups. SDOCT was used to measure choroidal thickness for all eyes. For each eye, the best SDOCT image with a clear posterior margin of choroid was chosen for analysis. Enhanced depth imaging spectral-domain optical coherence tomography (EDI-SDOCT) was used when available (20 of 138 eyes). SFCT was measured using Heidelberg Eye Explorer interactive software.

**Results:** Mean SFCT of RPD eyes (176.3 microns ± 60.5 SD) was significantly less than that of non-RPD eyes (216.5 microns ± 70.3 SD) by the Student’s t-test for independent samples (p = 0.0005).

**Conclusions:** These results support previous smaller studies that have shown RPD is associated with a thinner choroid. As RPD has been associated with increased risk of advanced AMD, SFCT may be integral to understanding the RPD process, as well as stratifying risk of AMD progression.

Images of an AMD patient without RPD. EDI-SDOCT (top) shows a SFCT of 451 microns. Infrared (middle) and autofluorescence (bottom) imaging depict absence of RPD.

Images of an AMD patient with RPD. SDOCT (top) shows a very thin SFCT of 32 microns. Infrared (middle) and autofluorescence (bottom) imaging support the presence of RPD throughout the fundus.

**Commercial Relationships:**
- Aakriti Garg, None;
- Maris Oll, None;
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**Program Number:** 4170 **Poster Board Number:** A0088

**Presentation Time:** 8:30 AM - 10:15 AM

Reticular pseudodrusen and their topographic relation to choroidal watershed zones and localized changes in choroidal volume and choroidal thickness

**Florian Alten, Christoph R. Clemens, Nicole Eter.** University Eye Hosp Muenster, Muenster, Germany.

**Purpose:** To identify a potential topographic relation of evolving reticular pseudodrusen (RPD) to choroidal watershed zones (CWZ) as well as to local changes in choroidal thickness (CT) and choroidal volume (CV).

**Methods:** 20 eyes of 20 patients with RPD in the posterior pole in an area < 10 mm² and no other phenotypic retinal alteration were included (16 females, 4 males; age 75.9 ± 7.0 years). Patients underwent fundus photography, spectral domain optical coherence tomography (SD-OCT), enhanced depth imaging OCT (EDI-OCT), fluorescence videoangiography (vFA), indocyanine green videoangiography (vICG) and confocal scanning laser ophthalmoscopy (cSLO) (Fundus autofluorescence [FAF, λ = 488 nm], near-infrared reflectance [IR, λ = 830 nm]) (Spectralis, Heidelberg Engineering, Germany).

vICG were evaluated for the presence, localization and configuration of CWZ. Retinal areas affected by RPD were measured and their localization was determined in relation to CWZ. Cursor lines marking the internal limiting membrane and the retinal pigment epithelium (RPE) in EDI volume scans were moved manually to the outer border of the RPE and the choroidal-scleral interface to construct a CT map.
of the posterior pole. CT and CV were measured using the ETDRS grid. An age and sex-matched control group of 20 healthy eyes underwent the same procedures.

**Results:** In all study eyes, RPD and no other retinal alteration could be clearly demonstrated in SD-OCT, EDI-OCT, vFA, vLCG and cSLO. CWZ were identified in 17 eyes (85.0%) in the study group and in 7 eyes (35.0%) in the control group. The area affected by RPD in the study group was 7.58 ± 2.39 mm². In 17 study eyes showing CWZ the RPD area was fully or partly located within the CWZ in 15 eyes (88.2%). Mean CV in the full ETDRS grid area was 4.76 ± 1.93 mm³ in the study group and 4.74 ± 1.24 mm³ in the control group. CV and CT in the grid sector mostly affected by RPD were 0.96 ± 0.37 mm³ / 181 ± 70.7 µm and 1.1 ± 0.3 mm³ / 207 ± 57.9 µm in the corresponding sector of the control eyes.

**Conclusions:** The localization of evolving RPD seems to be related to the presence and the site of CWZ. However, an association between the presence of RPD and macular CT and CV could not be shown in this population.

**Commercial Relationships:** Florian Alten, Novartis Pharma (F); Christoph R. Clemens, Heidelberg Engineering (F), Novartis (F); Nicole Eter, Novartis (F), Bayer (R), Heidelberg Engineering (R), Sanofi Aventis (C), Allergan (C), Bausch and Lomb (C)

**Program Number:** A0089

**Presentation Time:** 8:30 AM - 10:15 AM

**Long-term evaluation of drusen area and volume using polarization-sensitive OCT**

Ferdinand G. Schlanitz1, Bernhard Baumann2, Matthias Bolz2, Erich Gotzinger2, Michael Pircher1, Christoph K. Hitzenberger1, Ursula Schmidt-Erfurth1, Christoph Fleckenstein2, Frank G. Holz, Steffen Schmitz-Valckenberg2. Department of Ophthalmology, University of Bonn, Bonn, Germany.

**Purpose:** To evaluate drusen area and volume over time using polarization-sensitive OCT (PS-OCT).

**Methods:** 30 Patients with drusen due to age-related macular degeneration were imaged using PS-OCT every 6 months over three years. Patients were followed until a regression of drusen (spontaneous or due to a development of advanced AMD) occurred. The drusen area and volume in each macular volume scan were evaluated using an automated segmentation algorithm based on the depolarization information of the PS-OCT.

**Results:** In all eyes, a continuous and approximately linear increase of drusen area and volume was observed. Mainly, patients could be classified into two groups: Group A was characterized by a progression rate of more than 0.1 mm² in area and 0.01 mm³ in volume per six months (mean rate: 0.54 mm² resp. 0.03 mm³, SD: 0.14 resp. 0.01, range 0.32 - 0.76 resp. 0.02 - 0.05), and Group B a progression rate below 0.1 mm² in area resp. 0.01 mm³ in volume (mean rate: 0.08 mm² resp. 0.003 mm³, SD: 0.02 resp. 0.001, range 0.06 - 0.1 resp. 0.002 - 0.004). The progression rates were significantly related to the baseline drusen area and volume, which was 4.69 mm² and 0.21 mm³ in average for group A and 1.78 mm² resp. 0.07 mm³ for group B.

**Conclusions:** Drusen show a steady increase of area and volume over time, which can be measured precisely using PS-OCT. Interestingly, the progression rates were roughly linear and patients could be classified into a “fast progression group” and a “slow progression group”. Further studies will show the prognostic value of this classification. The exact measurements made by PS-OCT outranges any other drusen detection algorithm and enables future clinical studies investigating the influence of prophylactic treatments on the progression of early AMD.

**Commercial Relationships:** Ferdinand G. Schlanitz, None; Bernhard Baumann, Canon Inc. (F); Matthias Bolz, None; Erich Gotzinger, Canon Inc. Japan (F); Michael Pircher, Canon Inc. (F), Canon Inc. (C); Christoph K. Hitzenberger, Canon Inc. (F), Canon Inc. (C); Ursula Schmidt-Erfurth, Alcon (C), Bayer Healthcare (C), Novartis (C)

**Support:** Austrian Science Fund FWF Grant P19624-B02

**Program Number:** A0090

**Presentation Time:** 8:30 AM - 10:15 AM

**Longitudinal analysis of reticular drusen associated with age-related macular degeneration**

Julia S. Steinberg, Jasmin Anke Ilka Auge, Monika Fleckenstein, Frank G. Holz, Steffen Schmitz-Valckenberg. Department of Ophthalmology, Medical University of Vienna, Vienna, Austria.

**Purpose:** To evaluate longitudinal variations of reticular drusen (RDR) in patients with age-related macular degeneration (AMD) using spectral-domain optical coherence tomography (SD-OCT) imaging.

**Methods:** Simultaneous combined near-infrared confocal scanning laser ophthalmoscopy and SD-OCT imaging was performed in 6 eyes of 4 patients (mean age 83 years, range 80 - 85 years) with RDR associated with AMD. Dense volume scans (1 µm between sequential B-scans) were acquired at sites with RDR at baseline and at review examination (mean 6 months, range 5 - 9). For the latter, the AutoRescanTM tool (Heidelberg Engineering, Germany) was applied which allows for automatic alignment of follow-up scans at the same location as set at as baseline examination. The maximum width and the maximum height of 5 pre-selected individual RDR in each eye were quantified by two independent readers. The number of B-scan involvement was counted and the individual B-scan showing the maximum height was identified for each lesion, respectively.

**Results:** The mean height and width at baseline of 30 included RDR lesions were 99.5µm ± 13.7 (range 69.5-127µm) and 126.3µm ± 35.2 (range 60.5-193µm), respectively. Bland-Altman statistics showed a mean agreement of -0.8µm ± 8.8 (range -27-16µm) for lesion height and of 1.0µm ± 6.6 (range -12-19 µm) for lesion width. Over time, a mean change of 3.8 ± 7.3µm (range -12-14.5 µm) for height and of 15.45µm ± 27.3 (range -40-84µm) for width were determined. An average number of B-scan involvement of 7.5 ± 3.6 (range 1-16) for baseline and of 7.2 ± 3.5 (range 1-17) for follow-up was counted. The individual B-Scan showing the maximum height over time was identical for three lesions and varied in-between ± 6 scans.

**Conclusions:** Single B-scans may not be adequate for the assessment of dynamic RDR changes over time. Using dense volume SD-OCT imaging with the image analysis software tool applied herein, no complete disappearance of a single lesion was observed during the review period, while there was an overall trend of RDR lesion progression both in height and width. Exact and accurate location of follow-up SD-OCT scans as compared to baseline imaging appears to be crucial for further longitudinal analysis of RDR evolution.

**Commercial Relationships:** Julia S. Steinberg, Heidelberg Engineering, Germany (F), Carl Zeiss Meditec, Germany (F), Optos, UK (F); Jasmin Anke Ilka Auge, Heidelberg Engineering, Germany (F), Carl Zeiss Meditec, Germany (F), Optos, UK (F); Monika Fleckenstein, Heidelberg Engineering, Germany (F), Heidelberg Engineering, Germany (C), Heidelberg Engineering, Germany (R), Carl Zeiss Meditec, Germany (F), Optos, UK (F), Optos, UK (C); Frank G. Holz, Acucela (C), Allergan (C), Genentech (F), Heidelberg Engineering (F), Zeiss (F), Novartis (F), Novartis (C), Optos (F), Merz (C), Bayer (F), Bayer (C), Boehringer Ingelheim (C); Steffen Schmitz-Valckenberg, Heidelberg Engineering (F),
Preferential Hyperacuity Perimetry Monitoring in Patients During Treatment of Neovascular Age-related Macular Degeneration

Merina Thomas1,2, Yulia Wolfson1, Voraporn Chakitchompkol1,3, Neil M. Bressler1. 1Department of Ophthalmology, Retina Division, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, MD; 2Department of Ophthalmology, University of Illinois at Chicago, Chicago, IL; 3Department of Ophthalmology, Chiang Mai University, Chiang Mai, Thailand.

Purpose: To determine how often the home device preferential hyperacuity perimeter (PHP) detects changes in participants being treated with anti-angiogenic therapy for neovascular age-related macular degeneration (AMD), and how often those changes correspond to images of neovascular AMD obtained as part of standard care.

Methods: Patients with neovascular AMD requiring anti-VEGF treatment at a current visit were enrolled into a prospective longitudinal study to investigate the correlation between PHP test scores, quantitative measurements including the rate of normal and abnormal responses, the average size of the presented distortion, and maps of spatial representation of hyperacuity visual field defects to clinical findings including visual acuity and OCT data. Follow-up was at 4 weeks; if treated at 4 weeks, follow-up at 8 weeks also was obtained. An additional PHP test also was administered 1 week following each clinical examination.

Results: 90% (n = 19) of the study candidates had a reliable qualification test score and were followed. 76% (n = 16) of the participants were women. The mean age of participants was 77 years, (range 61 to 89 years). Mean visual acuity of the qualification eye was logMAR 0.25 (20/32-20/40). 57% (n = 12) of patients used bifocal eyeglasses during testing. The mean PHP test score improved (decrease in raw score) from baseline to week 1 (-0.10, P = 0.03) and deteriorated (increase in raw score) from baseline to week 4 (+0.09, P = 0.09). For patients who received injections in two subsequent months, the PHP test score improved (decrease in raw score) from week 4 to week 5 (-0.14, P = 0.13) and deteriorated (increase in raw score) to near baseline at week 8 (-0.12, P = 0.12). The mean visual acuity increased slightly (mean difference logMAR +0.06 or 3 letters, P = 0.27) over the 2 month follow-up period. The OCT CST decreased (-1.78 µ, P = 0.46) and the OCT volume increased (0.93 mm3, P = 0.02) over 2 months.

Conclusions: These data suggest that the PHP home device can detect changes during antiangiogenic therapy consistent with the course of the disease as determined by clinical and imaging findings. Further studies would be needed to determine if this device has a role in monitoring patients receiving anti-VEGF therapy in an as needed regimen.

Commercial Relationships: Merina Thomas, None; Yulia Wolfson, None; Voraporn Chakitchompkol, None; Neil M. Bressler, Abbott Medical Optics, inc (F), Alimera Sciences (F), Allergan (F), Bausch &Lomb, Inc (F), Bayer (F), Carl Zeiss Meditec, Inc (F), ForSight Labs, LLC (F), Genentech, Inc (F), Genzyme Corporation (F), Lumenis, Inc (F), Notal Vslion (F), Novartis Pharma AG (F), Pfizer, Inc (F), Regeneron Pharmaceuticals, Inc (F), Roche (F), Thrombogencis (F)

Support: Vanderbilt Medical Scholars Program (NIH Grant 5TL1RR024978-04), Notal Vision, Inc., Johns Hopkins University

Program Number: 4173 Poster Board Number: A0091
Presentation Time: 8:30 AM - 10:15 AM

Visual outcomes of an Inject and Extend protocol of intravitreal anti-vascular endothelial growth factor treatment in neovascular age-related macular degeneration over two years

Farshad Abedi, Sanjeewa Wickramasinghe, Amirul Islam, Kellie M. Inglis, Robyn H. Guymer. Ophthalmology, Centre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital, East Melbourne, VIC, Australia.

Purpose: To evaluate visual outcomes of an “Inject and Extend” protocol of intravitreal anti-vascular endothelial growth factor treatment for patients with neovascular age-related macular degeneration (AMD) over 24 months.

Methods: 120 consecutive treatment-naive patients with active subfoveal choroidal neovascularization (CNV) secondary to AMD, who were treated with intravitreal ranibizumab or bevacizumab using an “Inject and Extend” protocol over 24 months at the Royal Victorian Eye and Ear Hospital in Australia, were recruited to this study. Each patient received three initial monthly injections. Follow-up visits and injections were continued until monthly intervals until there was no sign of CNV activity (subretinal or intraretinal fluid on optical coherence tomography, loss of ≥5 letters in best corrected visual acuity [BCVA] or persistent or recurrent haemorrhage). Thereafter, the interval to the next follow-up visit and re-treatment was extended by two weeks out to a maximum of 12 weeks if there was no sign of recurrent CNV activity. The 12 weekly injections were continued until the end of the study period as long as there was no recurrence of CNV activity. In the presence of one or more signs of CNV activity at any visit, an injection was administered and the interval to the next follow-up visit was shortened by two weeks (from the last interval). The main outcome measure was the mean change in BCVA after 12 and 24 months and the number of injections required.

Results: Mean (standard deviation [SD]) baseline BCVA was 51.2 (12.1) Early Treatment Diabetic Retinopathy Study letter scores. Mean (SD) change in BCVA from baseline was +9.5 (10.9) and +8.0 (12.9) letters after 12 and 24 months with, on average, 8.6 (SD, 1.1) injections and clinic visits in the first year and 5.6 (SD, 2.0) injections and clinic visits in the second year. After 12 and 24 months, 97.5% and 95.0% of patients lost fewer than 15 letters and 30.8% and 29.7% gained ≥15 letters from baseline, respectively.

Conclusions: The “Inject and Extend” protocol delivered visual outcomes comparable to those of the pivotal phase III clinical trials of monthly ranibizumab injections. This was achieved with a lower number of injections and clinic visits, reducing the risks and the treatment burden for patients, their carers and the health care providers.

Commercial Relationships: Farshad Abedi, None; Sanjeewa Wickramasinghe, Novartis (R); Amirul Islam, None; Kellie M. Inglis, None; Robyn H. Guymer, Ellex Pty Ltd (F), Novartis (C), Bayer (C), Novartis (R)

Support: National Health and Medical Research Council (NHMRC) project grants 590205 and 1008979, an NHMRC- Clinical Research Excellence grant 529923, NHMRC practitioner fellowship (RHG)

Program Number: 4175 Poster Board Number: A0093
Presentation Time: 8:30 AM - 10:15 AM

PROSPECTIVE RANDOMIZED CONTROLLED TRIAL OF COMBINATION RANIBIZUMAB AND KETOROLAC FOR WET AGE-RELATED MACULAR DEGENERATION

Optos (F), Carl Zeiss Meditec (F), Heidelberg Engineering (R), Genentech (C), Novartis (C), Novartis (R), Roche (R), Novartis (F)
Purpose: To evaluate the effect of intravitreal aflibercept on patients with neovascular age-related macular degeneration (AMD) that developed resistance to bevacizumab or ranibizumab treatment.

Methods: This is a consecutive interventional case series. Eyes that were treated with every four weeks (Q4W) bevacizumab or ranibizumab that did not respond to treatment were switched to aflibercept 2 mg (0.5 mL) every 8 weeks (Q8W) (no induction). Resistance was defined as multiple recurrences or persistence of intraretinal (IRF) or subretinal fluid (SRF). Imaging was performed monthly initially and semi monthly thereafter. We determined changes in visual acuity, and retinal thickness and area. A subgroup of patients was tested with the Vimetrics instrument, which is a time-based vision, contrast and glare acuity test with read out in ETDRS notation.

Results: Forty-one eyes of 34 patients were treated. The mean age was 80.1 years old (range, 67-90) and there were an equal number of males and females. Mean number of prior bevacizumab or ranibizumab injections was 17.5 (range, 2-39). Mean best-corrected visual acuity (BCVA) at baseline was 20/112.5 on ETDRS. Maximum retinal thickness at baseline was 452 μm which significantly improved to 330 μm at 1 month (p<0.001) and to 376 μm at 2 months (p=0.004) after an initial injection. Seventy-seven percent of eyes had good response (i.e. showing >90% resorption of SRF and IRF) at 1 month. All the rest except for 1 eye had evidence of response to the initial injection. Of the eyes that showed good response at 1 month, 61% remained stable and maintained the initial response at 2 months. Mean BCVA improved to 20/74 at 1 month post-injection and this was maintained at 2 months (20/79), with a corresponding improvement in contrast sensitivity.

Conclusions: Aflibercept is an effective treatment even in bevacizumab- or ranibizumab-resistant patients and even given at a pharmacokinetically equivalent dose to bevacizumab or ranibizumab (i.e. bevacizumab or ranibizumab Q4W and aflibercept Q8W). This suggests that the potency of aflibercept overcomes bevacizumab or ranibizumab resistance and that much of this resistance is due to inadequate anti-VEGF activity. We’re continuing to follow this cohort of patients with semi-monthly aflibercept injections and data on durability of response and need for more frequent injections will be present.

Commercial Relationships: Cheryl A. Arcinue, None; Feiyin Ma, None; Giulio Barteselli, None; Su-Na Lee, None; Sharif El-Emam, None; Aubrey L. Doede, None; Maria Laura Gomez, Viternis LLC (C); William Freeman, OD-OS, Inc. (C)

Program Number: 4176 Poster Board Number: A0094
Presentation Time: 8:30 AM - 10:15 AM
Aflibercept Rescue of Bevacizumab- or Ranibizumab-Resistant Choroidal Neovascularization in Age-Related Macular Degeneration

Cheryl A. Arcinue, Feiyin Ma, Giulio Barteselli, Su-Na Lee, Sharif El-Emam, Aubrey L. Doede, Maria Laura Gomez, William Freeman. Jacobs Retina Center, UCSD Shiley Eye Center, La Jolla, CA.

Purpose: To evaluate the effect of intravitreal aflibercept on patients with neovascular age-related macular degeneration (AMD) that developed resistance to bevacizumab or ranibizumab treatment.

Methods: This is a consecutive interventional case series. Eyes that were treated with every four weeks (Q4W) bevacizumab or ranibizumab that did not respond to treatment were switched to aflibercept 2 mg (0.5 mL) every 8 weeks (Q8W) (no induction). Resistance was defined as multiple recurrences or persistence of intraretinal (IRF) or subretinal fluid (SRF). Imaging was performed monthly initially and semi monthly thereafter. We determined changes in visual acuity, and retinal thickness and area. A subgroup of patients was tested with the Vimetrics instrument, which is a time-based vision, contrast and glare acuity test with read out in ETDRS notation.

Results: Forty-one eyes of 34 patients were treated. The mean age was 80.1 years old (range, 67-90) and there were an equal number of males and females. Mean number of prior bevacizumab or ranibizumab injections was 17.5 (range, 2-39). Mean best-corrected visual acuity (BCVA) at baseline was 20/112.5 on ETDRS. Maximum retinal thickness at baseline was 452 μm which significantly improved to 330 μm at 1 month (p<0.001) and to 376 μm at 2 months (p=0.004) after an initial injection. Seventy-seven percent of eyes had good response (i.e. showing >90% resorption of SRF and IRF) at 1 month. All the rest except for 1 eye had evidence of response to the initial injection. Of the eyes that showed good response at 1 month, 61% remained stable and maintained the initial response at 2 months. Mean BCVA improved to 20/74 at 1 month post-injection and this was maintained at 2 months (20/79), with a corresponding improvement in contrast sensitivity.

Conclusions: Aflibercept is an effective treatment even in bevacizumab- or ranibizumab-resistant patients and even given at a pharmacokinetically equivalent dose to bevacizumab or ranibizumab (i.e. bevacizumab or ranibizumab Q4W and aflibercept Q8W). This suggests that the potency of aflibercept overcomes bevacizumab or ranibizumab resistance and that much of this resistance is due to inadequate anti-VEGF activity. We’re continuing to follow this cohort of patients with semi-monthly aflibercept injections and data on durability of response and need for more frequent injections will be present.

Commercial Relationships: Cheryl A. Arcinue, None; Feiyin Ma, None; Giulio Barteselli, None; Su-Na Lee, None; Sharif El-Emam, None; Aubrey L. Doede, None; Maria Laura Gomez, Viternis LLC (C); William Freeman, OD-OS, Inc. (C)
Program Number: 4504
Presentation Time: 11:00 AM - 11:15 AM

Anti-VEGF Gene Therapy for Wet AMD: Safety and Tolerability of Subretinal Delivery in a Phase I/II Clinical Trial

Ian Constable1, 2, Cora Pierce3, Sendhil K. Somasundaram4, May Lai5, 6, 7, Thomas W. Chalberg5, Myra S. Blumenkrantz8, Richard Samulski4, Elizabeth P. Rakocy9, 10, 11, 12, 13. 1Centre for Ophthalmology and Visual Sciences, University of Western Australia, Perth, WA, Australia; 2Lions Eye Institute, Perth, WA, Australia; 3Avalanche Biotechnologies, San Francisco, CA; 4Byers Eye Institute at Stanford, Palo Alto, CA; 5Pharmacology and Gene Therapy Center, University of North Carolina, Chapel Hill, NC.

Purpose: To evaluate the safety and tolerability of extraveeal, subretinal injection in elderly patients for the delivery of an anti-VEGF gene therapy agent for wet age-related macular degeneration (wAMD).

Methods: One week after injection with ranibizumab, subjects underwent standard pars plana vitrectomy (PPV) followed by subretinal injection of 100 microliters of therapeutic agent. Subjects could elect either general (GA) or local (LA) anesthesia. Subretinal injection was performed using a commercially available 41g cannula, and documented using a high-definition AJA Ki Pro video system. The adeno-associated viral vector construct rAAV.sFlt-1 was designed to confer multiyear local production of sFlt-1, a potent, naturally occurring anti-VEGF protein. Local and systemic safety parameters were assessed in 12 treated plus 5 control subjects. Control patients had ranibizumab injections on an extend program with monthly OCT review.

Results: The mean age of patients was 79 years and the cohort had a wide range of pre-existing age-related diseases. Four patients had GA and 8 had parabulbar LA only. Vitrectomy was performed and posterior vitreous detachment (PVD) was confirmed in all patients. The therapeutic agent was delivered via a 41 G retinotomy in the superior retina near the vascular arcades, adjacent to but not including the fovea. Delivery was successfully documented in all 12 subjects. The induced bleb was transient, able to be visualized clinically and via optical coherence tomography (OCT) at 2 hours, but invisible by 24 hours post injection. There were no serious surgical complications such as endophthalmitis, retinal tears, or detachments. All subjects tolerated the procedure well. There was no evidence of local or systemic toxicity. Adverse events were minor, not visually significant, and consistent with standard vitrectomy with PVD induction. No drug-related adverse events were observed.

Conclusions: PPV with extraveeal subretinal injection is a straightforward procedure that is compatible with parabulbar LA. Whereas a similar approach has been used for children and young adults undergoing gene therapy for retinal dystrophy, we show here that subretinal injection is well-tolerated by elderly patients with wAMD. Transfection of the retinal cells with subretinal rAAV.sFlt-1 may provide a promising strategy for long-term anti-VEGF therapy following a single procedure.

Commercial Relationships: Ian Constable, Lions Eye Institute (P), Avalanche Biotechnologies (C); Cora Pierce, None; Sendhil K. Somasundaram, None; May Lai, Lions Eye Institute (P); Thomas W. Chalberg, Avalanche Biotechnologies, Inc. (E), Avalanche Biotechnologies, Inc. (I), Avalanche Biotechnologies, Inc. (P), Avalanche Biotechnologies, Inc. (S); Mark S. Blumenkrantz, avalanche biotechnologies (I), avalanche biotechnologies (P), optimedia (I); Richard Samulski, Asklepios BioPharmaceutical, Inc. (I); Elizabeth P. Rakocy, Avalanche Biotechnologies (C), Lions Eye Institute (P)

Support: National Health and Medical Research Council of Australia Clinical Trial: NCT01494805

Program Number: 4505
Presentation Time: 11:15 AM - 11:30 AM

Phase I, Masked, Placebo-Controlled, Single and Multiple Ascending Intravenous Dose Studies Evaluating Systemic and Ocular Safety, Tolerability, and Visual Acuity Effects of RN6G (PF-04382923) in Subjects with Dry, Age-Related Macular Degeneration (ARMD)

Brian B. Berger1, Pamela D. Garzzone2, Ivana Gunderson1, Philip M. Fanning2, Gilbert Wong2, Kai H. Liao2, Steven Y. Hua2, John Lin2. 1Retina Research Center, Austin, TX; 2Pfizer Inc., South San Francisco, CA.

Purpose: To examine the safety (systemic and ocular) and tolerability of single and multiple ascending intravenous (IV) doses of RN6G (PF-04382923), a humanized IgG2a monoclonal antibody and to explore the effects of RN6G on best corrected visual acuity (BCVA) by ETDRS, low luminance BCVA (LLBCVA) and contrast sensitivity (CS).

Methods: In the Phase 1, first-in-human (FIH) study, 54 adult men and women with dry ARMD were assigned to a cohort (n=9) and randomized to receive either a single intravenous (IV) dose of RN6G (0.3 mg/kg to 40 mg/kg) or placebo (PBO), 2:1 ratio of active drug to PBO, within a cohort. Safety, BCVA, and LLBCVA were done at specified intervals with the last observation at week 24. In the multiple ascending dose (MAD) study, 24 adult men and women with advanced dry ARMD or geographic atrophy were enrolled into one of 3 cohorts (5 mg/kg, 10 mg/kg, or 15 mg/kg) and were randomized to active drug or PBO (3:1). Six IV treatments were administered monthly followed by safety observations over five months. BCVA, LLBCVA and CS were tested monthly through week 44.

Results: In the FIH study, 45 subjects (83.3%) had at least one treatment (Tx) emergent adverse event (TEAE); 28 subjects (51.9%) had at least one AE related to Tx. Headache was the most common AE followed by iritis. There was no dose response in either frequency or severity of AEs. All systemic and ocular AEs observed were considered mild to moderate in severity. There were no withdrawals due to AEs. One serious AE (SAE) unrelated to Tx was reported. BCVA was reduced in 2 subjects; 1 received RN6G and 1 received PBO. In the MAD study, 94% (17/18) of subjects receiving RN6G and 100% (6/6) receiving PBO reported TEAEs. The most frequently reported systemic TEAEs were infections (38%) and nervous system disorders (29%). Ocular TEAEs were reported in 58% of subjects and blepharitis was the most frequently reported TEAE. Preliminary BCVA, LLBCVA, and CS results were unchanged. Two SAEs that were considered not related to Tx were reported.

Conclusions: RN6G (PF-04382923) was safe and well tolerated by all subjects in Phase I. No effects on BCVA, LLBCVA or CS were observed. Based on the safety and tolerability profile, a Phase II study was initiated in July 2012.

Commercial Relationships: Brian B. Berger, Allergan Incorporated (F), Alcon Laboratories (F), Diabetic Retinopathy Clinical Research Network (F), Glaxo Smith Kline (F), Iconic Therapeutics (F), Lpath Incorporated (F), Lux Biosciences (F), Genentech (F), NeoVista Pharmaceuticals (F), Pfizer Incorporated (F), Thrombogenics (F), Allergan Advisory Panel (C), Alimera Sciences Advisory Panel (C), LuxBiosciences Advisory Board (C); Pamela D. Garzzone, Pfizer (E); Ivana Gunderson, None; Philip M. Fanning, Pfizer (E); Gilbert Wong, Pfizer, Inc (E); Kai H. Liao, Pfizer Inc (E); Steven Y. Hua, Pfizer, Inc. (E); John Lin, Pfizer (E)

Clinical Trial: NCT01003691

Program Number: 4506
Presentation Time: 11:30 AM - 11:45 AM

Clinical Trial: NCT01494805

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A Phase 2 Double-masked, Placebo-controlled, Dose Ranging Study of Emixustat Hydrochloride (ACU-4429) in Subjects with GA Associated with Dry AMD

Pravin U. Dugel1, Roger L. Novack2, Karl G. Csaky2, Preston P. Richmond2, David G. Birch2, Ryo Kubota1. 1Retinal Consultants of Arizona, Ltd, Phoenix, AZ; 2Retina-Vitreous Associates Medical Group, Beverly Hills, CA, Beverly Hills, CA; 3Texas Retina Associates, Dallas, TX, Dallas, TX; 4Central Florida Retina, Orlando, FL, Orlando, FL; 5Retina Foundation of Southwest, Dallas, TX, Dallas, TX; 6Acucela Inc., Seattle, WA, Seattle, WA.

Purpose: Emixustat HCl is a novel orally administered agent in clinical development for the treatment of geographic atrophy (GA) associated with dry age-related macular degeneration (AMD). Emixustat HCl acts as a rod visual cycle modulator by inhibiting isomerase (RPE65) activity and reducing retinal toxins (eg, A2E) that damage the RPE and overlying photoreceptors. The purpose of the study was to assess the biologic activity and safety of emixustat in subjects with GA compared with placebo. Four dose levels (2, 5, 7, and 10 mg) and 2 dose regimens (AM and PM dosing) were evaluated.

Methods: Subjects (n=72) were randomly assigned to emixustat HCl (2, 5, 7 or 10 mg AM, or 5 mg PM) or placebo orally daily for up to 90 days in a 3:1 ratio. Adverse events and other safety parameters were collected. After 30 min of dark adaptation, ERGs were recorded, then eyes were photo bleached and ERGs were recorded immediately and at 10, 20, and 30 min. Rod b-wave amplitudes were expressed as a percentage of the prebleach dark-adapted rod amplitude from baseline. The rate of rod recovery (slope) for each emixustat HCl group was compared to the placebo group.

Results: Emixustat HCl suppressed ERG b-wave rod recovery after light exposure in a dose-related manner. Suppression plateaued by Day 14 of dosing, and reversed within 7-14 days after cessation. No systemic adverse events (AEs) of concern were noted. Choromatosia and delayed dark adaptation were the most common ocular AEs. There were 2 subjects with a treatment-related serious AE (both were moderate chromatopsia; at 5 mg). All ocular AEs resolved upon drug cessation; most events were mild and no severe events were observed.

Conclusions: This proof of concept study demonstrated a dose-dependent biologic effect and emixustat’s ability to modulate the visual cycle. Despite oral dosing, systemic adverse events were minimal. The common ocular AEs are explainable based on the understood mechanism of action. Results suggest that emixustat HCl has the potential to be a useful agent in the treatment of geographic atrophy associated with dry AMD. A long-term Phase 2b/3 study is underway to evaluate emixustat HCl in GA subjects.

<table>
<thead>
<tr>
<th>Placebo</th>
<th>2 mg AM</th>
<th>5 mg AM</th>
<th>5 mg PM</th>
<th>7 mg AM</th>
<th>10 mg AM</th>
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<tr>
<td>N=48</td>
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<td>N=11</td>
<td>N=11</td>
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<tr>
<td>Rate of Recovery (slope)</td>
<td>2.6%</td>
<td>1.77</td>
<td>0.99</td>
<td>0.96</td>
<td>0.89</td>
</tr>
<tr>
<td>% Suppression*</td>
<td>34%</td>
<td>63%</td>
<td>64%</td>
<td>67%</td>
<td>90%</td>
</tr>
</tbody>
</table>

*[(slope of placebo - slope of emixustat HCl)]/[slope of placebo] × 100

Note: Total sample size = 72; only 68 subjects are presented due to 1 subject in each of the 5 mg AM, 5 mg PM, 7 mg AM and 10 mg AM groups having missing data.

ERG b-wave Rod Recovery vs Placebo - Day 14

Commercial Relationships: Pravin U. Dugel, Abbott (C), Allcon (C), Allergan (C), Artic Dx (C), Alimera Sciences (C), Acucela (C), Digisight (C), Genentech (C), LUX (C), Macusight (C), Neovista (C), ORA (C), Ophthotech (C), Regeneron (C), Thomobogens (C); Roger L. Novack, Genentech (R), Acucela (F), Thomobogens (F);

Karl G. Csaky, Genentech (F), Acucela (C), QLT (C), Pfizer (C), Regeneron (C), Santen (C), Ophthotech (C), Thomobogens (C); Preston P. Richmond, None; David G. Birch, Acucela (C), QLT (C), Neurotech, USA (C); Ryo Kubota, Acucela Inc. (I), Acucela Inc. (E), Acucela Inc. (P)

Clinical Trial: NCT01002950

Program Number: 4507
Presentation Time: 11:45 AM - 12:00 PM
Photodynamic Therapy vs Combination Therapy in Polypoidal Choroidal Vasculopathy: Changes of Aqueous Vascular Endothelial Growth Factor

Meeyon Lee1, Won Ki Lee2. 1Chung ang University hospital, Seoul, Republic of Korea; 2Seoul St. Mary hospital, Seoul, Republic of Korea.

Purpose: To investigate the influence of photodynamic therapy (PDT) and combination of PDT and ranibizumab on aqueous humor levels of vascular endothelial growth factor (VEGF) in polypoidal choroidal vasculopathy (PCV).

Methods: Prospective, randomized clinical trial. We included twenty eyes with treatment-naive PCV and 20 eyes undergoing cataract surgery as controls. Eyes with PCV were randomized to treatment with PDT alone or to a combination of ranibizumab and PDT on same day. During 3 months of follow-up, retreatment was not performed. Aqueous humor samples were collected at baseline and at 1 week, 1 month and 3 months after treatment in PCV group and during cataract surgery in the control group. VEGF levels were measured using multiplex bead immunoassay.

Results: At baseline, concentrations of VEGF were significantly increased in PCV eyes compared with control eyes. A significant decrease in VEGF levels were found at 1 week after PDT treatment (n=8), and at all time points after combination treatment (n=12). With combination treatment, VEGF levels were decreased to values below the detection limit in all eyes at 1 week and 1 month, and in 7 of 12 eyes at 3 months.

Conclusions: Decreased levels of VEGF detected 1 week after PDT for PCV seems to reflect acute damage of vascular endothelial cells, one of VEGF expression sites. Concomitant ranibizumab resulted in a further decrease in VEGF expression to negligible levels. This effect persisted for at least 1 month and as long as 3 months in more than half of the cases.

Commercial Relationships: Meeyon Lee, None; Won Ki Lee, Novartis (F), Novartis (C), Bayer (C)

Support: This article was supported by funding from NOVARTIS KOREA, Seoul, Korea. The sponsor or funding organization had no role in the design or conduct of this research.

Clinical Trial: NCT 01360151

Program Number: 4508
Presentation Time: 12:00 PM - 12:15 PM
Twelve Months Results Comparing Ranibizumab or Bevacizumab Treatment in Patients with Neovascular Age-related Macular Degeneration(AMD) Multicenter Anti-VEGF Trial in Austria The Manta Study

Susanne Binder1, Ilse Krebs2, Leopold Schnatterer2.
1Ophthalmology, Rudolf Foundation Clinic, Vienna, Austria; 2Department of Clinical Pharmacology, Medical University, Vienna, Austria.

Purpose: Report of an observer and subject masked trial comparing the visual outcome after treatment with Ranibizumab or Bevacizumab in patients with neovascular age-related macular degeneration

Methods: Non inferiority study based on the Data of MARINA,
ANCHOR and FOCUS studies. 320 patients with NV AMD included and randomized to either Bevacizumab or Ranibizumab treatment. Three initial monthly injections with either 0.5mg ranibizumab(Lucentis*, Novartis) or 1.25 mg bevacizumab(Avastin *, Genentech). Retreatment if: VA loss a minimum of 5 letters, increase of central retinal thickness of more than 100µm (optical coherence tomography (OCT)), fresh intra-or sub retinal hemorrhage, new classic CNV, persistent intra retinal fluid (OCT+FA).

**Results:** 321 patients were randomized, 4 excluded (1 had previous anti-VEGF treatment, 3 received wrong drug), so that a total of 317 eyes were evaluated. Mean age, sex, baseline BCVA and central retinal thickness was comparable in both groups. BCVA after one year was equivalent between bevacizumab (highest gain 6.2 letters after 4 months and 4.9 letters after 12 months) and ranibizumab (highest gain 5.8 letters after 3 months and 4.1 letters after 12 months). The two drugs were also not different when adjusted for age and baseline BCVA. Mean number of treatments was also similar: 5.8x in the ranibizumab group and 6.1x in the bevacizumab group. Adjusted retinal thickness measurements showed also similar reductions over one year (decrease of 89.9µm for ranibizumab and 86.3µm for bevacizumab, p=0.81). Lesion size did decrease in both groups equally (p= 0.55). Serious adverse events were observed in 9.2% in the ranibizumab group and in 11.6% in the bevacizumab group. Also NR of death (2 resp3), cardiac disorders as well as gastrointestinal disorders were comparable. No serious ocular event (endophthalmitis, pseudoendophthalmitis) did occur in both groups.

**Conclusions:** Bevacizumab was equivalent to ranibizumab at all time points for one year. Neither the total number nor the number of adverse events in any subgroup was sign. different.

**Commercial Relationships:** Susanne Binder, None; Ilse Krebs, None; Leopold Schmetterer, None

**Support:** The study was assigned and financed by the Austrian Ophthalmologic Society

**Clinical Trial:** NCT00710229

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**426 Macular Disease other than AMD II**

Wednesday, May 08, 2013 11:00 AM-12:45 PM

6E Paper Session

**Program #/Board # Range:** 4510-4516

**Organizing Section:** Retina

**Program Number:** 4510

**Presentation Time:** 11:00 AM - 11:15 AM

**Occult Central Serous Chorioretinopathy**

K Bailey Freund1,2, David Warrow3, Roberto Gallego-Pinazo1,5, Quan V. Hoang1,1, Ophthalmology, Vitreous Retina Macula Consultants New York, New York, NY; 2Ophthalmology, New York University, New York, NY; 3Ophthalmology, Columbia University, New York, NY; 4Ophthalmology, University and Polytechnic Hospital La Fe, Valencia, Spain

**Purpose:** To describe the clinical and multi-modal imaging findings of a new variant of central serous chorioretinopathy: occult central serous chorioretinopathy (OCSC).

**Methods:** Retrospective review of the clinical histories and multi-modal imaging findings of patients with the diagnosis of OCSC based on a characteristic funduscopy appearance, fundus autofluorescence (FAF) imaging abnormalities, and increased subfoveal choroidal thickness as measured with enhanced depth imaging optical coherence tomography (EDI-OCT).

**Results:** Fourteen eyes of 7 patients (5 females and 2 males; age: 27-89 years) were diagnosed with OCSC. Each patient had mild or no visual symptoms. The funduscopy appearance was characteristic in all cases with either diffuse or focal areas of decreased choroidal vascular markings suggestive of increased choroidal thickness, that was confirmed with EDI-OCT (mean subfoveal choroidal thickness = 462.6 microns). Each patient demonstrated a variety of drusenoid and pigmentary changes in the macula of one or both eyes with occasional small serous retinal pigment epithelial detachments (PED) detectable only on OCT. No subjects had a history of, or subsequently developed, macular edema or subretinal fluid over the course of follow-up, and patients showed mean vision improvement over the follow-up period (16-192 months).

**Conclusions:** OCSC should be suspected in patients with a
Results: Immunocytochemistry studies showed no effect of somatostatin on expression of Occludin and Zonula Occludens-1 under both hypoxic and normoxic conditions. However, mRNA expression of Occludin, Zonula Occludens-1 and urokinase plasminogen activator receptor was increased (twofold, p<0.001, threefold, p<0.001 and threefold, p<0.001, respectively) under normoxic conditions. We did not observe any effect of vascular endothelial growth factor on tight junctions and urokinase plasminogen activator receptor expression in both immunocytochemistry and real-time PCR studies. Exposure to both vascular endothelial growth factor and somatostatin neither showed any effect.

Conclusions: Our results suggest that somatostatin may contribute to decrease permeability through the external blood retinal barrier by enhancing components of the tight junctions. Hence, a decrease in somatostatin activity may contribute to macular edema development, at least in retinal diseases in which ischemia is not a predominant event.

Commercial Relationships: Alex Fonollosa, None; Joseba Artaraz, None; Agustin Martinez-Berriotxoa, None; Elena Vecino, None

Program Number: 4512
Presentation Time: 11:30 AM - 11:45 AM
Selective Laser Photocoagulation of Peripheral Non-perfused Retinal Areas May Improve the Vision in Patients with Central Retinal Vein Occlusion Treated with Ranibizumab
Matus Rehak1∗, Annegret Franke1, Peter M. Wiedemann1.
1Department of Ophthalmology, University of Leipzig, Leipzig, Germany; 2Clinical Trial Centre (ZKS) Leipzig, University of Leipzig, Leipzig, Germany.

Purpose: To evaluate the efficacy and safety of the combination of intravitreal injections of ranibizumab and selective laser photocoagulation of peripheral retinal areas of capillary non-perfusion in patients with macular edema due to central retinal vein occlusion (CRVO).

Methods: The prospective, proof-of-concept study randomized 22 CRVO patients into 2 arms. The experimental group (ranibizumab+laser; n=10) received intravitreal ranibizumab with additional laser photocoagulation; the control group (n=12) was treated with ranibizumab only. All patients received 3 initial ranibizumab injections (loading phase) followed with the pro re nata (PRN) regimen according to pre-defined criteria. The changes in the Best Corrected Visual Acuity (BCVA) using the ETDRS charts (primary endpoint) and central retinal thickness (CRT) were documented until 10 months after randomization. Means/ medians of the between-group differences with corresponding 95% confidence limits were estimated. Furthermore, the proportion of subjects with neovascularizations developed and the number and kind of adverse events (AEs) were evaluated.

Results: Patients treated with ranibizumab and laser improved from BCVA=61.6±12.7 ETDRS letters at baseline to 72.5±11.5 letters on month 10. In the control group improvement from 58.6±12.4 to 64.5±17.2 ETDRS letters was observed. CRT decreased between baseline and 10 months’ visit in the experimental group from 560.6±247.4 µm to 267.4±93.7 µm and in the control group from 696.0±212.9 µm to 282.5±175.0 µm. More pronounced improvements were seen in the experimental group.

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in BCVA change were seen in the index arm in descriptive statistics although all observed group differences were not significant due to small samples. No patient in the experimental group and 2 patients in the control arm developed neovascularizations of retina requiring the rescue scatter laser photocoagulation. **Conclusions:** The selective laser photocoagulation of peripheral areas of capillary non-perfusion seems to lead to additional visual improvement in patients with CRVO treated with ranibizumab. A replication trial with larger patient samples is necessary to enhance existing evidence and confirm the results of this proof-of-concept study.

**Commercial Relationships:** Matus Rehak, Novartis Pharma (F); Annegret Franke. None; Peter M. Wiedemann, Novartis (F), Bayer (F), Novartis (R), Bayer (R)

**Support:** German Federal Ministry for Education and Research (Grant Nr: DLR-KKZ-01KN0702)

**Clinical Trial:** EudraCT-No.: 2010-020441-27

**Program Number:** 4513

**Presentation Time:** 11:45 AM - 12:00 PM

**Macular Bruchs Membrane Defects and Axial Length:**

**Association with Gamma Zone and Delta Zone in Peripapillary Region**

Joscht B. Jonas¹, Kyoko Ohno-Matsui², Richard F. Spaide³, Leonard Holbach³, Songhomitra Panda-Jonas⁴. ¹Ophthalmology, Medical Faculty Mannheim-Heidelberg, Mannheim, Germany; ²Department of Ophthalmology and Visual Science, Tokyo Medical and Dental University, Tokyo, Japan; ³Vitreous-Retina-Macula Consultants of New York and the LuEsther T. Mertz Retinal Research Center, Manhattan Eye, Ear, and Throat Hospital, New York, NY; ⁴Department of Ophthalmology, Friedrich-Alexander University Erlangen-Nürnberg, Erlangen, Germany.

**Purpose:** To examine histomorphometrically the macular region of highly myopic eyes.

**Methods:** On horizontal anterior-posterior histological sections, we examined the region of the macula and optic nerve head of 138 human globes (axial length:20-35mm). In the parapapillary region, we differentiated between beta zone (Bruchs membrane without retinal pigment epithelium (RPE)), gamma zone (parapapillary region without Bruchs membrane), and delta zone (elongated and thinned gamma zone).

**Results:** In 12 (8.7%) eyes, a macular Bruchs membrane defect (MBMD) was detected. The MBMD showed a complete lack of RPE and choriocapillaris, and an almost complete lack of photoreceptors. Presence of MBMD was associated with longer axial length (P<0.001), longer gamma zone (P=0.04) and delta zone (P<0.001), thinner peripapillary scleral flange, and lower thickness of the sclera just outside of the optic nerve meninges (P<0.001) and at the posterior pole (P<0.001). A MBMD was found only in eyes with an axial length of ≥27 mm. Presence of a MBMD was not significantly related to length of beta zone of parapapillary atrophy (P=0.09). In multivariate binary regression analysis, MBMD presence was significantly (P<0.001) associated only with axial length.

**Conclusions:** Highly myopic eyes (axial length ≥27mm) can show a MBMD associated with complete loss of RPE and choriocapillaris, and marked reduction of photoreceptors and large choroidal vessels. MBMD presence was strongly associated with axial length and indirectly with parapapillary gamma zone and delta zone. The myopia associated secondary MBMDs may occur parallel to the myopia associated widening of Bruchs membrane opening around the optic nerve head.

**Commercial Relationships:** Joscht B. Jonas, Allergan (C), MSD (C), Alimera (C), CellMed AG (P); Kyoko Ohno-Matsui. None; Richard F. Spaide, Topcon (P), Thrombogenics (C), Bausch and Lomb (C); Leonard Holbach. None; Songhomitra Panda-Jonas. None

**Program Number:** 4514

**Presentation Time:** 12:00 PM - 12:15 PM

**Treatment Experience with Intravitreal Aflibercept Injection (IAI) After Switching to PRN Dosing in Patients with Macular Edema Secondary to Central Retinal Vein Occlusion (CRVO)**

David M. Brown¹, Frank G. Holz². ¹Retina Consultants of Houston, Houston, TX; ²Department of Ophthalmology, University of Bonn, Bonn, Germany.

**Purpose:** The 52-week results of COPERNICUS and GALILEO studies demonstrated that visual and anatomical improvements after six monthly IAI at week 24 were largely maintained at week 52 following switching to PRN dosing. This analysis evaluated the treatment experience between weeks 24 and 52.

**Methods:** Two double-masked, multicenter, phase 3 trials (COPERNICUS and GALILEO) randomized patients to receive either IAI 2 mg or sham every 4 weeks up to week 24. In COPERNICUS, all patients received IAI pro re nata (PRN) from week 24 to week 52. In GALILEO, the IAI group received IAI PRN from week 24 through week 52, and the sham group continued to receive monthly sham injections through week 52. Treatment experience was evaluated in patients who received IAI from baseline.

**Results:** In COPERNICUS, IAI patients (n = 110) received a mean (SD) of 2.7 ± 1.7 injections (range: 0–7) from week 24 to 52. Percentages of patients who had ≤ 3 or ≥ 4 injections were 70.9% and 29.1% respectively. Thirty-two patients (29.1%) received IAI at week 24 and had a mean (SD) of 4.1 ± 1.6 injections (range: 1–7) from week 24 to 52 while 78 patients (70.9%) did not require IAI at week 24 and had a mean (SD) of 2.1 ± 1.3 injections (range: 0–6) from week 24 to 52. In GALILEO, IAI patients (n = 97) received a mean (SD) of 2.5 ± 1.7 injections (range: 0–6) from week 24 to 52. Percentages of patients who had ≤ 3 or ≥ 4 injections were 72.2% and 27.8%, respectively. Nineteen patients (19.6%) received IAI at week 24 and had a mean (SD) of 3.8 ± 1.8 injections (range: 1–6) from week 24 to 52 while 78 patients (80.4%) did not require IAI at week 24 and had a mean (SD) of 2.1 ± 1.6 injections (range: 0–6) from week 24 to 52. The most frequent ocular serious adverse events were macular edema and vitreous hemorrhage.

**Conclusions:** Across both studies, over 70% of patients received ≤ 3 injections during PRN dosing. Most patients (> 70%) did not receive IAI at week 24. Patients who did not receive IAI at week 24 had fewer injections during PRN dosing than those who received IAI at week 24.

**Commercial Relationships:** David M. Brown, Regeneron Pharmaceuticals, Inc. (F), Regeneron Pharmaceuticals, Inc. (C), Regeneron Pharmaceuticals, Inc. (R), Bayer HealthCare (F), Bayer HealthCare (C), Bayer HealthCare (R), Genentech (C), Roche (C), Alimera (C), Alcon (C), Novartis (C), Thrombogenics (C), Genentech (F), Roche (F), Thrombogenics (F), GSK (F), Alimera (F), Alcon (F), Allergan (F), Eli Lilly (F); Frank G. Holz. Acucela (C), Allergan (C), Genentech (F), Heidelberg Engineering (F), Zeiss (F), Novartis (F), Novartis (C), Optos (F), Merz (C), Bayer (F), Bayer (C), Boehringer Ingelheim (C)

**Support:** Regeneron Pharmaceuticals, Inc., and Bayer HealthCare

**Clinical Trial:** NCT00943072

**Program Number:** 4515

**Presentation Time:** 12:15 PM - 12:30 PM

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Two-Year Results of the COPERNICUS Study Evaluating Intravitreal Aflibercept Injection (IAI) for Macular Edema Secondary to Central Retinal Vein Occlusion (CRVO)

W. Lloyd Clark, Palmetto Retina Center, West Columbia, SC.  

Purpose: To evaluate the efficacy and safety of IAI for treatment of macular edema due to CRVO.  

Methods: This double-masked, multicenter, 2-year, phase 3 trial randomized CRVO patients with macular edema to receive either IAI 2 mg (IAI 2q4) (n = 115) or sham (n = 74) injections every 4 weeks up to week 24. From week 24 to 52, all patients were evaluated monthly and received IAI pro re nata (PRN) (IAI 2q4-PRN) and sham-IAI PRN. From week 52 to week 100, patients were evaluated quarterly to receive IAI PRN. If needed, patients could receive IAI as frequently as every 4 weeks. The primary efficacy endpoint was the proportion of patients who gained ≥ 15 letters at week 24.  

Results: The proportion of patients who gained ≥ 15 letters was 56.1% vs 12.3% (P < .001) at week 24, 55.3% vs 30.1% (P < .001) at week 52, and 49.1% vs 23.3% (P < .01) at week 100 in the IAI 2q4-PRN and sham-IAI PRN groups, respectively. The mean change from baseline visual acuity was +17.3 vs -4.0 letters (P < .001) at week 24, +16.2 vs +3.8 (P < .001) at week 52, and +13.0 vs +15.5 letters at week 100 in the IAI 2q4-PRN and sham-IAI PRN groups. The mean reduction from baseline central retinal thickness was 457.2 vs 144.8 µm (P < .001) at week 24, 413.0 vs 381.8 µm at week 52, and 390.0 vs 343.3 µm at week 100 in the IAI 2q4-PRN and sham-IAI PRN groups. The mean (SD) number of PRN IAI injections was 2.7 (1.7) vs 3.9 (2.0) from week 24 to 52 and 6.0 (3.4) vs 7.1 (3.4) from week 24 to 100 in the IAI 2q4-PRN and sham-IAI PRN groups, respectively. Over the 100 weeks, the most frequent ocular serious adverse events in the IAI 2q4-PRN and sham-IAI PRN groups were vitreous hemorrhage (0.9% vs 6.8%), glaucoma (0% vs 4.1%), and cataract (3.5% vs 1.4%). Antiplatelet Trials’ Collaboration arterial thromboembolic events occurred in 2 (1.8%) IAI2q4-PRN patients (nonfatal) from baseline to week 100, and in 2 (2.7%) sham patients (fatal) from baseline to week 24.  

Conclusions: The visual and anatomic improvements observed at the end of the fixed dosing period were diminished after changing to PRN dosing with a reduced monitoring frequency from Week 52 to 100. IAI was generally well tolerated.

Commercial Relationships: Yuichiro Ogura, None. Jean-Francois Korobelnik, Alcon (C), Allergan (C), Bayer (C), Carl Zeiss Meditec (C), Novartis (C), Thea (F); Johann Roider, Novartis (F), Bayer (F); Robert Vitti, None. Frank G. Holz, Acucela (C), Allergan (C), Genentech (F), Heidelberg Engineering (F), Zeiss (F), Novartis (F), Novartis (C), Optos (F), Merz (C), Bayer (F), Bayer (C), Boehringer Ingelheim (C); Florian Hiemeyer, Bayer AG (E), Bayer AG (I); Brigitte Stempel, Bayer Pharma (E); Oliver Zeitz, Bayer HealthCare (E); Rupert Sandbrink, Bayer HealthCare (E), Bayer HealthCare (I)  

Support: Study sponsored by Regeneron and Bayer  

Clinical Trial: NCT01012973

Program Number: 4516  

Presentation Time: 12:30 PM - 12:45 PM  

Eighteen-Month Results of the GALILEO Study Evaluating Intravitreal Aflibercept Injection (IAI) for Macular Edema Secondary to Central Retinal Vein Occlusion (CRVO)

Yuichiro Ogura, Jean-Francois Korobelnik, Johann Roider, Robert Vitti, Frank G. Holz, Florian Hiemeyer, Brigitte Stempel, Oliver Zeitz, Rupert Sandbrink.  

1Department of Ophthalmology, Nagoya City University Medical School, Nagoya, Japan; 2Department of Ophthalmology, CHU Bordeaux, Universite Bordeaux, Bordeaux, France; 3Department of Ophthalmology, University Medical Center Schleswig-Holstein, Kiel, Germany; 4Regeneron Pharmaceuticals Inc., Tarrytown, NY; 5Department of Ophthalmology, University of Bonn, Bonn, Germany; 6Bayer Healthcare, Berlin, Germany.  

Purpose: To evaluate the efficacy and safety of IAI for treatment of macular edema due to central retinal vein occlusion (CRVO).  

Methods: This double-masked, multicenter, 18-month, phase 3 trial randomized patients to receive either IAI 2 mg (IAI 2q4) (n=106) or sham (n=71) injections every 4 weeks up to Week 24. From Week 24 to 52, IAI patients were evaluated monthly and received IAI pro re nata (PRN) (IAI 2q4-PRN), and sham patients continued to receive monthly sham injections. From Week 52 to Week 76, all patients were evaluated every 8 weeks and received IAI PRN (IAI 2q4-PRN and sham-IAI PRN). The primary efficacy endpoint was the proportion of patients who gained ≥15 letters at Week 24.  

Results: The proportion of patients who gained ≥15 letters was 60.2% vs 22.1% at Week 24 (P<0.0001), 60.2% vs 32.4% (P=0.0004) at Week 52, and 57.3% vs 29.4% at Week 76 (P<0.01) in the IAI 2q-4PRN and sham-IAI PRN groups, respectively. The mean increase from baseline visual acuity was 18.0 vs 3.3 letters (P<0.0001) at Week 24, 16.9 vs 3.8 letters (P<0.0001) at Week 52, and 13.7 vs 6.2 letters at Week 76 in the IAI 2q4-PRN and sham-IAI PRN groups. The mean reduction from baseline central retinal thickness was 448.6 vs 169.3 µm (P<0.0001) at Week 24, 423.5 vs 219.3 µm (P<0.0001) at Week 52, and 389.4 vs 306.4 µm at Week 76 in the IAI 2q4-PRN and sham-IAI PRN groups. The mean (SD) number of PRN IAI injections was 2.5 (1.7) in the IAI 2q4-PRN group from Weeks 24 to 52, and 1.3 (1.1) vs 1.7 (1.1) injections in the IAI 2q4-PRN and sham-IAI PRN groups, respectively, from Weeks 52 to 76. Over the 76 weeks, the most frequent ocular serious adverse events in the IAI 2q4-PRN and sham-IAI PRN groups were macular edema (3.8% vs 2.9%), glaucoma (0% vs 2.9%), reduced visual acuity (1.9% vs 1.5%), and vitreous hemorrhage (1.0% vs 1.5%). No Antiplatelet Trials’ Collaboration-defined arterial thromboembolic events occurred during the study.  

Conclusions: The visual and anatomic improvements observed at the end of the fixed dosing period were diminished after changing to PRN dosing with a reduced monitoring frequency from Week 52 to 76. IAI was generally well tolerated.  

Commercial Relationships: Yuichiro Ogura, None. Jean-Francois Korobelnik, Alcon (C), Allergan (C), Bayer (C), Carl Zeiss Meditec (C), Novartis (C), Thea (F); Johann Roider, Novartis (F), Bayer (F); Robert Vitti, None. Frank G. Holz, Acucela (C), Allergan (C), Genentech (F), Heidelberg Engineering (F), Zeiss (F), Novartis (F), Novartis (C), Optos (F), Merz (C), Bayer (F), Bayer (C), Boehringer Ingelheim (C); Florian Hiemeyer, Bayer AG (E), Bayer AG (I); Brigitte Stempel, Bayer Pharma (E); Oliver Zeitz, Bayer HealthCare (E); Rupert Sandbrink, Bayer HealthCare (E), Bayer HealthCare (I)  

Support: Study sponsored by Regeneron and Bayer  

Clinical Trial: NCT01012973

Program Number: 4898  

Presentation Time: 11:00 AM - 12:45 PM  

Organizing Section: Retina

Program #/Board # Range: D0337-D0355  

446 Imaging I, RE  

Wednesday, May 08, 2013 11:00 AM-12:45 PM  

Exhibit Hall Poster Session

Program Number: 4898  

Poster Board Number: D0337

Presentation Time: 11:00 AM - 12:45 PM

Qualitative and quantitative changes of cystoid macular edema treated with Ozurdex therapy

Raeba Mathew, Elizabeth Pearce, Sobha Sivaprasad.  

1Ophthalmology, King’s College Hospital, London, London, United Kingdom; 2Ophthalmology, Moorfields Eye Hospital, London, United Kingdom.  

Purpose: To describe progression, resolution and relapse of cystoid macular edema (CME) over 9 months following Ozurdex therapy, to
understand the prognostic values of various morphological features of CME.

**Methods:** Twenty-eight eyes with cystoid macular edema were examined at monthly intervals to assess the resolution and relapse of macular edema following Ozurdex therapy in a prospective study. The quantitative measures included central retinal thickness (CRT), central subfield thickness (CST), macular volume, number of zones with >300um, the foveal, parafoveal and perifoveal distribution of edema at monthly intervals. The qualitative measures included the presence, resolution and reappearance of cysts in different layers at each time points. Other structural changes included the persistence of foveal ellipsoid layer and external limiting membrane. Applying repeated-measures ANOVA, morphological findings were evaluated as predictive factors for relapse free period and treatment outcome.

**Results:** At baseline, all patients presented with cystoid edema. 60.7% had both outer nuclear layer/Henle’s-layer (ONL/HL), 21% had ONL cysts only and the rest had only inner nuclear layer (INL) cysts. Following Ozurdex therapy, ONL/HL-cysts diminished before INL-cysts (p=0.0008). Subretinal fluid disappeared in all cases by 3 months and recurrence in these cases were dominated by INL cysts. Subretinal fluid recurred in 31% of cases. SRD at baseline predicted a relapse-free clinical-course within the 9 months period (p=0.025).

**Conclusions:** Different morphologic patterns in CME resolve and relapse at different time-points and may represent different stages of disease progression.

**Commercial Relationships:** Raeba Mathew, Allergan (R); Elizabeth Pearce, Novartis (R); Sohba Sivaprasad, Allergan (F), Bayer (F), Novartis (F)

**Support:** Allergan

**Clinical Trial:** n/a

**Program Number:** 4901 Poster Board Number: D0340

**Presentation Time:** 11:00 AM - 12:45 PM

**Prediction of visual prognosis with spectral domain optical coherence tomography in outer retinal atrophy secondary to closed-globe trauma**

**Haoyu Chen, Yufang Lu, Huichun Huang, Jianlong Zheng, Ping Hou, Weiqui Chen.** Joint Shantou International Eye Center, Shantou, China.

**Purpose:** To investigate the structural features of outer retinal atrophy secondary to closed-globe trauma and their correlation with visual prognosis, using spectral domain optical coherence tomography (OCT).

**Methods:** In this retrospective study, patients with outer retinal atrophy secondary to closed-globe trauma were examined with Topcon 3D OCT-1000. The foveal thickness was measured. The severity of outer retinal atrophy was graded into three levels: disruption of inner/outter segment (IS/OS) layer, reduced thickness of outer nuclear layer (ONL), and disappearance of ONL. Cases with > 180 days of follow-up were included. The correlations between OCT features and best-corrected visual acuity at the last follow-up were analyzed.

**Results:** Overall, 52 eyes of 52 patients were included, with mean follow-up of 286 ± 200 days. Spectral domain OCT revealed disruption of the inner/outter segment (IS/OS) layer with atrophy of outer nuclear layer and disorganization of inner retina in severe cases. The final best-corrected visual acuity was significantly correlated with foveal thickness (r = 0.813, p<0.001) and grade of outer retinal atrophy (r = 0.796, p<0.001).

**Conclusions:** Spectral domain OCT revealed disruption of IS/OS layer and atrophy of outer nuclear layer in cases of commotio retinae. Foveal thickness and grade of outer retinal atrophy were predictors for final visual outcome in these cases.

**Commercial Relationships:** Haoyu Chen, None; Yufang Lu, None; Huichun Huang, None; Jianlong Zheng, None; Ping Hou, None; Weiqui Chen, None

**Support:** National Nature Science Foundation of China (30901646 and 81170853), Guangdong Science and Technology Project (2011B031300013), Guangdong Medical Research Foundation (B2010230), Science and Technology Project of Shantou City, China (2009-70) and the Research Fund of Joint Shantou International Eye Center (2010-025)

**Program Number:** 4899 Poster Board Number: D0338

**Presentation Time:** 11:00 AM - 12:45 PM

**Retinal Blood Flow Velocities in Patients with Retinal Vein Occlusion**


**Purpose:** To evaluate retinal blood flow velocities in patients with retinal vein occlusion (RVO) by using Retinal Function Imager (RFI).

**Methods:** Seventeen patients with unilateral retinal vein occlusion underwent testing with the RFI in both eyes. Mean arterial and venous blood flow velocities in the eyes with RVO were compared to the velocities in fellow, unaffected eyes.

**Results:** In the eyes with retinal vein occlusion, mean arterial and venous blood flow velocities were measured as 3.09±1.45 mm/sec and 2.54±1.02 mm/sec, respectively. When compared to fellow normal eyes (4.42±1.79 mm/sec for arteries and 3.38±0.64 mm/sec for veins), both arterial and venous velocities were found to be significantly reduced (p=0.042 for arterial and p=0.018 for venous blood flow velocity).

**Conclusions:** Reduced retinal blood flow velocities in the eyes with retinal vein occlusion may serve as a new parameter for evaluation of patients with retinal vein occlusion.

**Commercial Relationships:** Gennady Landa, None; Nicole K. Scripsema, None; Richard B. Rosen, Opko-OTI (C), Optos (C), Clarity (C), OD-OS (C), Topcon (R), Zeavision (F), Genetech (F), Optovue (C)

**Support:** n/a
Comparison. The automated measurements of the total area of the cysts and the convex hull around them (convex area) were compared to the manual measurements. The convex hull area correlated significantly ($r=0.63$, $p<0.001$) with the manual measurement, though the automated area measurement did not ($r=0.67$, $p=0.065$). Additionally, automated determination of cyst locations (inner retinal layers, outer retinal layers, or both) was compared to manual annotation. Cysts existing in both inner and outer layers were located with 95% sensitivity and 66% specificity; cysts in the inner layers were located with 96% sensitivity and 70% specificity; and cysts in the outer layers were detected with 77% sensitivity and 62% specificity. Further sub-location analysis resulted in 81% sensitivity and 67% specificity for detecting cysts in the IPL; 96% sensitivity and 70% specificity for detection in the OPL; and 70% sensitivity and 72% specificity for detection in the ONL.

Conclusions: This novel system can detect cyst area as well as cyst location in eyes with DME. These measurements may help characterize patient status and predict prognosis.

Both images; Automated segmentation of retinal layers and diabetic cysts. RFNL (Blue), IPL/GL (Cyan), INL (Red), ONL (Yellow), PIS (Magenta), POS (Black), PE (Green), Cysts (White).

Commercial Relationships: Sohini RoyChowdhury, None; Dara D. Koozekanani, None; Salma Radwan, None; Keshab K. Parhi, Leansics Corporation (S); Leansics Corporation (E)
Support: MMF: Minnesota Medical Foundation

Program Number: 4902 Poster Board Number: D0341
Presentation Time: 11:00 AM - 12:45 PM
Evaluation Of Functional And Morphological Parameters In Patients With RVO Treated With Intravitreal Steroid Implant Simone Donati, Ettore Melardi, Muna Al Oum, Carlo Gandolfi, Marco Bianchi, Riccardo Vinciguerra, Claudio Azzolini. Department of Morphological and Surgical Sciences, University of Insubria-Circolo Hospital, Varese, Italy.

Purpose: To analyze the role of both morphological and functional retinal parameters evaluating the efficacy of a long term intravitreal steroid implant.

Methods: This prospective study included 12 eyes of 12 consecutive patients affected by Retinal Vein occlusion who underwent intravitreal implant of Ozurdex. Morphological examinations and functional assessments were evaluated at baseline and at day 30 and 90 after treatment. Morphological examination was performed by Spectral OCT (OTI, Toronto, Canada) evaluating macular retinal and choroidal thickness. Functional assessment included LogMAR visual acuity, retinal sensitivity and fixation pattern using the microperimeter (MP1, Nidek Technologies, Padova, Italy).

Results: Baseline morphological quantitative evaluation showed mean retinal thickness (RT, mean±standard deviation) of 430.00±295.13μm and choroidal thickness (CT) of 296.25±76.71μm; after treatment, at day 30 we found a RT of 201.43±27.34μm, CT of 238.57±39.34μm; at day 90 a RT of 326.67±210.79μm and CT of 256.67±30.55μm. Baseline functional evaluation showed mean visual acuity of 0.81±0.66 LogMAR and retinal sensitivity of 6.16±4.22 dB; after treatment, at day 30 we found 0.59±0.37 (p<0.05) and 8.23±4.42 dB (p<0.05); at day 90, 0.46±0.74 (p<0.05) and 7.06±4.66 dB (p<0.05). Fixation pattern improved significantly (p<0.05), showing a stable fixation in 4 of 12 patients (33%) at baseline, in 7 of 12 patients (58%) at day 30 and in 9 of 12 patients (75%) at day 90, suggesting a significative recovery on visual performances.

Conclusions: Our study shows significative results on retinal thickness reduction, significantly related to visual function increase. Moreover, functional evaluation underlined the role of microperimetry (retinal sensibility and fixation pattern) to complete visual acuity examination for a better definition of the efficacy of the treatment. To be further investigated the role of choroid that showed a significative thickness reduction during the follow up not elsewhere documented in literature.

Commercial Relationships: Simone Donati, None; Ettore Melardi, None; Muna Al Oum, None; Carlo Gandolfi, None; Marco Bianchi, None; Riccardo Vinciguerra, None; Claudio Azzolini, None

Program Number: 4903 Poster Board Number: D0342
Presentation Time: 11:00 AM - 12:45 PM
Macular Thickness Evaluation in Young Patients With Type 1 Diabetes Mellitus and Healthy Controls Muna Al Oum1, Simone Donati1, Carlo Gandolfi1, Laura Premoli1, Maurizio Chiaravalli1, Matteo Marrazzo1, Alessandro Sultavari1, Claudio Azzolini1. 1Department of Surgical and Morphological Science, University of Insubria-Circolo Hospital, Varese, Italy; 2Department of Clinical and Experimental Medicine, University of Insubria-Del Ponte Hospital, Varese, Italy.

Purpose: The objectives of this study were to (1) compare macular thickness (MT) in young patients with type 1 diabetes mellitus (DM) versus healthy controls and (2) evaluate the influence of metabolic control, blood glucose excursion and disease duration on macular thickness in patients with type 1 diabetes mellitus (DM).

Methods: 50 eyes of 25 young patients with type 1 diabetes mellitus without signs of diabetic retinopathy and 26 eyes of 13 young healthy controls were considered. Mean patients age was 15 years (range 7-18). Diabetic patients were divided into 2 groups: 22 eyes (Group 1) with poor metabolic control (HbA1c > 8.1%), 28 eyes (Group 2) with good metabolic control (HbA1c < 8.1%). Group 1 and 2 were respectively compared with healthy controls (Group 3). All patients underwent full clinical examination and instrumental evaluation included Spectral Domain OCT macular cross sectional and macular thickness studies for the pericentral and peripheral area of the macula. All statistical analysis was performed using Mann-Whitney test.

Results: All eyes presented a visual acuity of 20/20. All diabetic patients (Group 1 and 2) showed in comparison to Group 3 a no significant difference (p>0.05) on average MT (216.17 ± 14.38 μm vs 228.14 ± 13.84 μm), a significant lower (p<0.05) pericentral MT (228.08 ± 4.35 μm vs 301.75 ± 7.84 μm) and no significant difference in peripheral MT (224.52 ± 0.46 μm vs 230.19 ± 12.78 μm). Group 1 showed in comparison to Group 2 a significant (p<0.05) difference on average MT (206 ± 23.00 μm vs 226.34 ± 14.91 μm), a significant lower pericentral MT (225 ± 14.64 μm vs 301.75 ± 7.84 μm).
231.16 ± 14.50 μm) and no significant difference in peripheral MT (224.19 ± 14.49 μm vs 224.85 ± 14.57 μm). Statistically significant inverse simple correlations were present between RT and blood glucose excursion (p<0.01), blood glucose (p<0.02) and insulin requirement (p<0.05). No correlation were found between RT and disease duration.

**Conclusions:** Our study shows (1) a significant reduction in pericentral macular thickness in young type 1 diabetic patients versus healthy controls; (2) a mean MT and pericentral MT reduction in type 1 diabetic patients with poor metabolic control vs good metabolic control. MT reduction can represent the first sign of retinal involvement by diabetic microangiopathy and is associated with poor metabolic control but not with disease duration.

**Commercial Relationships:** Muna Al Oum, None; Simone Donati, None; Carlo Gandolfi, None; Laura Premoli, None; Maurizio Chiavralli, None; Matteo Marazza, None; Alessandro Salvatoni, None; Claudio Azzolini, None

**Program Number:** 4904

**Poster Board Number:** D0343

**Presentation Time:** 11:00 AM - 12:45 PM

**Yearly Loss of Retinal Thickness and Macular Volume Estimated from SPECTRALIS OCT Measurements in Patients with Stargardt Macular Dystrophy**

Rupert W. Strauss1, 2, Emily Fletcher1, 3, Yulia Wolfson1, Hendrik P. Scholl1.
1 Wilmer Eye Institute, Johns Hopkins University, Baltimore, MD; 2 Dept. of Ophthalmology, Medical University Graz, Graz, Austria; 3 Dept. of Ophthalmology, Cheltenham General Hospital, Gloucestershire Hospitals NHS Foundation Trust, Cheltenham, United Kingdom.

**Purpose:** To estimate disease progression based on analysis of retinal thickness and macular volume measured by SPECTRALIS™ spectral-domain optical coherence tomography (Spectralis OCT) in a prospective longitudinal natural history study in patients affected by Stargardt Macular Dystrophy (STGD).

**Methods:** 60 eyes of 30 STGD patients were included. The study was approved by the Institutional Review Board. Total macular volume (TMV), retinal thickness and volumes of all nine Early Treatment of Diabetic Retinopathy Study (ETDRS) subfields, 116 macular scans were analyzed. Numbers and types of segmentation errors of the Heidelberg Eye Explorer software (Version 5.4.6) were recorded and manually corrected. In a subgroup of 18 patients, TMV and retinal thickness and volumes of all 9 ETDRS subfields were registered, differences between visits calculated and difference per time (loss of retinal thickness and volume per year) estimated.

**Results:** 4424 line scans from 116 macular scans were analyzed. 1373 (31%) of those showed segmentation errors and were manually corrected. Mean observation period was 12 months (range 3 to 34 months). Mean change in TMV (mean baseline=6.713 ± 0.932 mm³) was -0.15 mm³ per year. Mean volume change was -0.007 mm³ per year in the central subfield (mean baseline=0.129 mm³), -0.011 mm³ per year in the inner ETDRS circle (inner four subfields; mean baseline=0.381 mm³), and -0.022 mm³ per year in the outer ETDRS subfields (mean baseline=1.33 mm³). Change of retinal thickness was -0.15 μm per year in the central subfield, -7.21 μm per year in the inner ETDRS circle and -4.68 μm per year in the outer ETDRS circle.

**Conclusions:** The Spectralis OCT allows to measure decline in retinal thickness and volume in neurodegenerative disease of the retina such as STGD. However, automated analysis shows segmentation errors in about a third of scans and requires manual correction. The level of variability of OCT-derived measurements of retinal thickness and volume that we observed suggests that an observation period of about 12 months is needed to detect definite progression above the noise level in the majority of patients with STGD. OCT-derived measurements of retinal thickness and volume may serve as outcome measures for clinical trials of clinical intervention that targets the progression of loss of the neuroretina in STGD.

**Commercial Relationships:** Rupert W. Strauss, None; Emily Fletcher, None; Yulia Wolfson, None; Hendrik P. Scholl, None

**Support:** Schroedinger Stipend Fonds zur Foerderung der wissenschaftlichen Forschung Project-number J3383-B23. Wynngund Translational Research Acceleration Program Enhanced Research and Clinical Training Award, Clinical Research Institute (CRI) - Foundation Fighting Blindness (FFB; NNCD-CL-0310.0049-JHU-WG); Clinical/Research Fellowship Award in Inherited Orphan Retinal Degenerations 2011 of FFB; Macular Degeneration Research Award, American Health Assistance Foundation (AHAF; M2010042); BAYER Clinical Training Award, BAYER Global Ophthalmology Awards Program; Unrestricted grant to the Wilmer Eye Institute from Research to Prevent Blindness. H.P.N.S. is the Dr. Frieda Derdeyn Bambas Professor of Ophthalmology.

**Program Number:** 4905

**Poster Board Number:** D0344

**Presentation Time:** 11:00 AM - 12:45 PM

**Choroidal Thickness in Healthy Pregnant Women Using EDI-OCT**

Eric K. Chin, Khoo V. Lam, Karishma Chandra, Ellen F. Redenbo, Susanna S. Park, Ophthalmology, UC Davis Eye Center, Sacramento, CA.

**Purpose:** Pregnancy is associated with an increase in blood volume and cardiac output by 30 to 50%. Various ocular conditions, such as central serous chorioretinopathy, hypertensive retinopathy/chorioretinopathy, retinal artery occlusion, myopic shift or spontaneous orbital hemorrage have been described and associated with pregnancy. This pilot study compared the choroidal thickness of asymptomatic otherwise healthy pregnant women to age-matched normal subjects using enhanced depth imaging optical coherence tomography (EDI-OCT) to study the effect of pregnancy on choroidal thickness.

**Methods:** A prospective, case-control pilot study of five female patients with uncomplicated pregnancy were imaged using the Heidelberg Spectralis OCT with EDI analysis. Subfoveal choroidal thickness measurements were obtained at various time points throughout the pregnancy in all five patients. These measurements were compared to five healthy age-matched female controls with similar refractive error range and no significant ocular abnormality. Statistical analysis was performed using an unpaired Student T-test.

**Results:** All subjects were asymptomatic and had normal eye examination and BCVA. Mean age in the pregnant group was 29.0 years, versus 28.2 years in the control group (p = 0.83). All five pregnant subjects were imaged at least once during the second and/or third trimester of pregnancy at mean 31.3 weeks gestation (range, 22-37 weeks). Mean choroidal thickness measurement was 315.6 μm (range, 150-532 μm) in pregnant females and 209.7 μm (range, 163-271 μm) in controls (p = 0.01). The average change in choroidal thickness was 56.8 μm (range 18-111 μm), with a downward trend in choroidal thickness during the third trimester in four out of five patients. None of the subjects had intraretinal or subretinal fluid by OCT imaging.

**Conclusions:** Subfoveal choroidal thickness may be elevated during pregnancy. This small pilot study shows a possible downward trend in choroidal thickness as patients advance from second to third trimester. Further research is needed to better understand the pathophysiologica significance of these findings which may be associated with pregnancy.

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Purpose: To evaluate the prevalence of epiretinal membrane (ERM) in eyes that underwent primary repair of rhegmatogenous retinal detachment (RD) treated with scleral buckle (SB) and cryopexy when imaged with spectral domain optical coherence tomography (SD-OCT).

Methods: 62 patients were included in the study. All patients were phakic, non-diabetic and had undergone SB surgery with cryopexy at least 2 months prior to enrollment. Patients underwent complete clinical evaluation and SD-OCT macular scans were obtained using Spectralis® SD-OCT. Two scans were acquired; fast mode volume scan, with 20° OCT scan width x 20° of height, and a section scan at the level of the umbus. The scans were read by an independent observer and graded based on the presence of a hypereffective layer on the surface of the retina in any of the scans reviewed. If there was an ERM, it was further subdivided as grade 1 if it did not distort the foveal depression and grade 2 or macular pucker if altered it. Further analysis was taken regards alteration of internal segment/outer segment junction (IS/OS), presence of vitreomacular traction, macular hole and subretinal fluid in the macular area.

Results: 62 subjects were studied with a 1:1 male:female ratio and a mean age of 42.5 years-old (±13.8 years). The mean time between initial symptoms of RD and SB surgery was 29.5 days (0 to 240 days). The number of retinal breaks (holes, tears or dyalisis) responsible for RD were: 1 in 69.3% of cases and more than 2 in 30.6% of cases. In 47 patients (75.8%) the RD was caused by a retinal hole or tear, while in 15 subjects (24.2%) was caused by retinal dialysis. The time period between surgery and SD-OCT scan was 6.9 years (60 days to 26.5 years). The presence of ERM was observed in 24 patients (38%): 91.6% were grade 1 and 8.3% were macular puckers. Alteration in the IS/OS was observed in 14 eyes (22.5%). A macular lamellar hole was present in 3 eyes; 3 eyes exhibited vitreomacular traction syndrome; while in 6 eyes subretinal fluid was recognized.

Conclusions: SD-OCT enable us to objectively measure the prevalence of ERM in patients that had undergone SB surgery with cryopexy for primary repair of RD. We found an ERM prevalence of 38%. To the best of our knowledge, this is the first study that analyzes ERM prevalence based on objective data gather though SD-OCT technology.

Commercial Relationships: Rosa E. Martinez-Munoz, None; Jans J. Fromow-Guerra, Virgilio Morales-Canton, Valentina Franco-Cardenas, Retina and Vitreous, Asociacion Para Evitar la Ceguera en Mexico, Mexico, Mexico.

Purpose: To reproduce any abstract, contact the ARVO Office at arvo@arvo.org.
Genentech (R), Regeneron (F), Regeneron (C), Regeneron (R), Optos (F), Optos (C), Optos (R), Eyetech (C), Merge/OIS (C), Merge/OIS (I)

Program Number: 4908 Poster Board Number: D0347
Presentation Time: 11:00 AM - 12:45 PM
Correlation of Posterior Inflammatory Leakage and Cystoid Macular Edema with Retinal Pigment Epithelium Atrophy in Retinitis Pigmentosa Evaluated with Optos Wide-field Fluorescein Angiography and Spectral Domain OCT
Carlos A. Medina-Mendez, Matthew B. Kaufman, Andrew W. Eller, Thomas R. Friberg, Ophthalmology, University of Pittsburgh Medical Center, Pittsburgh, PA.

Purpose: To utilize an Optos P200A (Dunfermline, Scotland) wide-field fluorescein angiographic (FA) system and SD-OCT to determine what characteristic changes in retinal pigment epithelium (RPE) atrophy correlate with posterior inflammatory changes in patients with retinitis pigmentosa (RP).

Methods: Patients diagnosed with RP who had been evaluated with Optos wide-field FA and SD-OCT were identified through a search of billing records. Two masked retina faculty members analyzed the images for the presence of late phase diffuse leakage as well as, amount, and location of RPE atrophy. RPE atrophy was classified as mild (< 33 %), moderate (33-66 %) and severe (> 66%) depending on what percent of the total RPE area was involved. The location was determined as predominantly posterior, peripheral or diffuse. Leakage was graded subjectively as mild, moderate or severe. SD-OCT was used to determine the amount of macular atrophy and the presence of cystoid macular edema (CME).

Results: A total of 39 eyes in 21 patients were analyzed. CME was found in 81% (13/16), 35% (7/20) and 0% (0/3) of patients with mild, moderate and severe RPE atrophy respectively. CME was seen in 66% (10/15) of patients with predominantly peripheral RPE changes, but was found in only 44% (7/16) and 37% (3/8) of eyes when predominantly diffuse or predominantly posterior RPE atrophy was observed. Leakage was observed in 19 of 39 eyes (35%). In eyes where leakage was observed, macular atrophy correlated with the amount of leakage seen on wide-field fluorescein angiography. A MCV of 11.98, 10.45, and 9.42 was seen in eyes with mild, moderate and severe leakage respectively. Interestingly the average MCV of non-leaking eyes was only 9.45.

Conclusions: Eyes with mild RPE atrophy where more likely to have CME. The location of the RPE atrophy is important as eyes with peripheral atrophy are more likely to have CME that those with posterior or diffuse atrophy. Macular atrophy correlated with late stage vascular leakage on FA. Further studies are needed to identify the prevalence, mechanism, treatment, and effect on prognosis of these findings but selectively performance of Optos wide-field FA and SD-OCT on these patients could be a valuable assessment tool.

Commercial Relationships: Carlos A. Medina-Mendez, None; Matthew B. Kaufman, None; Andrew W. Eller, None; Thomas R. Friberg, 13/581,518 (P)

Support: NIH P30 EY008098, Eye and Ear Foundation of Pittsburgh, Unrestricted Grant from Research to Prevent Blindness, New York, NY

Program Number: 4909 Poster Board Number: D0348
Presentation Time: 11:00 AM - 12:45 PM
Correlation between Visual Acuity and Spectral Domain Optical Coherence Tomography Findings in Birdshot Chorioretinopathy Patients
Vincent Y. Ho1, Jessica Shantha1, Farzin Forooghian2, Chris Bergstrom1, G B. Hubbard1, Timothy W. Olsen1, Purnima Patel1, Steven Yeh1

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Comparison of Optical Coherence Tomography Scan Patterns and Clinical Review Strategies in the Management of Neovascular Age-related Macular Degeneration

Robert J. Courtney, Jedediah McClintic, Justis P. Ehlers.

Ophthalmology, Cole Eye Institute, Cleveland Clinic Foundation, Cleveland, OH.

Purpose: To compare various OCT scan patterns and review strategies to identify an optimal OCT imaging strategy for NVAMD.

Methods: A retrospective chart review was performed to identify patients with exudative AMD and concurrent Cirrus (Zeiss) OCT imaging with horizontal 5-line rasters, vertical 5-line rasters, and macular cube analysis. For each encounter, a single published report was reviewed for each of the horizontal and vertical rasters within the clinical image review software (Zeiss Forum), while the cube was reviewed line-by-line in the Cirrus reader software. When available, enhanced depth imaging (EDI) and macular thickness analysis reports were also included in the image review tool. The primary variables compared were the presence or absence of definite exudation as defined by “unequivocal” intra- or subretinal fluid. In addition to “unequivocal fluid,” images were also scored for “any possible fluid” to assess the sensitivity of these review strategies with a “zero-tolerance” strategy. The gold standard for both unequivocal and the zero-tolerance strategy were the sum total findings of all scan patterns (e.g., fluid on any scan).

Results: 558 OCT scans were reviewed for 100 clinical encounters for 26 eyes of 23 patients. For unequivocal fluid, 75% of encounters showed exudation. The sensitivity of the line-by-line review (macular cube) and reports (rasters/thickness map) were 97% and 87%, respectively. For the zero-tolerance strategy, 94% of encounters showed possible fluid. The sensitivity of the line-by-line review and reports were 94% and 92%, respectively (p = 0.2). When utilizing a zero-tolerance strategy for interpreting the reports, only 2% of eyes were missed that had unequivocal fluid on the line-by-line review of the macular cube.

Conclusions: Different strategies for acquiring and reviewing OCT data differ in their ability to identify features of exudation. Optimizing both clinical accuracy and diagnostic testing efficiency is critical to successful management of NVAMD. Line-by-line review of the macular cube can be time consuming particularly when the reader software is housed separately from the image report review software. In this study, a zero-tolerance strategy with vertical/horizontal raster scans and thickness maps provides similar sensitivity to the line-by-line review of the cube.

Commercial Relationships: Robert J. Courtney, None; Jedediah McClintic, None; Justis P. Ehlers, Provisional patents filed related to intraoperative OCT technology. No company relationships (P)

Program Number: 4911 Poster Board Number: D0350
Presentation Time: 11:00 AM - 12:45 PM

Perivascular fundus autofluorescence abnormalities in autoimmune retinopathy


Purpose: To present a novel association of perivascular fundus autofluorescence abnormalities with the diagnosis of autoimmune retinopathy (AIR).

Methods: The retinal images of patients seen over the past two years (2010 to 2012) with the eventual diagnosis of AIR whose workup included fundus autofluorescence photographs were reviewed. The diagnosis of AIR was established based on a positive anti-retinal antibody titer and supported by compatible visual field and electroretinography studies. For all seven subjects meeting these criteria, a detailed chart review was performed. Demographic and clinical data were recorded, including gender, age, ethnicity, disease duration, visual acuity, and biomicroscopy and dilated fundus exam findings. Color fundus photographs, spectral domain optical coherence tomography (SD-OCT), and fundus autofluorescence imaging from the Spectralis HRA+OCT machine (Heidelberg Engineering, Heidelberg, Germany) and, when available, images from the P200CAF Wide-field-Autofluorescence scanning laser ophthalmoscope prototype (532-nm; Optos) were reviewed.

Results: Four patients with AIR had characteristic changes of perivascular hypofluorescence in very close association with the inner retinal vessels (see figure), thought to correspond to areas of retinal pigment epithelial (RPE) damage. Two patients had a less obvious pattern of perivascular hyper- and hypofluorescence, with hyperautofluorescence likely corresponding to active areas of RPE dysfunction. One patient had speckles of hyperautofluorescence distributed near but not adjacent to the vasculature as in the aforementioned cases. OCT confirmed the expected photoreceptor outer segment and RPE changes in areas of hyper- and hypofluorescence.

Conclusions: Characteristic perivascular autofluorescence abnormalities can be seen in AIR. Autofluorescence testing with both standard modalities and widefield imaging may have a role in the early detection and diagnosis of AIR, prompting testing for anti-retinal antibodies in the appropriate clinical context.

Widefield images of the right and left eye demonstrating the perivascular autofluorescence changes seen in four patients diagnosed with AIR.

Commercial Relationships: Damien C. Rodger, None; Grace M. Richter, Hossein Nazari Khanamiri, Narsing A. Rao, None

Program Number: 4912 Poster Board Number: D0351
Presentation Time: 11:00 AM - 12:45 PM

The clinical and spectral-domain optical coherence tomography findings in focal choroidal excavation

Christopher S. Lee1, Se Joon Woo2, Duck Jin Hwang2, SungChul lee2.

1Ophthalmology, Yonsei Univ College of Medicine, Seoul, Republic of Korea; 2Ophthalmology, Seoul National Univ College of Medicine, Seoul, Republic of Korea.

Purpose: To report the clinical and spectral-domain optical coherence tomography (SD-OCT) finding of focal choroidal excavation(FCE) in Korean population.

Methods: The medical records of 27 patients (30 eyes) with FCE diagnosis were analyzed. The clinical data were recorded, including gender, age, ethnicity, disease duration, visual acuity, and biomicroscopy and dilated fundus exam findings. Color fundus photographs, spectral domain optical coherence tomography (SD-OCT), and fundus autofluorescence imaging from the Spectralis HRA+OCT machine (Heidelberg Engineering, Heidelberg, Germany) and, when available, images from the P200CAF Wide-field-Autofluorescence scanning laser ophthalmoscope prototype (532-nm; Optos) were reviewed.

Results: Four patients with AIR had characteristic changes of perivascular hypofluorescence in very close association with the inner retinal vessels (see figure), thought to correspond to areas of retinal pigment epithelial (RPE) damage. Two patients had a less obvious pattern of perivascular hyper- and hypofluorescence, with hyperautofluorescence likely corresponding to active areas of RPE dysfunction. One patient had speckles of hyperautofluorescence distributed near but not adjacent to the vasculature as in the aforementioned cases. OCT confirmed the expected photoreceptor outer segment and RPE changes in areas of hyper- and hypofluorescence.

Conclusions: Characteristic perivascular autofluorescence abnormalities can be seen in AIR. Autofluorescence testing with both standard modalities and widefield imaging may have a role in the early detection and diagnosis of AIR, prompting testing for anti-retinal antibodies in the appropriate clinical context.
were reviewed. Demography, clinical histories, and SD-OCT findings were analyzed.

**Results:** The mean age of patients was 51 years (range, 25-76). Seventeen (63%) patients were men. The mean refractive error was -3.7 diopters (range, +2.5 to -9.0). In 19 (63%) eyes, SD-OCT showed no separation between the outer retinal layers and the retinal pigment epithelium (RPE) (conforming type). There was a separation between the outer retina and RPE (non-conforming type) in 11 (37%) eyes. The mean largest diameter and the height of lesions were 833 μm and 104 μm, respectively. The mean subfoveal choroidal thickness was 275 μm (range 70-571). Ten (33%) eyes were associated with central serous chorioretinopathy (CSC), nine in the affected eye and one in the unaffected fellow eye. Five (17%) eyes were associated with choroidal neovascularization. Non-conforming type FCE was associated with greater lesion height (P=0.008) and the presence of CSC (P=0.001). There was one case of conforming type FCE with CSC, which spontaneously was converted to non-conforming type with CSC progression, and then re-converted to conforming type following intravitreal bevacizumab.

**Conclusions:** Focal choroidal excavation is a recently described idiopathic entity, which may be more common in Asian population. There appears to be an association between FCE and CSC. Choroidal neovascularization may be associated in some patients.

Focal choroidal excavation in a 43 year-old woman

**Commercial Relationships:** Christopher S. Lee, None; Se Joon Woo, None; Duck Jin Hwang, None; SungChul lee, None

**Program Number:** 4913 **Poster Board Number:** D0352
**Presentation Time:** 11:00 AM - 12:45 PM

**Purpose:** To report the usefulness of wide field imaging and angiography in patients with Coat’s disease.

**Methods:** In 5 consecutive patients, wide field imaging using scanning laser ophthalmoscopy and angiography (Optomap) was performed before treatment. The laser was performed on the basis of wide field images. Once the ophthalmologist considered that the treatment was complete, the imaging was repeated including late phase angiographic images. After reviewing the images, the ophthalmologist decided whether further treatment was required.

**Results:** Among all patients, wide field imaging enabled to monitor the localization of laser treatment with respect to the vascular abnormalities and non perfusion areas displayed on angiography. In all cases, additional laser treatment was performed on the basis of the image lecture although the treatment had been considered to be sufficient by the ophthalmologist.

**Conclusions:** Wide field imaging and angiography enables to target laser treatment in Coat’s disease.

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the macula was also evaluated for error analysis.

**Results:** 12 eyes from 10 patients were included, 8 with dry AMD and 4 with wet AMD. The average age was 72 years, with 8 females and 2 males. Average PED via automated segmentation was 0.14 mm² in the central 3 mm circle and 0.21 mm² in the 5 mm circle. Average automated PED area was 2.37 mm² in the central 3 mm circle and 3.77 mm² in the 5 mm circle. Manual segmentation yielded an average PED volume of 0.30 mm³ in the 3 mm and 0.92 mm³ in the 5 mm circles.

The ICCs across the three automated measurements were 0.954 for the volume in the 3 mm circle, 0.983 for the volume in the 5 mm circle, 0.971 for the area in the 3 mm circle, and 0.992 for the area in the 5 mm circle. The ICC between the manual and automatic volume is 0.033 for the 3 mm circle and 0.296 for the 5 mm circle.

In the center 1 mm region, 11 of the 12 scans showed ‘true RPE’ line breakdown, while 8 of the 12 scans showed ‘true PED’ line breakdown.

**Conclusions:** RPE analysis software allowed for reproducible calculation of PED volumes and areas. Agreement between manual and automated volumetric measurements was low secondary to a high incidence of segmentation line breakdown.

**Commercial Relationships:** Jessica N. Taibl, None; Samir I. Sayegh, None

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**Program Number:** 4915 Poster Board Number: D0354

**Presentation Time:** 11:00 AM - 12:45 PM

**Use of SD-OCT/SLO as an alternative to ultrasonography to monitor patients with recurrent retinal detachments and silicone oil tamponade**

Jessica N. Taibl1,2, Samir I. Sayegh1.1. The EYE Center, Champaign, IL; 2University of Illinois, Urbana-Champaign, IL.

**Purpose:** To evaluate SD-OCT/SLO as an alternative to B-mode ultrasonography in cases of inferior recurrent retinal detachment with silicone oil tamponade. If repair is done by pars plana vitrectomy and silicone oil tamponade, ultrasound upon follow-up is more difficult, as significant artifact is present. It is therefore necessary to look for alternate ways of evaluating the integrity of the retina after surgical repair that can provide relevant diagnostic information.

**Methods:** 3 patients with rhegmatogenous inferior retinal detachments underwent pars plana vitrectomy with a silicone oil tamponade. After surgery, ultrasonography no longer yielded good diagnostic images and another way of determining retinal integrity needed to be explored. The Spectralis HRA/OCT (Heidelberg Engineering, Germany) generates both a high quality en face image (SLO) and OCT image (SD-OCT). OCT is most commonly used to image and section the fovea and peri-foveal area. However, directing the patient to look nasal, temporal, superior, or inferior allows areas in the periphery to be viewed. Once the en face image of interest is visible, the OCT scan can be directed to view a specific area of interest. One of the three patients suffered corneal decompensation, making it difficult to capture a strong SLO/OCT image. In this case, as well as in the other cases, “live” viewing can be achieved and recorded.

**Results:** The combined use of SD-OCT/SLO can pinpoint the origin of detachment and characterize the extent and amount of fluid and fluid resorption. The OCT set up as implemented in our clinic can propagate a signal through a decompensated edematous cornea and silicone oil. Images can be captured in a regular fashion through use of the software, or live video can be recorded of the session for those patients who are difficult to image.

**Conclusions:** Using SD-OCT/SLO to image and monitor retinal integrity after detachment repair and silicone oil tamponade is a good alternative to ultrasound, especially in situations where ultrasound is limited. Additionally, SD-OCT/SLO provides more diagnostic information than ultrasonography alone, has higher resolution and works in difficult-to-image patients, and, being non-contact, is more comfortable for the patient.

**Commercial Relationships:** Jessica N. Taibl, None; Samir I. Sayegh, None

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**Program Number:** 4916 Poster Board Number: D0355

**Presentation Time:** 11:00 AM - 12:45 PM

**Long-term changes of fudus autofluorescence in central serous chorioretinopathy**

Tetsuji Sekiryu, Hiroshi Oyamada, Kimihiro Imaizumi, Takafumi Mori, Ichiro Maruko. Ophthalmology, Fukushima Medical University, Fukushima, Japan.

**Purpose:** Hyperautofluorescence appears in the area of serous retinal detachment in central serous retinopathy (CSR). The constituents in the subretinal hyperautofluorescent materials may be different from that in the retinal pigment epithelium. We investigated that a long-term change of hyperautofluorescence that appeared in the subretinal space in the eyes with CSR.

**Methods:** Observational case series. Seventeen eyes of 17 patients were followed over 5 years after resolution of serous retinal detachment. All eyes showed hyperautofluorescence in the area of serous retinal detachment at the baseline. The eyes that showed recurrence of serous retinal detachment during the follow-up period were excluded. Fundus autofluorescence was taken with HRA2 (Heidelberg engineering). We measured the intensity of autofluorescence in the hyperautofluorescent area. The autofluorescence intensity was corrected by that in the unaffected area. Changes of the autofluorescence intensity during the follow-up period were calculated.

**Results:** Hyperautofluorescence remained at the final visit in all eyes. The intensity of autofluorescence was -0.046 log unit at the first visit and -0.093 log unit at the final visit (P=0.0005). The intensity of hyperautofluorescence decreased 0.009 log unit per year.

**Conclusions:** Hyperautofluorescence in the area of serous retinal detachment in CSR remains over 5 years, although the intensity of hyperautofluorescence decreases very slowly.

**Commercial Relationships:** Tetsuji Sekiryu, None; Hiroshi Oyamada, None; Kimihiro Imaizumi, None; Takafumi Mori, None; Ichiro Maruko, None

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**Program Number:** 4917 Poster Board Number: D0356

**Presentation Time:** 11:00 AM - 12:45 PM

**Correlations between Retinal Morphological Changes and Concentrations of Cytokines in Eyes with Diabetic Macular Edema**

447 DME: OCT and Function

Wednesday, May 08, 2013 11:00 AM-12:45 PM

Exhibit Hall Poster Session

**Program #/Board # Range:** 4917-4937/D0356-D0376

**Organizing Section:** Retina

**Program Number:** 4917 Poster Board Number: D0356

**Presentation Time:** 11:00 AM - 12:45 PM

**Correlations between Retinal Morphological Changes and Concentrations of Cytokines in Eyes with Diabetic Macular Edema**

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Correlation between Diabetic Macular Edema (DME) and extraocular complications observed during diabetes


Purpose: Diabetic macular edema is the main cause of visual loss during diabetes. Some clinical (hypertension, nephropathy) or biological parameters (glycated hemoglobin) are well-known risk factors for DME. The objective of the study was to identify clinical factors that may be associated with the presence of the DME.

Methods: This is a longitudinal study including type 2 diabetic patients to evaluate the risk of complications related to diabetes. The diagnosis of DME was established with retinal coherence tomographic (OCT) images were evaluated to determine the presence of serous retinal detachments (SRDs), retinal cysts, and retinal swelling. The concentrations of VEGF, interleukin (IL)-6, and IL-8 in vitreous samples collected during vitrectomy were determined. The correlations between the OCT parameters and the concentration of the cytokines and other clinical data were calculated. The effects of intravitreal triamcinolone (IVTA) or bevacizumab (IVB) on the SRD was also examined in other eyes.

Results: Fifty-two eyes (52 patients) were investigated. A SRD was found in 36.5% (19/52) of the eyes. Multivariate regression analysis showed that IL-6 was the only factor significantly associated with the presence of a SRD (P=0.001, odds ratio 1.024, 95% confidence interval 1.010-1.038). Retinal cysts were found in 69.2% (36/52) of the eyes, and retinal swelling was found in 75.0% (39/52) of the eyes. The presence of cysts was not significantly associated with the presence of any of the retinal pathologies. Among 24 DME eyes with a SRD, the SRD disappeared significantly more frequently after IVTA (9/12 eyes) than after IVB (2/12 eyes; P=0.012).

Conclusions: The significant association of a SRD with the level of intravitreal IL-6 and its better responsiveness to IVTA indicates that inflammation plays an important role in the development of SRD in DME eyes. SRD may be important in determining the type of treatment for DME.

Commercial Relationships: Shozo Sonoda, None; Takehiro Yamashita, None; Makoto Shirasawa, None; Hiroki Otsuka, None; Yasushi Sonoda, None; Taiji Sakamoto, None

Support: Grant-in-Aid for Scientific Research from the Ministry of Education, Science, and Culture of the Japanese Government

Program Number: 4918 Poster Board Number: D0357

Evaluation of choroidal thickness by enhanced depth imaging OCT in the LUCIDATE study: a randomised clinical trial to compare outcomes of ranibizumab with laser in diabetic macular oedema

RISHMA GOHIL, Oliver Comyn, Pearse A. Keane, Praveen J. Patel, James W. Bainbridge, Sobha Sivaprasad, Philip G. Hykin.

Purpose: The Enhanced Depth Imaging (EDI) technique of OCT allows visualisation of the choroid. Studies have shown that changes in choroidal thickness may accompany diabetic retinopathy and diabetic macular oedema (DMO). In this exploratory, post-hoc analysis from a clinical trial, we evaluated the effect of laser and ranibizumab therapy on choroidal thickness in DMO.

Methods: Randomised clinical trial. 36 subjects with centre-involving DMO, BCVA 55-79 ETDRS letters, moderate macular haemoglobin 7.7%).

In univariate analysis, DME was significantly associated with the duration of diabetes (OR=1.04, p<0.0001), glycated hemoglobin levels (OR=1.18, p=0.001), systolic blood pressure (OR=1.02, p<0.0001), history of cardiovascular disease (OR=2.4, p<0.0001), renal impairment (OR=7, p<0.0003) and with any history of amputation (OR=3.7, p<0.0001).

In multivariate analysis, DME was significantly associated with the duration on diabetes (OR adjusted=1.03, CI 95% 1.01-1.05, p=0.002), glycated hemoglobin (OR adjusted =1.2, CI 95% 1.1-1.4, p=0.0003), systolic blood pressure (OR adjusted =1.01, CI 95% 1.01-1.02, p=0.01), renal impairment (OR adjusted=5, p<0.006) and with any history of amputation (OR adjusted =2.6, CI 95% 1.4-5, p=0.003).

Conclusions: This study demonstrates a strong association between DME and any history amputation. Our study provides other associations between DME and extraocular events that have been previously investigated in other studies. A common microvascular determinism may be explained the relationship between amputation and DME.

The identification of clinical and biological risk factors for DME could lead to define more precisely the at-risk population. Based on these risk factors, a prospective follow-up of patients may lead to validate predictive models for development of DME.

Commercial Relationships: Olivier Lichtwitz, None; Nicolas Leveziel, None; Michèle Boissonnot, None; Aurélie Miot, None; Xavier Piguet, SANOFI (F), NOVONORDISK (F), BMS (F), NOVARTIS (F); Florence Torremocha, None; Pierre-Jean Saulnier, None; Richard Maréchaud, None; Samy Hadjadj, None

Program Number: 4919 Poster Board Number: D0358
ischaemia only and no recent laser or anti-VEGF therapy were randomised 2:1 to receive ranibizumab injections (RBZ) or macular laser therapy. Subjects had Spectralis OCT EDI scans at baseline and at 12 weeks to the primary endpoint at 48 weeks. Repeat scans were performed in “follow up” mode. Choroidal thickness was measured at 500 µm intervals across the macula from a high quality single horizontal line scan using measuring software incorporated within the HEYEX software, by a grader masked to treatment allocation. Results were evaluated for longitudinal change in either group and for between-group differences.

**Results:** 33 subjects completed 48 weeks follow up. The two groups were comparable in terms of age, grade of retinopathy, duration of DMO, HbA1C level and previous laser treatments. At baseline, subfoveal choroidal thickness was 278.5 ±0.70 µm and 297.0 ±0.72 µm in the ranibizumab and laser groups respectively. At 48 weeks, thickness was 278.7 ±75.2 µm (RBZ) and 308.2 ±81.8 µm (laser) (p=0.31). Mean choroidal thickness across the central 5 mm of the macula was 243.5 ±58.8 µm at baseline and 245.3 ±58.3 µm at 48 weeks for ranibizumab; for laser it was 264.6 ±51.8 µm at baseline and 255.7 ±52.9 µm at 48 weeks (p=0.63). At baseline and 48 weeks, there was a weak correlation between subfoveal choroidal thickness and BCVA (baseline: r=0.31, p=0.082; 48 weeks r=0.29, p=0.096). Change in choroidal thickness did not correlate with change in retinal thickness (r=0.21, p=0.25).

**Conclusions:** This study found no change in choroidal thickness at 48 weeks with ranibizumab or laser therapy. Choroidal thickness did not correlate with retinal thickness but correlated weakly with visual acuity at baseline and 48 weeks. Further study is warranted to investigate the importance of choroidal thickness measurements in the evaluation of DMO.

**Commercial Relationships:** RISHMA GOHIL, None; Oliver Comyn, Novartis (F), Novartis (R); Pearse A. Keane, None; Praween J. Patel, Allergan (R), Bayer (C), Novartis UK (C), Heidelberg UK (R), Topcon UK (R). Thrombogenics (C); James W. Bainbridge, Novartis (F), Alimera (C), Gene Signal (C), Advanced Cell Technology (F), Targeted Genetics (P), Oxford Biomedica (C), GSK (F), Sobha Sivaprasad, Allergan (F), Bayer (F), Novartis (F); Philip G. Hykin, BAYER (C), NOVARTIS (C), ALLERGAN (C), BAYER (R), NOVARTIS (R), ALLERGAN (F), NOVARTIS (F).

**Support:** NIHR Moorfields Biomedical Research Centre; Novartis Pharmaceuticals (UK) Ltd.

**Clinical Trial:** NCT01223612

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**Quantifying Correlation Between Choroidal Thickness and Macular Sensitivity Using the CAD Test in Subjects Undergoing Treatment with Ozurdex**

**Program Number:** 4920 Poster Board Number: D0359

**Presentation Time:** 11:00 AM - 12:45 PM

**Chromatic sensitivity in diabetic patients treated with Ozurdex Afmed H. Abdel-hay,1,2 Sobha Sivaprasad,1 Ahalya Subramanian,1 Evgenia Konstantakopoulou,2 David F. Edgar,1 John L. Barbur3.1 Ophthalmology, King’s College Hospital, London, United Kingdom; 2Applied Vision Research Centre, City University London, London, United Kingdom.

**Purpose:** Clinical trials that compare treatment modalities for diabetic macular oedema (DME) rely on measurements of macular thickness using Optical Coherence Tomography (OCT) to monitor the effectiveness of therapy. Changes in macular thickness do not, however, correlate with change in visual acuity. It is therefore of interest to establish whether changes in colour thresholds can be used to evaluate the efficacy of Ozurdex in the treatment of DME. The purpose of the study was to measure the changes in red-green (RG) and yellow-blue (YB) thresholds during treatment with Ozurdex using the CAD (Colour Assessment & Diagnosis) test which isolates the use of colour signals and provides age-corrected, normal statistical limits (Expert Rev.Ophthalmol. 6:409-420, 2011). The test quantifies accurately the severity of colour vision loss and indicates statistically significant changes in both RG and YB thresholds.

**Methods:** 13 patients (mean age 56 ±9.3 years) with DME undergoing treatment with Ozurdex were recruited. RG and YB colour thresholds were measured using the CAD test at baseline and 24 weeks post-injection. Visual acuity was measured using ETDRS letter chart and central sub-field retinal thickness (CST) using the Heidelberg Spectralis SD-OCT scan.

**Results:** All diabetic patients (n=13 eyes), had significant loss of RG and YB chromatic sensitivity at the baseline measurement (p<0.05). The age specific, monocular, upper normal limits for a 56 years old subject (i.e., μ±2σ) are 2.66 for RG and 2.85 for YB. In this study, the mean ±σ for RG was 22.08 ± 11.57 and for YB was 16.12 ± 9.0 pre-injection. There was significant improvement in mean RG threshold post-injection: mean= 19.93 ± 10.92 (p<0.05). No significant changes were found in YB threshold: mean= 15.72 ± 4.76 (p=0.23). The severity of colour vision loss (RG and YB) measured with the CAD test showed negligible correlation with visual acuity or central sub-field thickness (r2=0.05) and (r2=0.17), respectively.

**Conclusions:** RG and YB colour thresholds provide a sensitive measure of functional change in diabetics, but the loss of colour vision shows poor correlation with visual acuity and central retinal thickness. These preliminary findings also suggest that RG loss, as measured with the CAD test, can be used to monitor the efficacy of treatment in DME.

**Commercial Relationships:** Ahmed F. Abdel-hay, None; Sobha Sivaprasad, Allergan (F), Bayer (F), Novartis (F); Ahalya Subramanian, None; Evgenia Konstantakopoulou, None; David F. Edgar, None; John L. Barbur, None

**Support:** Allergan

**Clinical Trial:** ISRCTN66216819 - OCTOME study

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**OCTOME Study: An OCT Assessments of Central Macular Edema and Its Relationship with Macular Sensitivity and Thickness**

**Program Number:** 4921 Poster Board Number: D0360

**Presentation Time:** 11:00 AM - 12:45 PM

**Longitudinal Comparison of Visual Acuity as Measured by ETDRS Chart and by Potential Acuity Meter in Eyes with Macular Edema and Its Relationship with Macular Sensitivity and Thickness Elham Hatef Naimi,1,2 Mostafa Hanoun1, Owhofasa O. Agbedia1, Ahmedreza Moradi1, Diana V. Do1, David L. Gayton1, Quan Dong Nguyen1.1 Ophthalmology, Wilmer Eye Inst, Johns Hopkins Univ, Baltimore, MD; 2General Preventive Medicine, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.

**Purpose:** To conduct a longitudinal comparison of visual acuity measured by the ETDRS chart and by the Potential Acuity Meter (PAM) in eyes with macular edema under medical treatment for edema and its relationship with macular sensitivity and thickness

**Methods:** Patients with macular edema (ME) are enrolled in an ongoing prospective study. Patients have follow up visits every 2–4 weeks. At the initial and each follow up visit, best refractive correction for all patients is determined using the ETDRS protocol, and best-corrected visual acuity (BCVA) is assessed using the ETDRS chart as well as by the PAM. Macular sensitivity and thickness are measured by an automatic fundus perimeter/tomography system [OPKO/OTI]. The relationships between BCVA measurements with each of the two systems and macular sensitivity/ thickness are evaluated using mixed-effect modeling.

**Results:** Thirty-eight eye-visits of 14 patients are included in the study. Five patients (10 eyes) had one follow up visit after the initial one. Ages range from 49 to 84 years (median: 66 yrs). BCVA using the ETDRS chart ranges from 20/20 to 20/200 (median: 20/50). BCVA measured by the PAM ranges from 20/20 to 20/400 (median:...
Macular thickness ranges from 112 to 743 microns (median: 346). Macular sensitivity ranges from 0 to 20 dB (median: 10). Differences between BCVA measured with the two systems are evaluated using LogMAR values. The mean LogMAR value using the ETDRS chart is 0.45 (95% confidence interval (CI): 0.35, 0.56) while it is 0.44 (95% CI: 0.31, 0.57) using the PAM (P-value > 0.05). The LogMAR values using the ETDRS chart as well as the PAM are correlated (r= 0.88%). The difference between LogMAR value for BCVA measured with PAM and the ETDRS chart changes by an average of 0.004 (95% confidence interval (CI): 0.002, 0.011) per 1 unit increase in macular thickness while adjusted for macular sensitivity and other confounders.

Conclusions: There is a high correlation between VA measurements with the PAM and the ETDRS chart. VA values measured with the PAM are very close to those measured with the ETDRS chart, although a better VA median may be obtained for PAM values. The difference between LogMAR values for BCVA measured with PAM and the ETDRS chart changes slightly with every micron increase in macular thickness.

Commercial Relationships: Elham Hatef Naimi, None; Mostafa Hanout, None; Owhofesa O. Agbedia, None; Ahmadreza Moradi, None; Diana V. Do, Genentech (F), Regeneron (F); David L. Guyton, Smith-Kettlewell Eye Research Inst (S), U. S. 6,027,216 - Rebscan (P); Quang Dong Nguyen, Genentech (F), Regeneron (F), Lux Biosciences (F), Abbott (F), GSK (F), Santen (F), Santen (C), Bausch and Lomb (C), Optos (F), Heidelberg Engineering (F)

Program Number: 4922 Poster Board Number: D0361
Presentation Time: 11:00 AM - 12:45 PM

Retinal Perifoveal Inner Layer Disorganization as a Predictor of Visual Acuity Outcomes in Eyes with Center-involved Diabetic Macular Edema

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Purpose: To assess parameters on spectral domain optical coherence tomography (SDOCT) that may better correlate with visual acuity (VA) outcomes than central subfield thickness (CST) in eyes with center-involved DME (cDME).

Methods: Patients with cDME underwent ETDRS VA testing and SDOCT imaging on Spectralis (20x20°, 49 b scans, 16 ART Mean, high res setting) at baseline and 8 months. The central 1 mm area on 7 b scans centered on the fovea was graded in masked fashion to evaluate presence, location and extent of retinal perifoveal inner layer disorganization (PILD: inability to distinguish boundaries between any of the inner retinal layers), hyperreflective foci, cysts, subretinal fluid, epiretinal membranes (ERM), and external limiting membrane (ELM) or inner segment-outner segment junction (ISOS) disruption.

Results: 24 eyes of 19 patients were evaluated. Baseline mean±SD logMAR VA was 0.33±0.30, and CST was 423±121µm. Mean age was 61±15 years, diabetes duration 25±14 years, 47% were male and 57% type 1 DM. Eyes with better baseline VA had fewer OCT lines affected by PILD (2.8±2.8 vs. 4.0±2.1), although this and all other OCT variables did not reach statistical significance in relation to baseline VA. Over 8 months follow-up, 20 eyes (83%) received intravitreal anti-VEGF and 1 (4%) macular laser treatment for cDME. Mean CST decreased by 92±108µm, and logMAR VA improved by 0.07±0.13. In unadjusted analyses, improvement in VA was associated with worse baseline VA (improved VA vs unimproved VA: 0.45±0.27 vs 0.16±0.10, respectively, p=0.002), higher percentage of baseline b scans with PILD (57±29% vs 43±29%, p=0.03) and greater decrease in PILD (291±259µm vs 115±129µm, p=0.02), but not to other baseline OCT values or changes in the variables over time. In a multivariate model adjusting for baseline VA, VA improvement remained significantly associated with PILD decreases (1 mm decrease in PILD = 2 line VA improvement, p=0.03).

Conclusions: In eyes with cDME, change in PILD over time is more closely related to VA outcomes than either CST or disruption of outer layer structures including the ELM and ISOS junction. If validated in larger prospective studies, these findings suggest that PILD may serve as a readily measured surrogate biomarker for VA and help predict functional response to cDME treatment over time.

Commercial Relationships: Michael M. Lin, None; Rutuparna Sarangi, None; Jan Lammer, None; Allen Y. Ganjiel, None; Salma Radwan, None; Ahmed Z. Soliman, None; Paolo S. Silva, Optos plc (F); Lloyd P. Aiello, Genentech (C), Genzyme (C), Thrombogenetics (C), Ophthotech (C), Kalvista (C), Pfizer (C), Proteostasis (C), Abbott (C), Vantia (C), Optos, plc (F); Jennifer K. Sun, Boston Micromachines (F), Abbott Laboratories (C), Novartis (C), Genentech (F)

Support: Harvard Medical School Scholars in Medicine Office, Eleanor Chesterman Beaton Childcare Ambassador Program Foundation Grant, JDRF 17-2011-359, Massachusetts Lions Eye Research Fund

Program Number: 4923 Poster Board Number: D0362
Presentation Time: 11:00 AM - 12:45 PM

The effect of hard exudates and epiretinal fibrosis on the retinal thickness as calculated by optical coherence tomography (OCT) in diabetic macular edema

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Purpose: Central retinal thickness and macular volume are major factors in the assessment and treatment of diabetic macular edema. OCT is used as a primary tool to objectively document and calculate retinal thickness using special algorithms based on definition of inner and outer retinal border. The purpose of the study was to evaluate the frequency and type of algorithm challenges and their impact on thickness and volume calculation.

Methods: 129 diabetic patients with clinically significant macular edema (CSME) were enrolled in the study. All eyes were evaluated with OCT before treatment and one month after 3 injections of Ranibizumab. Retinal thickness of the central 1 mm region and retinal volume of the 6 mm region were calculated using 6 lines radial scan pattern (Spectral-domain, Topcon OCT 3D) ignoring decentralization errors. All 6 scan lines were evaluated for algorithm errors and when present, retinal thickness and volume was recalculated after manual correction of the artefacts.

Results: A total of 1740 scan lines were evaluated, algorithm errors were found in 24%. The major reason for the errors was: hard exudates (10 %), epiretinal fibrosis (5 %), optical opacities (5 %), serous detachment (3 %) and others (1 %). The mean signal quality was 60 (SD 20), 7 % were below 30 and for these examinations the percentage of algorithm errors of the scans was 55 %. Correction for epiretinal fibrosis caused a 7 % decrease in total macular volume (p=0.007) and 2 % decrease in central retinal thickness.

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Correlation of structural and visual function tests in patients with diabetic macular edema

Elizabeth Pearce, Raeba Mathew, Ahmed F. Abdel-hay, Sobha Sivaprasad. Ophthalmology, King’s College Hospital, London, United Kingdom.

**Purpose:** There is sufficient evidence to suggest that visual acuity does not correlate with macular thickness in patients with diabetic macular edema (DME). It is unclear whether other visual function tests would correlate with the central subfield thickness (CSF) as measured by spectral domain optical coherent topography. In this study, we assessed the correlation of various visual function tests in DME with CSF.

**Methods:** This is a prospective study on 22 eyes of diabetic patients with centre-involving macular edema. Best corrected visual acuity (BCVA), contrast sensitivity (Pelli Robson letter score) and foveal and retinal sensitivity measured by microperimetry (Nidek MP1) were recorded. Maximum reading speed (MRS) was evaluated using MNRead acuity charts. The central subfield thickness (CST) was performed using a standard protocol on the Heidelberg Spectralis SD-OCT. The Pearson correlation coefficient (r) was used to measure the linear association between visual function test score and between these scores and OCT-measured CST. P < 0.05 was considered statistically significant.

**Results:** The correlation coefficient for the association between CSF and BCVA was -0.273 (p=0.219), contrast sensitivity was 0.095 (p-value 0.673), MRS was 0.344 (p-value 0.116), foveal sensitivity was -0.365 (p-value 0.095) and retinal sensitivity was -0.271 (p-value 0.223). On the basis of multivariate regression models, none of these visual function parameters were significantly associated (P<0.05, after adjusting for multiple testing) with CST.

**Conclusions:** In DME, the combination of MRS, retinal sensitivity and visual acuity score is advocated to provide a more comprehensive assessment of retinal function. However, none of these tests correlated with CST suggesting that CST is not an appropriate measure to assess structure-function correlation in DME.

**Commercial Relationships:** Elizabeth Pearce, Novartis (R); Raeba Mathew, Allergan (R), Novartis (R); Ahmed F. Abdel-hay, None; Sobha Sivaprasad, Allergan (F), Bayer (F), Novartis (F)

**Support:** Allergan

**Clinical Trial:** ISRCTN66216819

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**Program Number:** 4924 Poster Board Number: D0363
**Presentation Time:** 11:00 AM - 12:45 PM
**Retinal Layer Thicknesses in SD-OCT Images for Diabetics with Hard Exudates

Joel A. Papay1, Ann E. Elsner2, Christopher A. Clark1, Victor Malinovsky3, Shane G. Brahm1, Stuart B. Young1, Andrea V. Walker1, Taras V. Litvin4, Glen Y. Ozawa5, Jorge A. Cuadros1, 2School of Optometry, Indiana University, Bloomington, IN; 3School of Optometry, UC Berkeley, Berkeley, CA.

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Purpose: To evaluate the retinal layer involvement and morphology in patients with a reduced retinal thickness area at the posterior pole.

Methods: This is a cross-sectional and retrospective study. Six hundred and 48 files were revised and only 67 patients were selected. The included patients had a reduced retinal thickness area at the posterior pole by using the Asymmetry Analysis Map in Heidelberg Spectralis (Heidelberg Engineering, Germany). Only one eye for patients was included in the study. Retinal thickness was measured in three different retinal areas: 1) the area involved by the pathology (IA), 2) the specular area in the opposite hemifield (SA), and 3) the corresponding IA in the contralateral eye (CIA). Retinal layer morphology was analyzed observing the Spectralis screen. When the distribution of the data was normal, t-test was used while when the distribution of the data was non-normal, Mann-Whitney test was used. A P value <0.05 was considered significant.

Results: The thickness of the IA was 235.54 µm +/- 39.95 (mean +/- standard deviation), while it was 269.84 +/- 36.16 µm and 293.81 +/- 37.52 µm for SA and CIA respectively. In all the optic neuropathy patients and in those with branch retinal artery occlusion, a reduction of the ganglion cell complex was observed, while in patients with central serous chorioretinopathy, post-PDT and chronic serous epiphiolathy, a reduction of the outer retinal layer was observed.

Conclusions: Different retinal layers could be involved in the reduction of the retinal thickness: a reduction of the inner layers was related to disease in which ciliar or retinal arterial vessel flow was involved, while a reduction of the outer retinal layer was related to pathologies related to choroidal flow diseases.

Commercial Relationships: Michele M. Iester, None; Luigi Borgia, None

Program Number: 4927 Poster Board Number: D0366
Presentation Time: 11:00 AM - 12:45 PM

Visual acuity evaluation in patients treated with ranibizumab for diabetic macular edema

Marc Stahel1, Peter P. Ciechanowski1, Frank Moser1, Sandra Lortz1, Heidi M. Fassnacht1, Nicole T. Graf1, Matthias D. Becker1, Stephan Michels1.
1Ophthalmology, Triemli Hospital Zurich, Zurich, Switzerland; Graf Biostatistics, Winterthur, Switzerland.

Purpose: In Switzerland ranibizumab (Lucentis) is licensed for the treatment of diabetic macular edema (DME) since fall 2011. Prior to this an off label use of restricted number of injections was possible in individual cases, when the specific health insurance company confirmed refunding. Review of the visual acuity (VA) outcome in clinical setting.

Methods: Retrospective analysis of VA in eyes with DME under ranibizumab treatment receiving at least one injection between April 2011 and April 2012. VA at baseline, month 3, 6, 12, 24 and at last visit were evaluated.

Results: At baseline 125 eyes with DME and a mean VA of 68.8 ETDRS letters were treated with ranibizumab. 39 of them in an off label setting prior to approval by Swissmedic. Mean follow up was 24 month. 13 eyes had a change of therapy, 11 to triamcinolon and 2 to bevacizumab, whereat 7 of these were switched back to ranibizumab and 1 had a second change to bevacizumab. Mean number of injections was 6.17. Over the observed period the VA remained stable with a mean VA of 69.3 (M3), 70.4 (M6), 66.1 (M12) and 62.7 (M24) letters respectively in the follow up visits. At the last recorded visit mean VA was 70.2 letters. These results didn’t differ statistically. No statistical significant difference in VA was reached as well in respect to the number of injections, HbA1c, insulin dependence, diabetic retinal proliferations, central laser coagulation and time since diagnosis of diabetes.

Conclusions: In this cohort of patients with DME treated with ranibizumab VA remained stable without a significant improvement. Limited visual acuity gain in this cohort is likely due to too infrequent treatment due to the prior off-label status of ranibizumab for DME.

Commercial Relationships: Marc Stahel, None; Peter P. Ciechanowski, None; Frank Moser, None; Sandra Lortz, None; Heidi M. Fassnacht, None; Nicole T. Graf, None; Matthias D. Becker, Novartis (F), Bayer (F), Allergan (F); Stephan Michels, Novartis (C), Bayer (C), Allergan (C), Alimera (C), Clonotech (C)

Program Number: 4928 Poster Board Number: D0367
Presentation Time: 11:00 AM - 12:45 PM

Differences in the topographic profile of retinal thickening in cases of diabetic macular edema with and without serous macular detachment

Hannah Shereef1,4, Oliver Comyn2, Sobha Sivarapasad2, Philip G. Hykin2, Gemmy C. Cheung3, Niro Narendran4, Yit C. Yang4.
1University of Birmingham, Birmingham, United Kingdom; 2National Institute for Health Research Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, London, United Kingdom; 3Singapore National Eye Centre, Singapore, Singapore; 4Royal Wolverhampton Hospitals NHS Trust, Wolverhampton, United Kingdom.

Purpose: To investigate if cases of diabetic macular edema (DME) associated with serous macular detachment (SMD) have a different topographic profile of retinal thickening compared to DME cases that are not associated with SMD.

Methods: Optical Coherence Tomography (OCT) scans from a total of 152 eyes from 152 patients with center-involving DME and central subfield thickness > 350 µm, were identified from departmental imaging databases in three centers; Royal Wolverhampton Hospitals NHS Trust, UK, Moorfields Eye Hospital NHS Foundation Trust, UK and Singapore National Eye Centre, Singapore. Measurements were taken of retinal thickness at the fovea (H) and extent of retina thicker than 350µm (W). H/W ratio was used as an “index for diffuseness” with lower values indicating a more diffuse spread of edema. Group means were compared between eyes with SMD and eyes without SMD.

Results: SMD was present in 55 eyes (36%). H (retinal thickness at the fovea) was lower in eyes with SMD than in eyes without SMD (396 µm vs. 550 µm, p<0.001) while W (extent of retina thicker than 350µm) was higher in eyes with SMD compared to eyes without SMD (4.74 mm vs. 4.18 mm, p=0.011). Eyes with SMD had significantly lower values of H/W compared with eyes without SMD (97.37 vs. 153.35, p=0.007).

Conclusions: In DME, the OCT profiles of retinal thickening differed between eyes with SMD and eyes without SMD. These observations may be explained by differences in the amount of retinal tissue expansion due to edema in the planes parallel to and perpendicular to the retinal surface. Our findings suggest the possibility of two morphological subtypes in DME, one of which may be associated with a higher probability of SMD. Our work generates a hypothesis that axial compliance of the retina may be an independent factor affecting the likelihood of developing SMD in DME.

Commercial Relationships: Hannah Shereef, None; Oliver Comyn, Novartis (F), Novartis (R); Sobha Sivarapasad, Allergan (F), Bayer (F), Novartis (F); Philip G. Hykin, BAYER (C), NOVARTIS (C), ALLERGAN (C), BAYER (R), NOVARTIS (R), ALLERGAN (F), NOVARTIS (F); Gemmy C. Cheung, Bayer (C), Bayer (R), Bayer (F), Novartis (C), Novartis (S), Glaxo Smith Kline (F), Roche (F); Niro Narendran, None; Yit C. Yang, Novartis (R)

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Program Number: 4929 Poster Board Number: D0368
Presentation Time: 11:00 AM - 12:45 PM
Use of a Retinal Acuity Meter (RAM) and Brightness Acuity Meter (BAM) to Identify Early Diabetic Macular Edema
Albert Li, David J. Sackel, Agnes Chen, Lisa Park. Ophthalmology, NYU School of Medicine, New York, NY.

Purpose: Diabetic retinopathy is among the leading causes of preventable vision loss in working-aged individuals, and early diagnosis may prevent progression to advanced disease. Our objective is to study the potential use of a retinal acuity meter (RAM) with a brightness acuity meter (BAM) as a screening tool to identify patients with early diabetic macular edema.

Methods: Three groups of patients were identified in the ophthalmology clinic at Bellevue Hospital Center in New York: diabetics with known macular edema, diabetics without edema, non-diabetic patients. Recovery time was measured after a 15-second macular photostress using the RAM and BAM. Macular edema was diagnosed by ophthalmoscopy and confirmed by measuring macular thickness via Heidelberg Spectralis optical coherence tomography (OCT). A Mann-Whitney test was used for statistical analysis.

Results: 38 eyes from 21 patients were analyzed. Retinal acuity ranged from 20/20 to 20/100 and macular photostress recovery time ranged from 10 to 46 seconds. When comparing eyes with macular edema to controls, macular photostress recovery was slightly delayed in patients with edema (mean recovery time 23.2s v. 21.0s), but did not reach statistical significance. There was a mildly positive correlation between recovery time and central foveal thickness by OCT (Pearson’s correlation coefficient, p=0.13). The relationship between central foveal thickness or photostress recovery and hemoglobin A1c (HbA1c) were also analyzed, but did not show significant correlation.

Conclusions: Patients with diabetic macular edema demonstrated slightly delayed macular photostress recovery time although the data did not reach statistical significance. A larger sample size may confirm this finding. Given the ease of use, the RAM and BAM may be used by non-ophthalmologists internists as a screening test of macular function in patients with diabetes. Early referrals to ophthalmologists based on these screening results may result in prevention of irreversible vision loss.

Commercial Relationships: Albert Li, None; David J. Sackel, None; Agnes Chen, None; Lisa Park, None

Program Number: 4930 Poster Board Number: D0369
Presentation Time: 11:00 AM - 12:45 PM
Optimal treatment strategy for Stage 5 Type 2A Idiopathic Macular Telangiectasia with anti-vascular endothelial growth factor (VEGF) agents - When to stop?
Sharad S. Malavade, Steven Cohen. Ophthalmology, University of South Florida, Tampa, FL.

Purpose: To evaluate long term follow-up of patients with Stage 5 (neovascular) Type 2A idiopathic macular telangiectasia treated with anti-vascular endothelial growth factor (VEGF) agents.

Methods: Retrospective review of three cases treated with bevacizumab and subsequently followed for an average 45 months (range 26 months - 61 months). The charts were reviewed to determine presenting symptoms, the baseline visual acuity at time of diagnosis of subretinal neovascular membrane (SRNVM), initial series of treatments with intra-vitreal bevacizumab injections, period of quiescence, recurrence and repeat therapy.

Results: All patients presented with acute vision loss. The average age was 71 years (range 60 years - 78 years) at time of presentation. The average Snellen visual acuity was 20/125 (range 20/50 to 20/200). Signs of neovascularization included pigment epithelial detachment, subretinal fluid and subretinal hemorrhage. Following treatment with intravitreal bevacizumab, each patient’s presenting symptoms abated and the average visual acuity improved to 20/63 (range 20/50 to 20/160). The treatment was stopped when the macula became dry and stable following a treat and extend treatment strategy. In all three patients, recurrent SRNVM was noted after a mean period of 22 months (range 6 months - 41 months) of their last injection. At recurrence, each eye developed similar signs and symptoms to the initial episode. The patients have all responded to re-institution of intravitreal bevacizumab.

Conclusions: It may not be safe to discontinue intravitreal injection of anti-VEGF agents in eyes of patients with neovascular Type 2A macular telangiectasia. Time to recurrence varied from 6 months to 41 months. The optimal treatment strategy for patients with stage 5 Type 2A macular telangiectasia is not known.

Commercial Relationships: Sharad S. Malavade, None; Steven Cohen, None

Program Number: 4931 Poster Board Number: D0370
Presentation Time: 11:00 AM - 12:45 PM
Safety, sterility and stability of direct- from- vial multiple dosing intravitreal injection of bevacizumab
Taraprasad Das1, Srinivas Volety*, Saad M. Ahsan2, Abhay K. Thakur2, Savitri Sharma1, Soumya Basu1, Tapas R. Padhi1, Mohan Rao2,1. Retina Vitreous Services, LV Prasad Eye Institute, Bhubaneswar, India; 2Center for Cellular and Molecular Biology, Hyderabad, India.

Purpose: To determine the stability, sterility and safety of bevacizumab multiple dosing from a single vial without prior aliquoting.

Methods: Six bevacizumab vials, used in multiple patients on a single day by direct withdrawal from the vial, and stored in 4 degree C up to six months, were tested for stability (High Performance Liquid Chromatography, (HPLC) and mass spectrometry, sterility (Culture), conformational stability by circular dichroism and fluorescence spectroscopy and the rubber cap structural integrity (Electron Microscopy, EM).

Results: HPLC of all six samples along with controls were similar. The culture was negative. The EM of the rubber cap did not show an open communication. Spectroscopic studies suggested the conformational stability of the drug. Further there was no infection or inflammation in 221 consecutive patients (973 injections) when bevacizumab was stored at 4 degree C and used for one week.

Conclusions: Bevacizumab does not lose stability when stored at 4 degree C for six months. It may be used for a week by direct withdrawal from the vial without fear of infection or inflammation if all standard precautions related to intravitreal injection are adhered to.

Commercial Relationships: Taraprasad Das, None; Srinivas Volety*, None; Saad M. Ahsan, None; Abhay K. Thakur, None; Savitri Sharma, None; Soumya Basu, None; Tapas R. Padhi, None; Mohan Rao, None

Support: Hyderabad Eye Research Foundation

Program Number: 4932 Poster Board Number: D0371
Presentation Time: 11:00 AM - 12:45 PM
Increased Healthcare Cost Related To Adding Dexamethasone Implant (Ozurdex®) To Bevacizumab (Avastin®) Monotherapy In Patients With Cystoid Macular Edema (CME) Due To Retinal Vein Occlusion (RVO) May Be Balanced By Less Frequent Follow-Up

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Omar Saleh, James Heroman, Shlomit Schaal. University of Louisville, Louisville, KY.

**Purpose:** To investigate the effect of adding intravitreal Ozurdex therapy to Avastin monotherapy for the treatment of CME due to branch RVO (BRVO) or central RVO (CRVO) on functional outcome, anatomical outcome, frequency of injections, and cost.

**Methods:** 35 patients (18 BRVO and 17 CRVO) treated initially with Avastin and later on with Ozurdex were included. Best corrected visual acuity (BCVA) and central macular thickness (CMT) on OCT were documented every 6 weeks for up to 228 weeks. Frequency of injections and cost of therapy were compared before and after Ozurdex was injected.

**Results:** Throughout 87 ± 60 (20-228) weeks of follow-up, BRVO patients received a mean of 1.6 ± 0.8 Ozurdex injections (39 ± 24% of all injections) and CRVO patients received 1.8 ± 1 injections (37 ± 19% of all injections).

In BRVO, an Ozurdex implant was received every 28 ± 14 weeks starting 30 ± 28 weeks after Avastin therapy and in CRVO an Ozurdex implant was received every 26 ± 12 weeks starting 37 ± 35 weeks after Avastin therapy.

After Ozurdex was added to Avastin therapy, the mean frequency of any intravitreal injection in BRVO decreased from injection every 10 ± 4 weeks to every 21 ± 15 weeks (p<0.01) and from injection every 11 ± 6 weeks to every 19 ± 7 weeks in CRVO (p<0.2). The mean number of fluid-free treatment-free visits increased from 1.3 ± 1.7 to 4.6 ± 3.7 visits in BRVO (p<0.01) and from 2.6 ± 3.4 to 5 ± 4.4 visits in CRVO (p>0.05).

Initiation of treatment with Ozurdex did not influence BCVA, which remained at 20/68 ± 20/76 in BRVO and at 20/105 ± 20/58 in CRVO, but decreased mean CMT from 399 ± 88 to 344 ± 96 µ in BRVO (p<0.01) and from 478 ± 86 to 348 ± 114 µ in CRVO (p<0.01). Mean monthly cost of therapy increased from 293 ± 60 $ to 408 ± 111 $ in BRVO (p<0.01) and from 478 ± 86 to 348 ± 114 µ in CRVO (p<0.01).

**Conclusions:** The addition of Ozurdex to Avastin therapy in the treatment of CME due to RVO reduced the overall frequency of intravitreal injections needed to control the disease, reduced CMT but did not affect BCVA, and increased the cost of treatment. Decreasing the frequency of follow-up for Ozurdex-injected patients from every 6 weeks to every 10 weeks may compensate for the increased healthcare cost.

**Commercial Relationships:** Omar Saleh, None; James Heroman, None; Shlomit Schaal, None

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**Program Number:** 4933 **Poster Board Number:** D0372

**Presentation Time:** 11:00 AM - 12:45 PM

**Reperfusion of ischemia with central retinal vein occlusion by activated protein C**

Motohiro Kamei, Nagakazu Matsumura, Mihoko Suzuki, Susumu Sakimoto, Hirokazu Sakauchi, Kohji Nishida. Ophthalmology, Osaka Univ Grad School of Medicine, Suita, Japan.

**Purpose:** To present two cases of ischemic central retinal vein occlusion (CRVO) in which reperfusion of large ischemic areas occurred after a novel treatment with intraocular activated protein C (APC) injection.

**Methods:** We intravitreally injected 3 µg of APC to treat two men (ages, 62 and 60 years) diagnosed with ischemic CRVO. We evaluated the retinal perfusion using fluorescein angiography (FA) before and after treatment. The safety and efficacy of the treatment were evaluated.

**Results:** In case 1, fluorescein angiography (FA) showed delayed retinal vascular filling and hypofluorescence due to non-perfusion of the retinal capillaries of 22.4 disc areas (DA). The area of non-perfusion decreased to 9.6 DA (by 57%) 3 months after treatment and completely resolved with almost normal microcirculation 10 months after treatment (Figure). In case 2, FA performed 6 months after treatment showed clearly improved microcirculation with shrinkage of the area of non-perfusion from 52.6 to 6.1 (by 88%). The treatment had no adverse effects and the visual acuity improved in both cases (20/400 to 20/250, and 20/300 to 20/150).

**Conclusions:** The current clinical report is the first to show that APC may be a potential treatment to achieve reperfusion of ischemic lesions. Although we reported only two cases, APC may be useful for treating not only ischemic CRVO but also other ischemic disorders such as diabetic retinopathy, acute myocardial infarction, or stroke.
THE EFFICACY OF SINGLE INTRAVITREAL RANIBIZUMAB INJECTION IN ACUTE NONARTERITIC ISCHEMIC OPTIC NEUROPATHY

Ali Osman Saatci, Okan Taskin, Ozlem Barut Selver, Aylin Yaman, Meltem Soylev Bajin. Ophthalmology Department, Dokuz Eylul University, Izmir, Turkey.

Purpose: To evaluate the effect of a single intravitreal ranibizumab injection in eyes with acute nonarteritic ischemic optic neuropathy (NAION).

Methods: In this retrospective clinical data analysis, 17 eyes of sixteen patients who experienced a visual loss with a duration of 15 days or less comprised the study group. In addition to standard ophthalmic examination, retinal nerve fiber layer thickness (RNFLT) analysis with spectral domain OCT was also performed prior to injection, one, three, six months and one year after the injection. Two subgroups were also statistically analyzed according to the visual loss duration. (Group one, visual loss duration less than eight days and group two, visual loss duration between eight and 15 days.)

Results: The mean time between visual loss and intravitreal injection was 7.5 days (Range, 2-15 days). Mean age of patients was 59 years (Range, 41-90 years). Male to female ratio was 6:10. After a single dose of ranibizumab injection, visual gain was noted in 14 of 17 study eyes. In two eyes, visual acuity was minimally reduced and no change was noted in the remaining eye with an initial visual acuity of hand motions. While preinjection mean best-corrected visual acuity (BCVA) was 1.45 ±0.88 logMar unit, postinjection mean BCVA was 1.00 ±0.68, 0.86 ±0.70, 0.80 ±0.71, 0.77 ±0.70 logMar unit respectively at the first week, first month, third month and first year. In all patients, the mean RNFLT dramatically decreased after the injection during the follow-up period. While preinjection mean RNFLT was 210 ±38 µm, postinjection mean RNFLT was 162.11 ±40.2, 94.27 ±71.23 ±22.5 and 57 ±18 µm respectively at the first week, first month, third month and first year. The improvement in visual acuity and RNFLT was better in the group of eyes with disease duration less than eight days but statistical analysis was not significant when two groups were compared. No injection related complication was noted during the follow-up period.

Conclusions: Intravitreal ranibizumab may be a promising treatment option in eyes with acute NAION.

Commercial Relationships: Ali Osman Saatci, None; Okan Taskin, None; Ozlem Barut Selver, None; Aylin Yaman, None; Meltem Soylev Bajin, None

Program Number: 4935 Poster Board Number: D0374
Presentation Time: 11:00 AM - 12:45 PM

Influence of Axial Length and Degree of Injection Reflux on Sustained Intraocular Pressure Elevation Due to Intravitreal Anti-Vascular Endothelial Growth Factor Therapy

Luis Mendonça1,2, Quan V. Hoang1,3, Jesse J. Jung1,3, Sarah Mrejen4, K Bailey Freund2,4. Ophthalmology, Hospital de Braga, Braga, Portugal; 1Vitreous, Retina, Macula Consultants of New York, New York, NY; 2Ophthalmology, Columbia University Medical Center, New York, NY; 3Ophthalmology, New York University, New York, NY.

Purpose: We previously reported 7.1% of our patient population experienced sustained intraocular pressure (IOP) elevation among 449 eyes from 328 neovascular age-related macular degeneration (NVAMD) patients injected with ranibizumab and/or bevacizumab. Here, we assess for an association of axial length with sustained IOP elevation in this population. Additionally, we determine whether axial length or the degree of immediate post-injection fluid reflux is associated with the severity of transient IOP elevation.

Methods: A prospective study was performed on a subset of 147 eyes from 74 consecutive NVAMD patients that presented to a single physician over a 2 month period. All patients had axial lengths measured by IOLMaster. 21 of these patients also had pre- and immediate post-injection IOP measured by Tonopen, as well as the degree of immediate post-injection reflux graded by an single experienced retinologist (KBF).

Results: Among the 147 eyes studied, 9.5% had been identified with sustained IOP elevation in our prior studies. Axial length did not correlate with experiencing sustained IOP elevation. Specifically, eyes that had experienced sustained IOP elevation showed an axial length of 23.96 +/- 0.66 mm (mean +/- standard deviation, n = 14), which was not significantly different than that found in eyes that had not experienced sustained IOP elevation (23.44 +/- 1.24 mm, n = 133), with p = 0.12 (2-tailed t-test). Axial length also did not correlate with the degree of transient IOP elevation. Eyes with axial length ≤ 23.5 mm had an immediate post-injection IOP of 18.4 +/- 17.4 mmHg (n = 9), which was not significantly different than that found in eyes with axial length > 23.5 mm (17.8 +/- 16.7 mmHg, n = 12), with p = 0.94 (2-tailed t-test). Eyes without appreciable post-injection reflux had an immediate post-injection IOP of 30.2 +/- 9.3 mmHg (n = 12), which was significantly higher than those with reflux (1.1 +/- 7.2 mmHg, n = 9), with p < 0.001 (2-tailed t-test).

Conclusions: Axial length does not appear to be a predictor of experiencing transient or sustained IOP elevation. Repeated trabecular meshwork trauma related to the degree of post-injection reflux and immediate, post-injection IOP elevation may be a contributing factor.

Commercial Relationships: Luis Mendonca, None; Quan V. Hoang, None; Jesse J. Jung, None; Sarah Mrejen, None; K Bailey Freund, Genentech (C), Regeneron (C), ThromboGenics (C), Bayer (C), DigiSight (C)

Program Number: 4936 Poster Board Number: D0375
Presentation Time: 11:00 AM - 12:45 PM

Ranibizumab versus Bevacizumab in the Treatment of Subfoveal Choroidal Neovascular Membrane Secondary to Pathologic Myopia

Ramón Domínguez Fernández1, ANDREA GOVETTO1, Maria Teresa Alves Perez2, Ramon Lorente1. Ophthalmology, CHU Ourense, Ourense, Spain; 1Biostatistics, CHU Ourense, Ourense, Spain.

Purpose: To report the short-term safety and efficacy of intravitreal ranibizumab (IVR) compared to intravitreal bevacizumab (IVB) in patients with subfoveal choroidal neovascular membrane (CNVM) secondary to pathologic myopia (PM).

Methods: 18 consecutive eyes of 15 patients with subfoveal choroidal neovascular membrane (CNVM) secondary to pathologic myopia (PM) were retrospectively reviewed. 8 patients received 0.05 ml of IVR while the other 8 received 0.05 ml of IVB. Retreatment criteria were: decrease in visual acuity of 5 letters and any fluid on OCT, or persistent or increased fluid on OCT. Main outcome measures were occurrence of treatment-related ocular or systemic complications, mean change in best corrected visual acuity (BCVA) and change in CNVM thickness (CNVMT).

Results: The mean follow-up was 6.5 months for IVR group and 10.13 months for IVB group. Mean number of injections was 1.6 for IVR group and 2.9 for IVB group. Mean baseline BCVA was 0.14 (±0.09) for IVR group and 0.12 (±0.08) for IVB group. In the IVR group, mean BCVA gain during the first month was 0.1 (±0.13), at 3, 6 and 12 months was respectively 0.16 (±0.16), 0.19 (±0.13) and 0.17 (±0.1). In the IVB group, mean BCVA gain during the first month was 0.8 (±0.1), at 3, 6 and 12 months was respectively 0.07 (±0.1), 0.9 (±0.1) and 0.15 (±0.16). Mean CNVMT at baseline was
259 µm (±175) in the IVR group and 242 µm (±79) in the IVB group. In the IVR group, a mean CNVMT decrease of 78.63 µm (±87.3) in the first month, of 88.14 µm (±149.7) at 3 months, of 86.83 µm (±152.7) at 6 months and of 88.5 µm (±82.7) at 12 months were reported. In the IVB group, mean CNVM decrease during the first month was 10.7 µm (±49.5). At 3 months a mean increase of 31.5 µm was reported. At 6 and 12 months, mean CNVM decreases by respectively 40 µm (±33) and 75 µm (±31.2).

**Conclusions:** Short-term results suggest that intravitreal ranibizumab and bevacizumab provides significant functional and anatomical improvement with no significant adverse events in patients with CNVM. Although differences between groups did not reach statistical significance, we clinically noticed better improvements in BCVA and CNMVT in the group treated with intravitreal ranibizumab.

**Commercial Relationships:** Ramón Domínguez Fernández, None; Andrea Govetto, None; Maria Teresa Alves Perez, None; Ramon Lorente, None

**Program Number:** 4937 **Poster Board Number:** D0376
**Presentation Time:** 11:00 AM - 12:45 PM
**Changes in retinal layer morphology following intra-vitreal Ozurdex therapy for macular oedema secondary to Retinal Vein Occlusion**


**Purpose:** To characterise changes in macular morphology on SD-OCT following intravitreal dexamethasone implant (Ozurdex) for macular oedema in retinal vein occlusion.

**Methods:** The changes in morphology of retinal layers at macula on SD-OCT at 6 months following intravitreal Ozurdex in retinal vein occlusion (19 BRVO, 11 CRVO) were assessed retrospectively. Each scan was analysed at 4 intersection points of the ETDRS grid 1mm from the centre. The following morphological classification to analyse the presumed retinal layers was used. Nerve fibre layer (NFL) was recorded as normal, thickened or thinned; ganglion cell-inner plexiform layer (GCL-IPL) and the outer plexiform-outner nuclear layer (OPL+ONL) were graded as intact, cystoid or diffuse oedema or mixed. The integrity of the external limiting membrane and ellipsoid layer were classified as intact, disrupted or absent. Each layer was individually analysed for changes from the baseline to six months post treatment

**Results:** Of 30 eyes NFL was intact in 80%, thickened in 13% and thinned in 2% at baseline. At six months NFL was intact in 80%, thickened in 17% and thinned in 3%. At baseline GCL-IPL layer was intact in 13% eyes, cystic in 37%, diffuse in 27% and mixed in 23% eyes. At 6 months, GCL + IPL was intact in 13%, cystic in 3%, diffuse in 57% and mixed in 27% eyes. Thus the 34% decrease in cystic component and 30% increase in diffuse component was statistically significant (p value < 0.05). At baseline the OPL+ONL was intact in just 3%, cystic in 57%, diffuse in 7% and mixed in 33% eyes. At 6 months, no eyes showed intact OPL+PNL layer, 20% showed cystic change, 43% showed diffuse and 37% eyes showed mixed results. Thus the change from cystic to diffuse was statistically significant (p value < 0.05). At baseline the ELM was intact in 17%, disrupted in 13%, absent in 20% and mixed in 50% . At 6 months, the ELM was intact in 23% , disrupted in 13%, absent in 13% and mixed in 50% of eyes. At baseline ellipsoid is intact in 23%, disrupted in 7%, absent in 30% and mixed in 40%. At 6 months the ellipsoid layer was intact in 27%, disrupted in 7%, absent in 23% and mixed in 43% eyes.

**Conclusions:** The significant morphological feature is the cystic component settling into diffuse macular oedema in GCL + IPL and OPL + ONL layers. The NFL, ELM and Ellipsoid layers did not change in morphological characteristics.

**Commercial Relationships:** Rashmi Akshikar, None; Sobha Sivaraprasad, Allergan (F), Bayer (F), Novartis (F)

**460 ROP: Management**

Wednesday, May 08, 2013 2:45 PM-4:30 PM
6C Paper Session
**Program #/Board # Range:** 4945-4951
**Organizing Section:** Retina

**Program Number:** 4945 **Presentation Time:** 2:45 PM - 3:00 PM
**Length of daylight during early gestation is an independent predictor of risk for severe retinopathy of prematurity**

Michael B. Yang, Sujata Rao, David R. Copenhagen, Richard A. Lang, 1Ophthalmology/Visual Systems Group/Abrahamson Pediatric Eye Institute, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; 2Ophthalmology, University of Cincinnati, Cincinnati, OH; 3Ophthalmology, University of California San Francisco, San Francisco, CA; 4Physiology, University of California San Francisco, San Francisco, CA.

**Purpose:** We have identified in the mouse a light-response pathway via melanopsin stimulation that regulates the formation of retinal vasculature during a period that approximates the first trimester of gestation in humans. We were thus interested as to whether average day length (ADL) during early gestation was a predictor of severe ROP (SROP).

**Methods:** Institutional review board approval for this study was obtained. 712 eyes of 357 premature infants (401-1250 g birth weight (BW)) from 1998 to 2003 were included. Multiple logistic regression with generalized estimating equations to account for inter-eye correlation was performed. The outcome variable SROP was (1) classic threshold ROP in zone I or zone II, (2) type 1 zone I ROP, or (3) in a few eyes, type 1 ROP in posterior zone II that examiners chose to treat.

**Results:** Multiple logistic regression analysis evaluating all 712 eyes with 76 eyes developing SROP showed that BW, gestational age, per capita income in the zipcode area of the mother’s residence, multiple birth, black race, and ADL were independent predictors of eyes developing SROP. Each additional hour of ADL during the first 90 days after the estimated date of conception (EDC) decreased the likelihood of SROP by 29% (p = 0.014). In a model of 146 prethreshold ROP eyes with 76 eyes developing SROP, each additional hour of ADL during the first 105 days after EDC decreased the likelihood of SROP by 46% (p = 0.001).

**Conclusions:** The finding that longer average day length during early gestation lowers the risk for severe ROP supports the finding in fetal mice of a light-response pathway that regulates the formation of retinal vasculature and may have implications for light during early gestation as a prophylactic treatment to prevent severe ROP.

**Commercial Relationships:** Michael B. Yang, None; Sujata Rao, None; David R. Copenhagen, None; Richard A. Lang, Eye Devic Inc (P)

**Support:** Unrestricted Departmental Grant from Research to Prevent Blindness, Inc., New York, NY, to University of Cincinnati Department of Ophthalmology ( James J. Augsburger, Chairman)

**Program Number:** 4946 **Presentation Time:** 3:00 PM - 3:15 PM
**Long term outcomes of lens clarity following lens-sparing vitrectomy for retinopathy of prematurity**

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Eric Nudelman, Antonio Capone, Kimberly A. Drenger, Michael T. Trese. Associated Retinal Consultants, William Beaumont Hospital, Royal Oak, MI.

**Purpose:** This study aimed to evaluate the long term outcomes on lens status of lens-sparing vitrectomy surgery for retinopathy of prematurity (ROP) associated retinal detachments.

**Methods:** Retrospective review of 220 eyes (158 patients) who underwent lens-sparing vitrectomy surgery for stage 4A, stage 4B and stage 5 ROP from 1994-2012. Lens clarity was evaluated from the most recent office visit or exam under anesthesia. In addition, success rates of surgeries were calculated based on rate of reattachment and need for additional retinal surgeries. Visual acuity, refractive outcomes, and rate of glaucoma were also evaluated.

**Results:** Visually significant cataract formation was seen in 3 of 220 eyes (1.36%) following lens-sparing vitrectomy. Mean follow up was 3.2 years (range 64 days - 18 years). Forty nine eyes (22%) required lensectomy following lens-sparing vitrectomy due to progression of retinal traction and need for additional retinal surgery. Additional retinal surgeries were performed in 11% of eyes with stage 4A, 40% with stage 4B, and 82% with stage 5. Forty two eyes (19.0%) required drops to control intraocular pressure.

**Conclusions:** We present the largest series and the longest follow-up to date of outcomes following lens-sparing vitrectomy for ROP. We found the rate of cataract formation to be approximately one percent. Success rates for retinal re-attachment with a single surgery was approximately 89% for stage 4A, 60% for stage 4B and 18% for stage 5.

**Commercial Relationships:** Eric Nudelman, None; Antonio Capone, Alcon Laboratories, Inc. (C), Alimera Sciences (C), Allergan, Inc. (C), Allergan, Inc. (F), FocusROP, LLC (F), FocusROP, LLC (I), GENENTECH (C), GENENTECH (F), GlaxoSmithKline (F), Ophthotec (F), Retinal Solutions, LLC (I), Retina Solutions, LLC (P), Synergetics, Inc. (C), Thrombogenics (F); Kimberly A. Drenger, None; Michael T. Trese, Nu-Vue Technologies (F), Synergetics (C), Thrombogenics (I), Genentech (R), FocusROP (I), Retinal Solutions LLC (I)

**Program Number:** 4947

**Presentation Time:** 3:15 PM - 3:30 PM

**Risk factors for retinopathy of prematurity (ROP): insights from “outlier” infants with low or high birth weights**


1. Weill Cornell Medical College, New York, NY;
2. Ophthalmology, Weill Cornell Medical College, New York, NY;
3. Ophthalmology, Oregon Health & Science University, Portland, OR;
4. Medical Informatics and Clinical Epidemiology, Oregon Health & Science University, Portland, OR.

**Purpose:** Many risk factors for ROP, such as low birth weight (BW), systemic illness and supplemental oxygen, are known. However, clinicians are often unable to explain “outliers”: large infants with low apparent risk that develop ROP, and small infants with high apparent risk that never develop disease. This project aims to define features of “outlier” infants, with the goal of gaining insight about protective or predisposing factors.

**Methods:** We reviewed infants screened at WCMC and CUMC from 2002-2010. ROP exam results were recorded, along with clinical factors including sex, BW, gestational age, multiple gestation, maternal race, IVF status, mechanical ventilation, bronchopulmonary dysplasia, neonatal sepsis, intraventricular hemorrhage, and necrotizing enterocolitis. The cohort was stratified by weight, highest ROP stage, and need for ROP treatment. Descriptive and correlational statistics were performed.

**Results:** During the study period, 1377 infants were screened for ROP. For the overall cohort (n=1377), all clinical factors above and below 500g were significantly associated with ROP stage and need for laser treatment (p<0.05). Among 258 infants with BW <750g, 78/258 (30%) were “outliers” who developed no ROP. Among 469 infants with BW >1250g, 66/469 (14%) were “outliers” who developed ROP. For “outliers” with BW <750g or >1250g, the only statistically-significant differences between infants vs. without ROP were in multiple gestation and neonatal sepsis. Among infants with BW < 500g, there were no statistically-significant differences in any clinical risk factors between the 4 (23%) “extreme outliers” without ROP and the 13 (77%) with ROP (Table 1). For the 168 with BW >1500g, there were no significant differences in any clinical risk factors between 16 (9%) “extreme outliers” with ROP vs. the 152 (91%) without ROP.

**Conclusions:** In this large cohort, known clinical risk factors were predictive of ROP stage and need for laser treatment. However, these risk factors were not significantly associated with ROP at extremes of birth weight. This suggests that other clinical, maternal, or genetic factors may protect from or predispose to ROP pathogenesis.

**Comparison of ROP risk factors in infants with BW <500g and >1500g. Numbers shown are mean values or proportion of infants with risk factor. P-values are for difference between means calculated by two-tailed student’s t-test.**

**Commercial Relationships:** Alexander D. Port, None; R.V. Paul Chan, None; Susan Ostmo, None; Michael F. Chiang, Clarity Medical Systems (unpaid member of Scientific Advisory Board) (S)

**Support:** Supported by unrestricted departmental funding from Research to Prevent Blindness, New York, NY (MFC, RVPC); NIH grant EY19474 (MFC) and the St.Giles Foundation (RVPC)

**Program Number:** 4948

**Presentation Time:** 3:30 PM - 3:45 PM

**The postnatal weight-gain algorithm WINROP early identifies sight threatening retinopathy of prematurity in a nation based cohort of extremely preterm infant**

**Pia Landgren**1, 2, Elisabeth Soltz; Sjöström3, Magnus Domellöf4, Gerd Holmström5, Anna-Lena Härde1, Chatarina Lofqvist6, Ann Hellsström7, 1Ophthalmology, Umeå University, Umeå, Sweden; 2Ophthalmology, Sahlgrenska academy at University of Gothenburg, Gothenburg, Sweden; 3Pediatrics, Umeå University, Umeå, Sweden; 4Ophthalmology, Uppsala University, Uppsala, Sweden.

**Purpose:** Evaluation of a postnatal weight-gain algorithm WINROP, identifying sight threatening retinopathy of prematurity (ROP) in a population based extremely preterm cohort.

**Methods:** This study enrolled all 707 live-born extremely preterm, gestational age (GA) <27 weeks infants, born 2004-2007 in Sweden, of which 407 infants met the criteria of WINROP analysis. WINROP analysis was performed retrospectively using weekly weight gain to estimate the preterm infant’s risk of developing ROP type 1 requiring treatment. GA, birth weight (BW) and weekly postnatal weight...
Izatt

Tomography in premature infants undergoing Retinopathy of Prematurity

Presentation Time: 4:00 PM - 4:15 PM

Feasibility of Color Doppler Spectral Domain Optical Coherence Tomography in premature infants undergoing Retinopathy of Prematurity screening

Ramiro S. Maldonado,1 Eric L. Yuan,1 Du Tran-Viet,1 Sharon F. Freedman,2 David Wallace,2 Hansford C. Hendargo,2 Joseph A. Izatt1, Cynthia A. Toth1

1Duke University Eye Center, Durham, NC; 2Pediatrics, Duke University School of Medicine, Durham, NC; 3Biomedical Engineering, Duke University, Durham, NC.

Purpose: We have previously identified on Spectral Domain Optical Coherence Tomography (SDOCT), elevated hyporeflective vessels, perivascular changes, and scalloped retinal layers in neonates with plus disease. We aim to evaluate the feasibility of performing Color Doppler SDOCT (CD-SDOCT) in premature neonates undergoing screening for retinopathy of prematurity (ROP).

Methods: Retrospective analysis of all CD-SDOCT images obtained from January 2009 to October 2012 in preterm neonates ages 31-41 weeks postmenstrual age undergoing ROP screening. Images were obtained using an 840 nm wavelength SD-OCT system (Bioptigen, Inc). One randomly selected eye from each infant was used for analysis. Information on ROP status was obtained from case report forms. Feasibility was assessed by determining whether or not (1) a Doppler signal could be detected, and (2) an en-face retinal image (RI) could be generated. RI was graded as good (no motion artifacts), fair (few motion artifacts) or poor (undistinguishable vessel pattern). With increasing flow velocity, Doppler signal could be absent, present or present with phase-wraping (colored rings within vessel lumen indicating higher flow velocity).

Results: Ten subjects had plus disease and 10 had ROP stage 0-2 and no plus disease at time imaging. 17 scans were captured in the vertical direction while only 3 in the horizontal direction. Doppler signal was detectable in 15/20 (75%) eyes, 10/10 (100%) of the plus disease subjects and 6/10 (60%) of the non-plus subjects. RI was scored as Good in 9/20 (45%), Fair in 8/20 (40%) and Poor in 3/20 (15%). Phase-wraping phenomenon was detected only in 4 eyes, all of them with plus disease and stage 3 ROP.

Conclusions: CD-SDOCT signal was better detected in eyes with plus disease. The phase wrapigng phenomenon may represent flow abnormalities present in these subjects. CD-SDOCT may potentially aid in future analysis of flow changes in ROP and disease progression. Hardware and software improvements are required to increase quantification of flow in this imaging modality.

Commercial Relationships: Ramiro S. Maldonado, None; Eric L. Yuan, None; Du Tran-Viet, None; Sharon F. Freedman, Pfizer, Inc. (C); David Wallace, Allergan (C), Genentech (C), NEI (F), RPB (F); Hansford C. Hendargo, None; Joseph A. Izatt, Biopigen, Inc. (I), Biopigen, Inc. (P), Biopigen, Inc. (S); Cynthia A. Toth, Genetech (F), Biopigen (F), Physical Sciences Inc. (F), Unlicensed (P)

Support: The Hartwell Foundation

Program Number: 4951

Presentation Time: 4:15 PM - 4:30 PM

Use of Computer-Assisted Quantitative Analysis of Retinal Vascular Dilation and Tortuosity to Predict Need for Laser Treatment in Retinopathy of Prematurity

Katherine Wu1, David Wallace2, Sharon F. Freedman2, 1School of Medicine, Duke University, Durham, NC; 2Ophthalmology and Pediatrics, Duke University, Durham, NC.

Purpose: Our aim was to determine if computer-assisted quantitative analysis of retinal vascular dilation and tortuosity using ROPtool software can predict the need for laser treatment in retinopathy of prematurity (ROP).

Methods: Video indirect ophthalmoscopy recordings were done of the eyes of premature infants undergoing routine, clinically indicatedROP exams (1/1/2005-8/31/2012). Retrospectively, a high-quality still image of the posterior pole of one eye was selected from each exam for each infant. Infants were included if they had at least one exam prior to 35 weeks postmenstrual age and at least 2 exams with high-quality images prior to vessel maturation or prior to the exam determining need for laser treatment. All eligible infants who had laser were included, and twice as many infants without laser were
randomly selected as controls. ROPtool was used to calculate retinal vessel dilation, tortuosity, and Sum of Adjusted Indices (SAI, combining dilation and tortuosity) for each image. For each of the vessel characteristics (dilation, tortuosity, SAI), the following were calculated: maximum value from any one vessel across all exams (Max), largest increase per week in Max (Change in Max), highest mean value when all vessels were averaged from any one exam (Highest_Mean), and largest increase per week in Highest_Mean (Change in Highest_Mean). These parameters were compared between infants who received laser and those that did not. P values were Bonferroni corrected, with a critical p value of 0.002.

**Results:** Medians for maximum tortuosity indexes were 9.923 and 6.477 for laser (n=27) and no laser (n=55), respectively (p<0.001). Medians for highest mean tortuosity indexes were 5.145 and 3.617 for laser and no laser, respectively (p<0.001). Parameters involving dilation and SAI were not significantly different between eyes that received laser and those that did not (Table). In multivariable analysis, the variable with the most significant association with need for laser treatment was highest mean tortuosity (p<0.001).

**Conclusions:** ROPtool analysis of tortuosity from indirect ophthalmoscopy still images is able to predict need for laser treatment in retinopathy of prematurity. Highest mean tortuosity of all vessels averaged in an image is the best predictor of the need for laser treatment.

### Table: Medians and p values

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<th>Laser</th>
<th>No Laser</th>
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**Commercial Relationships:** Katherine Wu, None; David Wallace, Allergan (C), Genentech (C), NEI (F), RPB (F); Sharon F. Freedman, Pfizer, Inc. (C)

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**6E Paper Session**

**Wednesday, May 08, 2013 2:45 PM-4:30 PM**

### Program #/Board # Range: 4952-4958

**Organizing Section:** Retina

**Program Number:** 4952

**Presentation Time:** 2:45 PM - 3:00 PM

**The Management of Retinal Detachments in Patients with Severe Mental Disabilities**


1Ophthalmology, Oakland University William Beaumont School of Medicine, Royal Oak, IL.

**Purpose:** Patients with severe mental disabilities commonly develop retinal detachment (RD) due to self abusive behavior. Pathology is often severe due to presentation delay. Postop care and intraocular pressure (IOP) checks are often difficult. Surgical success is often far less than normal patients. This is the largest review to date of severely mentally disabled patients treated for RD.

**Methods:** 45 eyes/37 patients from 4 institutions underwent surgery for RD over a 21 year period. Preoperative, operative and postoperative records reviewed retrospectively. Acuity was not possible as patients were nonverbal. Results were defined as Probable Surgical Success (PSS) and Probable Surgical Failure (PSF). PSS required: 1. macula attached, 2. IOP controlled, 3. cornea clear, and 4. one or more present: a. monocular patient reaches for objects, b. eye photo-averse, c. disc color good. PSF defined if any of the following present: 1. macula detached, 2. IOP uncontrolled, 3. cornea decompensated, 4. monocular with nonvisual behavior, 5. not photo-averse, or 6. disc atrophic.

**Results:** 100% of patients had RD, with Grade C PVR in 78%. Other features: 96% - macula off; 42% - giant retinal tear; 22% - macular hole; 9% - dislocated lens; 22% - fellow eye phthisis; 22% - RD later in fellow eye. Surgery choice: laser wall-off (4%); buckle only (15%); vitrectomy & gas (TPPV-G) (16%); vitrectomy & oil (TPPV-O) (80%); inoperable (9%). 47% required ≥ 2 procedures; 15% ≥ 3 procedures. Mean follow-up: 6.3 yrs (6-183 mos.). PSS seen in 29/45 eyes (64%). PSS seen in: 71% of buckle-only (7 eyes); 43% in TPPV-G (7 eyes); 76% in TPPV-O (25 eyes). PSS was 57% in 7 eyes in which oil was removed, and 83% in 18 eyes with oil retained. PSF seen in 16/45 (36%). 3 eyes failed with fellow eye phthisis. 1 patient failed OU. Total blindness in 4/37 (9%). 540 postop exams reviewed. 47 EUA’s done. Fundus seen & IOP obtained in 215 exams (40%). IOP unable in 53% of exams. Fundus never seen in 10% patients. 24% never had IOP checked.

**Conclusions:** Overall PSS was 64%. TPPV-O with oil retention gave best results (83%)(p>0.01). Glaucoma and corneal problems common. Postop exams are difficult with IOP obtained in less than half of exams. EUA’s required commonly. Patients with severe mental handicap represent a difficult population however vision can be restored. The first eye should be considered for surgery since surgery often required in fellow eye.

**Surgical Success (PSS) and Probable Surgical Failure (PSF)**

<table>
<thead>
<tr>
<th>Surgical Technique</th>
<th>Probable Surgical Success (PSS)</th>
<th>Probable Surgical Failure (PSF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laser wall-off</td>
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<td>0 (0%)</td>
</tr>
<tr>
<td>Buckle only</td>
<td>5/7 (71%)</td>
<td>2/7 (29%)</td>
</tr>
<tr>
<td>TPPV – Gas</td>
<td>3/7 (43%)</td>
<td>4/7 (57%)</td>
</tr>
<tr>
<td>TPPV – Silicone Oil</td>
<td>19/25 (70%)</td>
<td>6/25 (24%)</td>
</tr>
<tr>
<td>TPPV – Retained Oil</td>
<td>15/18 (83%)</td>
<td>3/18 (17%)</td>
</tr>
<tr>
<td>TPPV – Removed Oil</td>
<td>4/7 (57%)</td>
<td>3/7 (43%)</td>
</tr>
<tr>
<td>Inoperable</td>
<td>0 (0%)</td>
<td>4/45 (9%)</td>
</tr>
</tbody>
</table>

**TOTAL Population**

29/45 (64%) 16/45 (36%)
Commercial Relationships: Kirk H. Packo, Alcon Surgical, Inc. (C), Regeneron (R), Genentech (F), Allergan (F), OD-OS, Inc (F), Eyetech (R), Alcon Surgical, Inc (F), Abbott Pharmaceutical (F);
Joseph M. Civantos, None; Jack A. Cohen, None; John S. Pollack, None; Pauline T. Merrill, None; Serge de Bustros, None; Bruce Garretson, None

Program Number: 4953
Presentation Time: 3:00 PM - 3:15 PM
Management of Uncomplicated Retinal Detachments: A Multicenter Study
Ron A. Adelman\(^1\), Aaron Parnes\(^1\), Didier Ducournau\(^2\), \(^1\)Ophthal & Visual Science, Yale Univ Sch of Medicine, New Haven, CT; \(^2\)Clinique Sourdirle, Nantes, France.

**Purpose:** To study success and failure in the treatment of uncomplicated rhegmatogenous retinal detachments.

**Methods:** Non-randomized, multi-center clinical study. 7,678 rhegmatogenous retinal detachments were included in the study. 176 surgeons from 48 countries spanning 5 continents provided information on the primary procedures for these patients. Reported data included specific clinical findings, the method of repair, and the outcome following intervention. The results were analyzed by the French INSEE (National Institute of Statistics and Economic Studies).

**MAIN OUTCOME MEASURES:** Failure of retinal detachment repair, remaining silicone oil, and need for additional procedures to repair the detachments.

**Results:** Of the 7,678 cases of rhegmatogenous retinal detachment, 4,179 “uncomplicated” retinal detachments were included in this report. Combining phakic, pseudophakic, and aphakic groups, those that were treated with scleral buckle alone (n = 1341) had a significantly lower final failure rate than those treated with vitrectomy, with or without a supplemental buckle (n = 2717) (p = 0.04). In phakic patients, final failure rate was lower in the scleral buckle group as compared to those who had vitrectomy, with or without a supplemental buckle (p = 0.028). In pseudophakic patients, the failure rate of the initial procedure was lower in vitrectomy compared to scleral buckle (p = 3 x 10^-8). There was no statistically significant difference in failure rate between segmental (n = 721) and encircling (n = 351) buckles (p = 0.5). Those that received vitrectomy with a supplemental scleral buckle (n = 488) had an increased failure rate compared to those that had vitrectomy without a supplemental buckle (n = 2242) (p = 0.048).

**Conclusions:** In the treatment of “uncomplicated” phakic retinal detachments, repair using scleral buckle may be a good option. There was no significant difference between segmental versus 360 degree buckle. For pseudophakic “uncomplicated” retinal detachments, the surgeon should balance the risks and benefits of vitrectomy versus scleral buckle and keep in mind that single-surgery reattachment rate may be higher with vitrectomy. However, if a vitrectomy is to be performed, this data suggests that a supplemental buckle is not helpful.

Commercial Relationships: Ron A. Adelman, None; Aaron Parnes, None; Didier Ducournau, None

Program Number: 4954
Presentation Time: 3:15 PM - 3:30 PM
Primary Scleral Buckling: A Safe and Effective Treatment Option for Retinal Detachment
Frank Ruda\(^1\), Adel Jirgis\(^2\), Nabil Jabbour\(^1,2\), \(^1\)West Virginia University Eye Institute, Morgantown, WV; \(^2\)ForSight Foundation, Morgantown, WV; \(^1\)National Eye Institute - Cairo, Cairo, Egypt.

**Purpose:** To evaluate primary scleral buckling (SB) for rhegmatogenous retinal detachments (RRD) frequently treated with vitrectomy with or without SB.

**Methods:** Primary SB performed in the past 5 years on all RRD cases that don’t qualify for pneumatic retinopexy or have significant proliferative vitreoretinopathy (PVR).

**Results:** 75 patients (eyes) underwent primary SB. 100% showed initial reattachment. 8 (11%) required additional treatment after 1 month (3 lasers and 5 buckle revisions). All 75 eyes remained reattached for the duration of follow up (average 12 M) with an average of 5.4 lines of improvement. 6 (8%) showed mild exposure requiring partial buckle removal (in the office). No other untoward effects or complications were encountered.

**Conclusions:** Primary SB without vitrectomy is a safe and effective treatment for many RRDs. It saves unnecessary complications and cost. Generations of vitreoretinal surgeons are being deprived of this effective therapy because of lack of exposure to it during their training. This deficiency affects the quality of SB, even as a secondary procedure.

Commercial Relationships: Frank Ruda, None; Adel Jirgis, None; Nabil Jabbour, None

Program Number: 4955
Presentation Time: 3:30 PM - 3:45 PM
Quantifying the Effects of Enzymatic Vitreolysis Reveals Biomechanical Roles of Structural Macromolecules in Shear and Extension
Benjamin Filas, Qianru Zhang, Ying-Bo Shui, David C. Beebe.
Ophthalmology and Visual Sciences, Washington University School of Medicine, St. Louis, MO.

**Purpose:** Clinical goals of enzymatic vitreolysis are two-fold: reduce vitreous stiffness and vitreoretinal traction to aid in separation of the vitreous from the retina. The purpose of this study was to develop a quantitative, in vitro method to simultaneously probe the viscoelastic response of the vitreous in shear (to gauge stiffness) and extension (to estimate traction) following enzymatic degradation of structural macromolecules.

**Methods:** Vitreous (10 mL total volume) from fresh bovine eyes was injected (200 μL) with PBS, purified collagenase (50-200 U/mL), or hyaluronidase (50-200 U/mL) and stored overnight at 4°C. The vitreous was isolated for analysis on a AR-G2 rheometer (TA Instruments) with a closed parallel plate (20mm) geometry. An oscillatory frequency sweep (Fig. 1A) (to estimate stiffness) at fixed 3% strain was followed by uniaxial extension (250 μm/sec; Fig. 1B) (to estimate traction) until detachment.

**Results:** Overnight exposure to hyaluronidase or collagenase significantly decreased the storage modulus (G\(^*\); solid-like structure) of the bovine vitreous relative to PBS controls (n > 7 per group) as assessed by oscillatory shear testing (G\(^*\)\(_{PBS} = 8.6 \text{ Pa} - \text{Fig. 1A} ; G\(^*\)\(_{Hyal}\) = ...
Pneumatic retinopexy (PR) is an office modality for primary RRD. Anatomic and visual outcomes are similar in RRD’s with traditionally accepted inclusion criteria compared to those with more extreme criteria. Outcomes are also similar in phakic and pseudophakic eyes.

**Conclusions**: Pneumatic retinopexy is an effective treatment modality for primary RRD. Anatomic and visual outcomes are similar in RRD’s with traditionally accepted inclusion criteria compared to those with more extreme criteria. Outcomes are also similar in phakic and pseudophakic eyes.
included demographics, etiology, presenting clinical examination findings, prior ocular surgery, predisposing factors and outcome. The primary outcome was anatomic success defined as retinal reattachment. Secondary outcomes included the number of subsequent surgeries and the requirement of silicone oil to maintain retinal attachment.

Results: We identified 103 eyes in 98 children who underwent segmental scleral buckling as an initial procedure for rhegmatogenous retinal detachment. The mean age was 12 years (standard deviation ±3.22; range 1 to 18 years) with 79.5% of patients being male. The mean follow-up interval was 25 months, with follow up ranging from 3 months to 13 years. Retinal reattachment was achieved with one operation in 71.8% (74 out of 103 eyes) and the final success rate was 95% (98 out of 103 eyes). Factors associated with an increased risk of failure included: more than one break; 3 or more quadrants of detachment; horse shoe tears; no breaks seen on pre-operative examination; congenital and developmental abnormalities.

Conclusions: The anatomic success rate for segmental scleral buckling in this study compares favorably with other studies and modalities and supports its use as a primary intervention in pediatric rhegmatogenous retinal detachments.

Commercial Relationships: Sidath E. Liyanage, None; Marie-Hélène Errera, None; Rene Moya, None; S. Chien Wong, None; Eric Ezra, None

Program Number: 4958
Presentation Time: 4:15 PM - 4:30 PM
Prophylactic Treatments for Retinal Tears/Detachment in Stickler Syndrome: Single Institution Experience

Purpose: To report various prophylactic treatment methods and outcomes for retinal tears and detachment in patients with Stickler Syndrome (SS).

Methods: A retrospective study of patients with SS from March 1991 to February 2012 was performed. Data analysis of 31 patients (62 eyes) included clinical features, systemic features, treatment (prophylactic scleral buckle, laser retinopexy and cryotherapy) and outcomes at the last follow-up (FU).

Results: The median age of the patients was 12 years (range 0.2- 68). Of the 31 patients, there were 9 females and 22 males. Systemic features of SS were present in 23 patients, of which most common was cleft palate in 13, musculoskeletal abnormalities in 7. High myopia was present in 19 patients. Anterior segment examination showed cataract in 10 eyes, pseudophakia in 7 eyes and aphakia in 4 eyes. Vitreous syneresis was present in 25 eyes, membranes, veins and opacities in 13 eyes, posterior vitreous detachment in 3, and empty vitreous cavity in 7 eyes. Peripheral retina examination showed small retinal tears in 4 eyes, lattice degeneration in 12, giant retinal tear in 2, chorioretinal atrophic scars in 15, vitreoretinal tufts in 8, retinal detachment (RD) in 5. No retinal abnormalities were noted in 13 eyes. Treatment was by laser retinopexy and or cryotherapy in 15 eyes, and combination of vitrectomy, laser retinopexy, cryotherapy and or sclera buckle in 6 eyes and close observation in 40 eyes. Five fellow eyes with extensive lattice degeneration with or without associated retinal tears were treated by prophylactic scleral buckle. The median FU duration was 65.5 months (range 5-226). Retinal detachment developed in seven fellow eyes. The median time to develop the retinal detachment was 22.5 months (range 5-123) months. Six eyes were treated by vitrectomy with sclera buckle and one eye with vitrectomy, silicon oil and laser retinopexy. Retinal tear in the fellow eyes occurred in 16 eyes and treated by laser retinopexy and or cryotherapy. None of the patients had RD at the last FU visit.

Conclusions: Prophylactic treatments such as scleral buckle, laser, and cryotherapy were effective in preventing the development of giant retinal tears or detachment not only in affected eyes but also in the fellow eyes of patients with Stickler syndrome.

Commercial Relationships: Kiran Turaka, None; Shepard Bryan, None; Alan J. Gordon, None; Henry M. Kwong, None; Clive H. Sell, None

516 Trauma
Thursday, May 09, 2013 8:30 AM-10:15 AM
Exhibit Hall Poster Session
Program #/Board # Range: 5754-5759/D0001-D0006
Organizing Section: Retina

Program Number: 5754 Poster Board Number: D0001
Presentation Time: 8:30 AM - 10:15 AM
High-Power Blue Laser Pointer-Induced Maculopathy
saluaiman M. Alsulaaiman1, Abdulaziz A. Alrushood,2 Juwai almasaoud,1 Sultan Alzaaidi,1 Yahya A. Alzahrani,1, J. Fernando Arevalo1,2, Nicola G. Ghazi,1 Emad B. Abboud,1 Saba Alreshaid1,1 king khaled eye specialist hospital, Riyadh, Saudi Arabia; 2Wilmer eye institute, Baltimore, MD.

Purpose: To report various forms of maculopathy caused by momentary exposure to high-power blue laser pointer.

Methods: A consecutive case series of patients who presented to the King Khaled Eye Specialist Hospital with a history of laser pointer exposure to the eye is reported. A full ophthalmic evaluation including fundus photography, spectral-domain optical coherence tomography and fluorescein angiography was performed.

Results: Ten eyes of 10 patients were evaluated. The clinical findings included a full thickness macular hole in 3 eyes, subhyaloidal/sub internal limiting membrane (ILM) hemorrhage in 4 eyes, an outer retinal disruption in one eye, an epiretinal membrane in 1 eye, and a schisis-like cavity in one eye. Nd:YAG hyaloidotomy was performed in three eyes with subhyaloidal hemorrhage and pars plana vitrectomy (PPV) with or without tamponade in four eyes. Visual acuity improved in all patients spontaneously or following intervention. Four eyes (40%) improved spontaneously whereas 6 eyes (60%) were managed by Nd:YAG hyaloidotomy or surgery.

Conclusions: Visual acuity improved in all patients spontaneously or following intervention. High-power handheld laser pointers are extremely dangerous to the eye and public awareness should be encouraged.

Commercial Relationships: sulaiman M. Alsulaaiman, None; Abdulaziz A. Alrushood, None; Juwai almasaoud, None; Sultan Alzaaidi, None; Yahya A. Alzahrani, None; J. Fernando Arevalo, None; Nicola G. Ghazi, None; Emad B. Abboud, None; Saba Alreshaid, None

Program Number: 5755 Poster Board Number: D0002
Presentation Time: 8:30 AM - 10:15 AM
The effects of repeated exposure to low level blast overpressure on rat ocular tissues
Jae Hyek Choi1,2, Whitney A. Greene1,2, Mikulas Chavko1,2, Anthony J. Johnson3, Jeffery M. Cleland,4 Heung-Ching W. Wang2,1 National Research Council, Washington, DC; 2Ocular Trauma Department, U.S. Army Institute of Surgical Research, Fort Sam Houston, TX; 3NeuroTrauma Department, Naval Medical Research Center, Silver Spring, MD.

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Purpose: Blast-induced ocular injury is a frequent cause of morbidity for survivors of improvised explosive devices (IEDs). A single exposure to a moderate level of blast overpressure (BOP) has been shown to cause damage to the eye in a rat model; however, during combat, military personnel may in fact be exposed to low levels of BOP multiple times. The purpose of this study is to characterize the effects of repeated exposure to low level BOP on rat ocular tissues. The pathophysiology of blast-induced ocular injury was examined by analysis of activated caspase 3 and expression of glial fibrillary acidic protein (GFAP) in ocular tissues from rats exposed five times to low level BOP.

Methods: A compressed air shock tube was used to deliver 70±7 KPa BOP of duration 2 ms to the frontal side of rats. Rats were exposed once daily for five days then euthanized on day 5, one hour after the last blast exposure. Rats subjected to a single blast exposure euthanized at 5 days after blast exposure and rats not exposed to blast were included as controls. Ocular tissues were collected and processed for immunohistochemistry to detect activated caspase 3 and GFAP. The number of positive cells was quantified.

Results: Activated caspase 3 was detected in the retina and optic nerve from all animals subjected to BOP exposure, whether one time exposure or repeated exposures. Similar levels of activated caspase 3 were detected in the ganglion layer (GL) and inner nuclear layer (INL) of the retina. Animals that had received repeated BOP exposures had significantly higher levels of activated caspase 3 in the optic nerve. In all animals subjected to BOP exposure, GFAP immunoreactivity was detected in the retinal Muller cells traversing the INL to the outer plexiform layer (OPL), while the central regions of the retina were negative for GFAP. Tissues from control animals not exposed to BOP were negative for activated caspase 3 and GFAP.

Conclusions: Both single exposure and repeat exposure to low level BOP resulted in damage to the retina in the GL and the INL. Repeated exposure to BOP caused increased apoptosis in the optic nerve as indicated by activated caspase 3, suggesting that repeated exposure to BOP causes more severe optic neuropathy than a single BOP exposure. Exposure to BOP caused a distinct pattern of gliosis at the periphery of the retina as indicated by GFAP immunoreactivity.

Commercial Relationships: Jae Hyek Choi, None; Whitney A. Greene, None; Mikulas Chavko, None; Anthony J. Johnson, None; Jeffery M. Cleland, None; Heuy-Ching H. Wang, None

Support: U.S. Army Military Operational Medicine Research Program (MOMRP) and Defense Medical Research and Development Program (DMRDP)

Program Number: 5757 Poster Board Number: D0004
Presentation Time: 8:30 AM - 10:15 AM

A prospective study on Terson’s syndrome and intraocular infections in critically ill patients

Daniel Barthelemes1, 2, Matthias Haenggi2, Tobias M. Merz2, Jakka Takala1, Michael Lensch2, Stephan M. Jakob2

1Biomedical Engineering, University of Texas at San Antonio, San Antonio, TX; 2WESMDPA, San Antonio, TX; 2Ophthalmology, University of Texas Health Science Center San Antonio, San Antonio, TX.

Purpose: Megadose steroids are an ineffective and potentially dangerous treatment for TON (Sarkies, Eye 2004;18:1122-5). Development of new treatments has been inhibited by the lack of a suitable animal model of TON. An ideal model would produce symmetric bilateral injury to both nerves without damaging the globe or compromising blood supply. Recent studies indicate that rapid rotation of the globe can produce partial or complete axonal avulsion immediately posterior to the lamina cribrosa (Sponsel et al, IOVS 2011;52:9624-8). Here, we present a robotic torsion device to test whether a rapid rotation could induce optic nerve damage similar to that observed in TON.

Methods: A robot was constructed (Fig. 1) to allow the application of rapid rotation to the eyes of a rat. The magnitude and velocity of rotation were both controlled to allow titration of damage to the optic nerve. The motor’s axis was fastened to the left eye using an elbow clamp holding a suction cup which attached to the eye using an ophthalmodynamometer. Initial testing of the device was carried out by producing torsional trauma to the left eye of a rat cadaver. In half of the animals, the right eye was left uninjured as a control while in the other half an identical injury was inflicted to examine symmetry. Both nerves were examined using biomicroscopy and histopathology.

Results: Controlled rotations up to 120 degrees at velocities of 13500 degrees/second were achieved. Optic nerve damage increased with both the magnitude and rate of rotation. Twisting the eye at a sufficiently high rate and magnitude resulted in a completely severed optic nerve. The control (right) eyes and optic nerves did not exhibit any degree of trauma or other damage induced by application of the device.

Conclusions: The robotic device successfully induced trauma limited to the selected eye, inducing optic nerve damage similar to that observed in human TON patients. The potential to produce isolated, titrated, symmetric injury to the retrolaminar nerve without traumatizing any of the remainder of the visual system using this focalized strain-rate effect offers the ideal model for placebo-controlled bilateral studies of topical, intraocular, or retrobulbar neuroprotective therapies to mitigate the effects of TON. This animal
model of torsion-induced TON will next be investigated in live rats by evaluating functional MRI and other measures of visual function.

Commercial Relationships: Matthew A. Reilly. None; Rick E. Sponser. New World Medical (P); Randolph D. Glickman. None

Program Number: 5758 Poster Board Number: D0005
Presentation Time: 8:30 AM - 10:15 AM
Pars Plana Vitrectomy with medium-term Perfluoro-N-Octane for severe ocular trauma and hemorrhage with or without retinal detachment
Ramanath Bhandari, Shulamit Schwartz, Carmen Gonzalez, Regina Victoria, Naresh Mandava, Hugo Quiroz-Mercado.
Purpose: To describe a retrospective series of patients post severe ocular trauma involving globe rupture and resultant vitreous hemorrhage and intra or subretinal hemorrhage treated with pars plana vitrectomy and post operative medium term tamponade with perfluoro-n-octane (PFO).
Methods: A chart review was conducted of patients with severe ocular trauma involving globe rupture and resultant vitreous hemorrhage with or without retinal detachment. All patients were treated with 23-gauge pars plana vitrectomy (PPV) and received a planned medium term tamponade with PFO. A second staged procedure was performed 10-17 days later with removal of the PFO and injection of 1000 centistoke Silicone Oil.
Results: Four Eyes of four patients were included in the present study. Mean follow-up time was 9 months +/- 4.2 months. The average time between primary repair of ruptured globe and PPV was 12 days +/- 5 days. All patients had active hemorrhage during PPV that was controlled with PFO injection. Two patients also had submacular hemorrhage that resolved post PFO tamponade. One patient was found to have concurrent retinal detachment which was repaired with primary PPV alone. PFO was found to compartmentalize the hemorrhage during the medium term tamponade with a majority of the hemorrhage draining into the anterior chamber. In addition, during PFO tamponade, all patients had some degree of anterior segment inflammation and a transient rise in intraocular pressure (IOP) above 21mm Hg, but none required an intervention beyond topical agents to control IOP. BCVA improved from light perception in all patients prior to procedure to count finger vision or better in 75% of patients post procedure.
Conclusions: Medium-term PFO tamponade was found to be efficacious in the treatment of active hemorrhage during secondary repair with PPV post globe rupture with or without retinal detachment. A larger randomized prospective trial is required to evaluate this treatment against PPV alone.

Organizing Section: Retina

517 Laser/Intravitreal Treatment
Thursday, May 09, 2013 8:30 AM-10:15 AM
Exhibit Hall Poster Session
Program #/Board # Range: 5760-5763/D0007-D0010

A comparison of anti-VGCEF therapy and laser in preserving visual function in patients with proliferative diabetic retinopathy
Marisol Estudillo, Victor H. Gonzalez. Ophthalmology- Retina, Valley Retina Institute, PA, McAllen, TX.
Purpose: To evaluate the effect on visual acuity and visual field sensitivity in patients with proliferative diabetic retinopathy (PDR)
treated with anti-VEGF monotherapy versus combination of anti-VEGF induction and selective laser versus standard panretinal photocoagulation (PRP).

**Methods:** The patients were randomly assigned to three groups and treated and followed for one year. They were evaluated baseline, week 3, week 6, and every 6 weeks thereafter. Twenty eyes of 20 patients were included. In Group A patients received 3 intravitreal pegaptanib (IVP) injections every 6 weeks (q6), then additional injections every 12 weeks. Eight eyes in Group B received 3 IVP q6 and after that selective laser treatment. Four eyes in Group C received standard PRP only. Humphrey Visual Fields (30-2) were performed in all groups at baseline and at 1 year follow up visit. Changes in mean deviation (MD) on HVF over the time period were assessed. Best corrected visual acuity (BCVA) was assessed at every visit.

**Results:**

- **Group A:** Baseline mean BCVA=77.25(20/32), MD=-9.63. One year visit mean BCVA=80.50(20/25), MD=-6.71.
- **Group B:** Baseline mean BCVA=78.56(20/32), MD=-6.10. One year visit mean BCVA=79.16(20/25), MD=-7.24.
- **Group C:** Baseline mean BCVA=66.16(20/50), MD=-10.08. One year visit mean BCVA=71.34(20/40), MD=-12.9.

**Conclusions:** The BCVA improved on average 3.25 letters at one year in group A, 0.6 letters in group B, and 5.18 letters in group C. The MD improved on average from baseline to one year after treatment in group A by 2.62 points. In group B it decreased by 1.14 points at one year, and group C got worse at one year by 2.82 points. Although BCVA in group C improved by more letters than group A, baseline BCVA in group C was lower to begin with and the ceiling effect might be responsible for this finding.

**Commercial Relationships:** Marisol Estudillo, None; Victor H. Gonzalez, Genetech (C), Regeneron (C), Pfizer (C), Valiant (C), Alimera (C)

**Clinical Trial:** NCT01486771

Program Number: 5761 Poster Board Number: D0008

**Program Number:** 5762 Poster Board Number: D0009

**Presentation Time:** 7:30 AM - 10:15 AM

**Intravitreal Ranibizumab Combined with Panretinal Photocoagulation in Patients with Treatment-Naive Proliferative Diabetic Retinopathy**

**Methods:** To evaluate the efficacy of combination therapy with ranibizumab (RBZ) and panretinal photocoagulation (PRP) versus PRP alone in patients with treatment-naive bilateral proliferative diabetic retinopathy (PDR) as measured by mean change in visual acuity (VA), mean change in central retinal thickness (CRT) as measured by time-domain optic coherence tomography (TD-OCT) and incidence of vitreous hemorrhage (VH).

**Results:** Thirty patients (n=56 eyes) completed the study; four eyes did not have complete VA and OCT data. Baseline demographics were well balanced between the groups (Table 1).

In eyes with clinically significant macular edema (CSME) and CRT greater than 250µm, VA increased by 4.1 letters in group 1 (p<0.02) and decreased by 5.0 letters in group 2 (p<0.01) at the primary endpoint (month 6). In group 1, CRT decreased by 52 um in group 2 (p<0.01), whereas in group 2, there was no significant change in thickness (p=0.09).

In eyes without edema (no CSME and CRT<250 µm), VA improved by 8.3 letters at month 6 in group 1 (p=0.05), with no significant change in group 2 (ΔVA =1.6, p=0.69). The CRT showed no significant changes in both groups: group 1, ΔCRT=1.9, p=0.58 and group 2, ΔCRT=17.1, p=0.19.

**Conclusions:** Intravitreal RBZ in conjunction with PRP can be an effective combination treatment in eyes with PDR and CSME.

### Table 1. Demographics

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (SD) /years</td>
<td>52.9 (7.5)</td>
</tr>
<tr>
<td>Gender / %</td>
<td>50.0</td>
</tr>
<tr>
<td>Mean duration of Diabetics / SD (years)</td>
<td>13.1 (1.9)</td>
</tr>
<tr>
<td>Mean Central Macular Thickness (DOCT) /µm</td>
<td>9.2 (1.9)</td>
</tr>
</tbody>
</table>

CDM = clinically significant macular edema; SD = standard deviation.

**Commercial Relationships:** Daniel A. Ferraz, None; Raaffay Sophie, None; Millena G. Bittencourt, None; Rony C. Preti, None; Lisa M. Vazquez, None; Augusto A. Motta, None; Mostafa Hanout, None; Yasir J. Sepah, None; Quan Dong Nguyen, Genetech (F), Regeneron (F), Lux Biosciences (F), Abbott (F), GSK (F), Santen (F), Santen (C), Bausch and Lomb (C), Optos (F), Heidelberg Engineering (F); Walter Y. Takahashi, Novartis (C), Bayer (C), Bayer (R)

Program Number: 5761 Poster Board Number: D0008

**Presentation Time:** 7:30 AM - 10:15 AM

**Rescue Laser Photo Stimulation for Diabetic Macular Edema Unresponsive to Anti-VEGF Therapy**

Yasir J. Sepah1, 2, Raaffay Sophie1, 2, Millena G. Bittencourt1, Rony C. Preti1, Lisa M. Vazquez1, Augusto A. Motta1, Mostafa Hanout1, Yasir J. Sepah2, Quan Dong Nguyen1, Walter Y. Takahashi3.

1Ophthalmology, University of São Paulo, São Paulo, Brazil; 2Retina Department, Wilmer Eye Institute, Johns Hopkins University, Baltimore, MD.

**Purpose:** Although, ranibizumab monthly improve vision and macular edema in patients with DME, a 30 to 50% of the patients may still require adjunctive and complementary therapy. The purpose of this investigation is to evaluate the safety and efficacy of sub-lethal continuous wave laser for the treatment of diabetic macular edema (DME) unresponsive to previously anti-VEGF therapy.

**Methods:** Twenty patients with DME that did not present improvement after 6 monthly injection of Ranibizumab, understood as a reduction of at least 10% of central macular thickness compared to the baseline visit and an increase of ≥5 letters in visual acuity, were assigned to receive rescue laser therapy. In brief, yellow diode laser (577 nm) clinically adjusted to show barely visible photocoagulation lesions at 20 ms exposure time. The mean retinal sensitivity within the central 10 degrees measured with a fundus-related microperimeter, MP1, ETDRS-best corrected visual acuity (BCVA), optical coherence tomography-determined central macular thickness (CMT), and fluorescein angiography (FA) were performed.
before, 1, 3 and 6 months after a single treatment.

**Results:** Central macular thickness decreased by an average of 198μm. At 6 months main change in visual acuity was 4 letters better. Mean macular sensitivity improved (P<0.005) at 3 and 6 months. Laser lesions were not clinically observed, but detected on the early phase of the FA examination.

**Conclusions:** In parallel with new pharmacologic agents for the treatment of DME, developments in new laser technologies, exploiting optimized parameters and treatment guidelines will be the key to progress DME treatment approaches for an ultimate anatomical and functional restoration

**Commercial Relationships:** Jose A. Cardillo, None; Alessandro J. Dare, None; Renato Peroni, None; Rodrigo Jorge, None

**Program Number:** 5763 **Poster Board Number:** D0010

**Presentation Time:** 8:30 AM - 10:15 AM

**A Simple Artificial Eye Model for Practicing Anterior and Posterior Segment Lasers**

Malav Joshi, Todd W. Altenbernd. Ophthalmology and Vision Science, University of Arizona, Tucson, AZ.

**Purpose:** To create a synthetic eye model system that allows residents to practice ophthalmic laser procedures before attempting them on human patients

**Methods:** The outer shell of the model was constructed using a ping pong ball cut in half and a corneal mold separated from used Ozil® Phaco Artificial Eyes. A 7 mm circle was cut out of one of the halves to mimic the pupil. Then, the corneal mold was glued anterior to it. The retina was simulated by carefully adhering two Tegaderm™ Films on the concave surface of the other half. Fundus details and the trabecular meshwork were drawn on using permanent markers. Finally, the two segments were taped together and placed on an extension clamp to position the eye on the slit lamp.

**Results:** Retinal photocoagulation was performed using a slit-lamp argon laser delivery system and a standard fundus contact lens, whereas trabeculoplasty was executed with a standard mirrored contact lens and either a frequency doubled Nd: YAG or argon laser. When the laser was applied to the model retina, a white treatment spot was created indicating a successful application. For trabeculoplasty, successful treatment resulted in focal blanching of the ink. Indirect laser retinopexy and focal grid laser were also practiced and produced comparable results. The eye model can be reused by simply replacing the Tegaderm film and re-inking the trabecular meshwork.

**Conclusions:** To our knowledge, this synthetic eye model, low in cost and simple to construct, is the first device of its kind to offer training for anterior and posterior segment laser procedures. Cadaveric and animal eye models for practicing laser procedures already exist, but are limited by postmortem corneal opacification, cost, availability, reusability, and biohazard. Our model closely simulates natural conditions and the hand-eye coordination required to perform laser procedures and allows residents to gain the skills and confidence needed to perform them on patients.

**Support:** Center grant from Research to Prevent Blindness (JMM)
The Effect of Internal Limiting Membrane Peeling in Epiretinal Membrane Including Pseudomacular Macular Hole

Jung Min Park1, Shin Yeop Oh2, Soo Jung Lee2. 1Ophthalmology, Maryknoll hospital, Busan, Republic of Korea; 2Ophthalmology, Haeundae paek hospital, Busan, Republic of Korea.

Purpose: To report the effect and visual improvement of internal limiting membrane(ILM) peeling, and epiretinal membrane(ERM) peeling in symptomatic epiretinal membrane with pseudomacular macular hole.

Methods: Twenty seven eyes in 26 consecutive patients with ERM including pseudomacular macular hole underwent a vitrectomy, ERM peeling, intravitreal gas tamponade and maintain a face-down position for 7 days. ILM peeling was performed only thirteen eyes in 13 patients. The patients were divided into two groups: eyes with(14 eyes) or without(13 eyes) ILM peeling and the follow-up period was 12 months or more in all cases. The postoperative anatomic results by Optical Coherence Tomography(OCT) and improvement of best corrected visual acuity (BCVA) were retrospectively compared in two groups.

Results: Anatomic closure after the surgery was achieved in 11 eyes(78.6%) of the non ILM peeling group and in 12 eyes(92.3%) of the ILM peeling group (p=0.596). The BCVA improved from 0.41±0.31(logMAR) to 0.33±0.21 in non ILM peeling group (p=0.479) and from 0.46±0.41(logMAR) to 0.28±0.25 in ILM peeling group (p=0.001).

Conclusions: The additional ILM peeling is an effective technique in BCVA improvement of ERM with pseudomacular macular hole. Vitrectomy, ERM peeling, Gas tamponade and ILM peeling were significant for anatomic and functional success in the ERM with pseudomacular macular hole.

Commercial Relationships: Jung Min Park, None; Shin Yeop Oh, None; Soo Jung Lee, None

Program Number: 5765 Poster Board Number: D0012
Presentation Time: 8:30 AM - 10:15 AM
Clinical Findings at Initial Pan Retinal Photocoagulation for Proliferative Diabetic Retinopathy Predict Future Need for Pars Plana Vitrectomy

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Purpose: To determine the incidence and probability of Pars Plana Vitrectomy (PPV) in insulin-dependent and non-insulin-dependent diabetic patients within 2 years of receiving Pan Retinal Photocoagulation (PRP).

Methods: Patient records from Vanderbilt Eye Institute from 2000-2008 with any diabetic retinopathy billing codes receiving PRP were reviewed. Patients were excluded if they had prior PRP for other primary diagnoses, such as retinal vein occlusions or rubecutive glaucoma. Patients were also excluded from the study if they had had prior PRP, destructive cryotherapy treatment, or PPV. Additional eyes were excluded if they had insufficient information.

Results: 374 eyes were included for analysis. We found statistically significant differences in the probability of receiving a PPV within two years following initial PRP based upon reason for initial PRP, insulin dependence, and age. Compared to patients receiving initial PRP for proliferative diabetic retinopathy (PDR) alone, patients receiving PRP for PDR and vitreous hemorrhage (VH) had 2.78 times the likelihood (p<.0001) of undergoing a PPV within 2 years. Similarly, a patient receiving PRP for PDR and other pathologies, defined as iris neovascularization; VH and traction; fibrosis and VH; or fibrosis, the likelihood of PPV within two years was 3.54 times (p<.0001) greater than PDR alone.

Eyes from insulin-dependent patients were 1.74 times as likely (p=0.021) to undergo PPV within 2 years than non-insulin dependent diabetics following initial PRP. Age at initial PRP was negatively correlated with receiving a PPV, as every one-year increase in age was associated with a 3% decrease in the likelihood of undergoing PPV within 2 years (p=0.0002).

The percentage of eyes receiving PPV within 1 and 2 years following PRP for PDR alone was 12.2% (95% CI: 7.97,18.4) and 21.1% (95% CI: 15.1, 29.1); for VH and PDR was 32.8% (95% CI: 25.2, 42.0) and 44.3% (95% CI: 35.8, 53.7); and for patients with PDR and other pathologies 44.5% (95% CI: 27.5, 65.9) and 58.3% (95% CI: 39.6, 78.1).

Conclusions: Patients who received PRP for PDR as well as VH, traction, fibrosis, or VH and fibrosis were more likely to undergo PPV in 1 and 2 years following initial PRP. Insulin-dependent diabetes was positively associated with PPV, while age was negatively associated.

Commercial Relationships: Ravi Parikh, None; Jacob Van Houten, None; Edward F. Cherney, None
Trends in choice of surgical technique and reimbursement for retinal detachment repair

Baseer Ahmad, Gaurav K. Shah, Kevin J. Blinder. The Retina Institute / Retina Consultants of St. Louis, St. Louis, MO.

**Purpose:** The aim is to evaluate current trends in surgeon choice of retinal detachment repair technique, particularly with a focus on changes in scleral buckling relative to vitrectomy over the past decade. Additionally, we wish to assess any significant changes in reimbursement for the techniques stated above.

**Methods:** The Medicare fee for service database (BESS, the Part B Extract Summary System) was analyzed over a 10 year period from 2000 to 2010 using CPT codes 67107 (scleral buckle), 67108 (vitrectomy), 67113 (complex repair), 67110 (pneumatic retinopexy), 67105 (laser demarcation), and 67101 (cryoretinopexy). Data collected included overall number of procedures performed, number of procedures with skilled assistants, average allowable billing per procedure, and average allowable skilled assistant supplement per procedure.

**Results:** During the period from 2000-2010, annual numbers of surgical procedures changed as follows: scleral buckling decreased from 6502 to 1938, vitrectomy increased from 14984 to 30259, laser retinopexy increased from 4379 to 5834, and cryoretinopexy decreased from 1306 to 924. Average reimbursement from 2000 to 2010 changed as follows: $498 to $1049 for scleral buckling, $1260 to $1316 for vitrectomy, $797 to $1049 for cryoretinopexy. Hence, there has been a clear trend away from scleral buckling toward primary vitrectomy for repair of retinal detachments over the past decade. Utilization of other techniques has remained stable. Although the higher reimbursement of vitrectomy may have played a role, reimbursement for both scleral buckling and vitrectomy have trended upward at approximately the same pace. It is likely that other factors such as advancements in small gauge vitrectomy surgery, industry involvement in vitrectomy instrumentation, and reduced emphasis on scleral buckling during fellowship training over the past decade have also contributed to these trends.

**Conclusions:** There has been a clear trend away from scleral buckling toward primary vitrectomy for repair of retinal detachments over the past decade. Utilization of other techniques has remained stable. Although the higher reimbursement of vitrectomy may have played a role, reimbursement for both scleral buckling and vitrectomy have trended upward at approximately the same pace. It is likely that other factors such as advancements in small gauge vitrectomy surgery, industry involvement in vitrectomy instrumentation, and reduced emphasis on scleral buckling during fellowship training over the past decade have also contributed to these trends.

**Medicare Part B National Database (BESS, 2000-2010): Surgeon Reimbursement, Per case**

![Medicare Part B National Database](image)

**Commercial Relationships:** Baseer Ahmad, None; Gaurav K. Shah, Alcon (C), Bausch and Lomb (C), Dutch Ophthalmic, USA (C); Kevin J. Blinder, Genetech (C), Regeneron (C), Ocusoft (F), Bausch & Lomb (C), Synergetics (C), Allergan (C)

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Anatomical outcomes of epiretinal membrane surgery with or without internal limiting membrane peeling

Sumeer Thinda, Rohan Flynn, None

Purpose: To compare the anatomical outcomes of epiretinal membrane (ERM) surgery with or without internal limiting membrane (ILM) peeling.

Methods: A retrospective chart review was performed on 45 eyes that underwent surgery for visually-significant ERM with and without ILM peeling by a single surgeon. A total of 17 eyes underwent ERM peeling without ILM peeling (group 1) and 28 eyes underwent ERM peeling with ILM peeling (group 2). Group 1 patients underwent surgery between 2004 and 2007 while group 2 patients underwent surgery between 2009 and 2011. Primary outcome measures were anatomical characteristics and included: central macular thickness (CMT), foveal umbo contour, and retinal surface irregularities. A secondary outcome measure was change in best-corrected visual acuity (BCVA). Eyes with secondary causes of ERM were excluded from this study.

Results: The mean follow-up was 8.4 months (range: 3 months to 12 months) for all eyes. CMT decreased significantly in both groups with a mean preoperative CMT of 460 microns to 257 microns at last visit in group 1 (p-value <0.0001) and mean preoperative CMT of 506 microns to 384 microns at last visit in group 2 (p-value <0.0001). Group 1 had a mean change of 194 microns while group 2 had a mean change of 121 microns (p-value = 0.02). The percentage of eyes with return of foveal umbo contour at one year was 80% in group 1 and 44% in group 2. The percentage of patients with resolution of surface irregularities in group 1 was 80% and 55% in group 2. Mean change in BCVA in group 1 was .23 (logMAR) and in group 2 was .19, which was not a statistically significant difference between the two groups.

Conclusions: The surgical technique for an ERM has evolved with the advent of vital dyes for staining the ILM. However, the functional and anatomical benefit of ILM peeling in ERM surgery remains unclear. Our data suggests that in terms of anatomical benefit, ILM peeling does not improve results as compared to without ILM peeling. Furthermore, functional outcomes as measured by improvement in BCVA appears unaffected by ILM peeling.

Commercial Relationships: alan sheyman, None; Jane S. Myung, Teddy Lyu, Ken Wald, department of ophthalmology, mount sinai school of medicine, New york, NY.

ARVO 2013 Annual Meeting Abstracts by Scientific Section/Group – Retina

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Retinal ganglion cells (RGC-5) were grown in the presence of 95% air and 5% CO2. Cells were exposed to two different concentrations of BBG (0.25 mg/mL and 0.5 mg/mL) in presence of halide light at 1 and 2.5 cm distances from the cell culture dishes. Cells were exposed to BBG at different time points of 1 min, 5 min and 15 min. Cells exposed to light source in the absence of BBG served as control. Intensity levels (800-1900 Fc) were standardized with light meter both at source as well as on surface of the cells. Cytotoxicity after dye exposure was analyzed using WST-1 assay. Morphological changes were observed using phase contrast brightfield microscopy.

**Results:** Results were normalized against cell viability rate of control (which represented 100% viability). At 0.25 mg/mL concentration, cell viabilities after 1, 5 and 15 min exposure to dye and light distance of 1 cm were 89.8±7.4%, 79.6±4.9% and 56.7±4.0% of control, respectively. At 0.5 mg/mL concentration, cell viability after 1, 5 and 15 min were 79±3.1%, 66.7±3.6% and 53.1±9.4% (p<0.05). In presence of medium illumination, at 0.25 mg/mL concentration cell viability was 104.6±3.3%, 94.4±5.9% and 73.7±4.7% after 1, 5 and 15 min of exposure, respectively. At 0.5 mg/mL concentration, cell viabilities at similar time points were 96.5±4.8%, 84.5±3.2% and 72.3±3.9% (p<0.05). However, at 2.5 cm distance of higher illumination, at 0.25 mg/mL cell viability was 97.5±16.4%, 96.7±15.2%, 92.4±15.2% and 98.9±12.6%, 94.8±12.4% and 82.7±15.7% at 0.5 mg/mL concentration.

**Conclusions:** Surgical illuminator placed at 2.5 cm for up to 5 minutes had a superior safety profile and was not toxic to RGC independent of the intensity of illumination.

**Commercial Relationships:** Jacob C. Meyer, None; Gaurav K. Shah, Alcon (C), QLT (C), Bausch and Lomb (C), Dutch Ophthalmic, USA (C)

**Program Number:** 5774 Poster Board Number: D0021
**Presentation Time:** 8:30 AM - 10:15 AM
**Outcomes of Transpupillary Posterior Chamber Intraocular Lens Removal with Pars Plana Vitrectomy and Placement of Anterior Chamber Intraocular Lens**

**Purpose:** To evaluate visual results, intra-operative and post-operative complications in eyes needing pars plana vitrectomy (PPV) with transscleral posterior chamber intraocular lens (PCIOL) removal and placement of anterior chamber intraocular lens (ACIOL).

**Methods:** We conducted a retrospective chart review on patients who underwent PPV for displaced PCIOL and concurrent placement of ACIOL at the University of Iowa Hospitals and Clinics from 1/1/2007 to 11/1/2012. IRB approval was obtained. Detailed pre-, intra-, and post-operative data were compiled, and statistical analysis was performed.

**Results:** 14 patients (5 males, 9 females) met the inclusion criteria and were analyzed. There were 8 right eyes and 6 left eyes. The mean age at time of surgery was 82.6 years (median = 82, range = 74 - 92).

Mean visual acuity (VA) at time of surgery was 20/225 (median = 20/250). Mean VA at final visit until 9 months post-operatively was 20/40 (median = 20/40), with mean improvement in visual acuity of the treated eyes at surgery of 20/200.
0.80 logMAR units. Intra-operative suprachoroidal hemorrhage occurred in 1 patient (7%) and post-operatively in 2 patients (14%); all resolved spontaneously; mean post-operative VA in these three patients was 20/40. There were no cases of intra-operative or post-operative choroidal detachment. Post-operatively, 5 (36%) developed cystoid macular edema; 3 (24%) had vitreous hemorrhage; 2 (14%) had hyphema; 2 (14%) developed epiretinal membrane; 2 (14%) had corneal decompensation, including one with perforation of penetrating keratoplasty graft requiring enucleation and the other with light perception vision after a detached DSAEK graft; 1 (7%) had ACIOL instability, corrected on the first post-operative day; 1 (7%) had iris capture of the ACIOL necessitating IOL exchange; 4 (28%) had no complications. There were no cases of post-operative glaucoma, uveitis-glaucoma-hyphema syndrome, or retinal detachment. Mean follow-up was 62 weeks (median = 13.5 weeks).

**Conclusions:** Transpupillary PCIOI removal with PPV and placement of ACIOL is in an effective procedure for improvement in VA, requiring proper management of post-operative complications. The most common post-operative complications were found to be cystoid macular edema and vitreous hemorrhage. The most detrimental complication in this series was corneal decompensation, resulting in very poor visual outcomes.

**Commercial Relationships:** Pavlina Kemp, None; A. T. Johnson, None; James C. Folk, None; Stephen R. Russell, IDX, LLC (I), IDX, LLC (P); Vinit B. Mahajan, None; H Culver Boldt, None; Thomas A. Oetting, None; Elliott H. Sohn, None

**Program Number:** 5775 Poster Board Number: D0022

**Presentation Time:** 8:30 AM - 10:15 AM

**Microfiltration of Brilliant Blue G Dye**

Sri Krishna Mukkamala. *Ophthalmology, Columbia University, New York, NY.*

**Purpose:** Brilliant Blue G (BBG) is a safe and effective dye used to highlight the internal limiting membrane during macular surgery. A recent outbreak of BBG associated Fusarium spp. endophthalmitis raises concerns about this off-label, non-FDA approved intraocular use. We propose that the utilization of a 0.22 μm filter intraoperatively can reduce the risk of inoculating an eye with contaminated BBG.

**Methods:** An in vitro model of contaminated BBG was prepared. Laboratory stock cultures of 7 organisms including Staphylococcus epidermidis, Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenza, Klebsiella pneumoniae, Fusarium spp., and Candida albicans were prepared in five 10-fold dilutions and injected into BBG vials. These mixtures were drawn with either a 5 μm filter, 0.22 μm, or without a filter and cultured on appropriate plates and growth conditions.

**Results:** No culture plates that had inoculate drawn through a 0.22 μm filter showed evidence of growth. There was evidence of growth for all organisms when no filter was used. A 5 μm was insufficient to filter Fusarium spp.

**Conclusions:** Using a 0.22 μm filter in the intraoperative processing of BBG would likely reduce the risk of infectiousendophthalmitis resulting from contaminated dye.

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Commercial Relationships: Sivashakthi Kanagalingam, None; Maziar Lalezary, None; Stephen J. Kim, None
Support: Supported in part by an unrestricted grant from Research to Prevent Blindness to the Vanderbilt University School of Medicine Department of Ophthalmology and Visual Sciences.
Clinical Trial: NCT01162356

Program Number: 5777 Poster Board Number: D0024
Presentation Time: 8:30 AM - 10:15 AM
Macular hole surgery: Does C3F8 provide better anatomical and functional outcomes than SF6 and C2F6?
Javier Zarranz-Ventura,1,2, Ahmed Sallam1, Pearse A. Keane2, Dawn A. Sim2, Nigel Kirkpatrick1, Robert Johnston2,1
Vitreo-Retinal Service, Cheltenham General Hospital, Cheltenham, United Kingdom;2Medical Retina Service, National Institute for Health Research (NIHR) Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, London, United Kingdom.
Purpose: To assess differences in anatomical and functional outcomes when using C2F6, SF6 or C3F8 gas tamponade in macular hole surgery with 20G pars plana vitrectomy+ILM peeling+gas in a single VR unit (2005-2012).
Methods: Clinical and surgical data were prospectively entered in electronic medical records. Data collection included: demographic details, tamponade type, stage of macular hole, preoperative and postoperative BCVA, anatomical success rate by OCT and secondary cataract surgery rate.
Results: 299 eyes of 276 patients with a mean age of 69.3±8.2 years (mean±SD)(median:69) and a 1:2.5 male to female ratio were included. The type of gas employed was C2F6 in 45.8% (137/299), SF6 in 18.1% (54/299) and C3F8 in 36.1% (108/299). No differences were observed in macular hole stage and type of gas employed at baseline. Mean preoperative BCVA was significantly worse in eyes treated with C3F8 compared to SF6 and C2F6 (0.94±0.37 logMAR vs 0.82±0.28 vs 0.84±0.28, p:0.034). No significant differences in postoperative BCVA were observed between gases at any timepoint but mean BCVA change from baseline was significantly better with C3F8 than SF6 and C3F8 at 12 months (-0.51±0.38 logMAR vs -0.43±0.30 vs -0.34±0.31, p:0.037). Closure rate assessed by OCT at 1 month was 95.5% for C3F8, 97.4% for SF6 and 92.3% for C2F6. However, closed holes with persistent foveal detachment on OCT 1 month post surgery were significantly less frequent in C3F8 treated eyes compared to SF6 or C2F6 (9.1% vs 37.8% vs 38.1%, p:0.056, p:0.036, respectively). At 3rd month, no significant OCT differences were observed between gases. Cataract surgery was performed at 11.61±6.1 months in C2F6 group, 9.62±5.5 in SF6 group and 11.54±7.19 in C3F8 group, with no significant differences between groups.
Conclusions: In our series, C3F8 was used in poorer vision eyes, provided better anatomical outcome at 1st month as assessed by OCT analysis and showed significantly higher vision gain at 12 months than SF6 and C2F6.
retrospectively examined. Surgery consisted of vitrectomy and internal limiting membrane peeling from arcade to arcade with adjunctive use of indocyanine green. Postoperative images were registered and scaled to preoperative images by using custom software. Vessel landmarks were identified in both images by using a point-and-click method to create coordinate point-pairs, and the displacement of each landmark was illustrated upon fundus images as vector plots (e.g. Figure 1). Total displacement was the largest movement in any direction and radial displacement was movement relative to the center of the macular hole. Relationships between displacement magnitudes and hole size and eccentricity (distance from center) were examined by using Pearson correlations. Differences in mean regional displacements (superior vs. inferior hemispheres) were examined by using Mann-Whitney tests.

**Results:** In each photo, we identified 20 point-pairs with mean eccentricity of 2175 ± 885 μm (± SD; range: 644 to 4898 μm). Vector plots depicted a general post-surgical movement nasally and toward the horizontal raphe (Figure 1). On average, displacement was nasal in all 9 patients (mean 91 ± 56 μm) and was also directed toward the center of the hole in 7 of 9 (78%) patients (mean 27 ± 108 μm). Displacement magnitudes were not correlated with hole size (total displacement, r=0.04, p=0.90) and were not correlated with eccentricity (radial r=0.07, p =0.99; total r=0.04, p=0.92). Regionally, mean radial and total displacements were not different between superior and inferior hemispheres (radial, p=0.29; total, p=0.82). Statistically, the minimum detectable difference in radial and total displacement was 117 μm (α=0.05, β=0.20, n=9).

**Conclusions:** After macular hole surgery, retinal vessels shift inward toward the hole, but also shift more nasally. This magnitude of shift is not correlated with hole size or eccentricity based on points sampled. This suggests that surgery relieves tractional forces directed away from the hole and also temporally.

Figure 1. Vessel displacements toward macular hole and also optic disc.

**Commercial Relationships:** Gene Chen, None; Raymond Iezzi, None; Jay W. McLaren, None; Ronald C. Gentile, None; Andrew J. Barkmeier, None

**Support:** Research to Prevent Blindness; Mayo Foundation

**Program Number:** 5779 Poster Board Number: D0026
**Presentation Time:** 8:30 AM - 10:15 AM

One-year results of the Prospective Retinal and Optic nerve Vitreectomy Evaluation (PROVE) Study: A controlled clinical trial


**Purpose:** To report 1-year outcomes of the Prospective Retinal and Optic Nerve Vitreectomy Evaluation (PROVE) Study.

**Methods:** This 5-year prospective, controlled, observational study enrolled 80 eyes of 40 patients requiring vitrectomy for epiretinal membrane (ERM), macular hole (MH), or vitreous opacities (VO). All participants underwent baseline evaluation of the study (surgical) and fellow (control) eye that included intraocular pressure (IOP), cup-to-disc ratio (CDR), Humphrey visual field (HV FG) testing, and optical coherence tomography (OCT) of the macula and peripapillary retinal nerve fiber layer (pRNFL). Evaluations were repeated at 3 months and 1 year after surgery.

**Results:** Thirty-seven of 40 patients completed 1-year follow up. Visual acuity (VA) in all study eyes at 1 year was improved from baseline (p=0.003), but remained worse than fellow eyes (p=0.0001). CDR did not change, but unlike baseline or 3 months, the MH group (n=14) had statistically higher mean IOP at 1-year (16.0±3.62 mm Hg) than fellow eyes (14.8±3.40 mmHg, p=0.002). Mean deviation (MD) on HVF improved in ERM study eyes (n=20) at 1-year when compared with baseline (-2.2 vs. -4.0, p=0.02), but remained worse than fellow eyes (-1.2, p=0.002). PSD increased in study eyes when compared with fellow eyes at 1-year (2.85vs.2.05, p=0.009), especially in the MH group (3.41vs.1.90, p=0.01). Postoperatively, the temporal and average pRNFL thickness decreased significantly in study eyes (p<0.05), and study eyes had thinner inferior pRNFL thickness (114±16.8 μm) when compared to fellow eyes (123±14.7 μm, p=0.004). Temporal pRNFL thinning was particularly evident in the ERM group (p=0.005) over time. Central subfoveal thickness (CST) and macular cube volume improved in all study eyes at 1-year, but remained significantly greater compared to fellow eyes (p < 0.05). Greater CST significantly correlated with less VA improvement (r=0.99). No significant OCT changes were present in the VO group (n=5).

**Conclusions:** One year after vitrectomy, VA, CST, and MD improve in study eyes, but not to the level of fellow eyes. Reduction in CST from baseline correlated with degree of VA improvement. MH eyes demonstrated significantly increased IOP and PSD, and both ERM and MH eyes had decreased inferior pRNFL thickness. Continued follow-up of this cohort will provide further insight into long-term changes after vitreectomy surgery.

**Commercial Relationships:** Rohan J. Shah, None; Maziar Lalezary, None; Stephen J. Kim, None; Rahul Reddy, None; Jeffrey Kammer, Allergan (C); Merck (F); Rachel W. Kuchtey, None; Karen M. Joos, Vanderbilt University (P); Franco Recchia, Alcon (C); Edward F. Cherney, None; Janice C. Law, None

**Clinical Trial:** NCT01162356

**Program Number:** 5780 Poster Board Number: D0027
**Presentation Time:** 8:30 AM - 10:15 AM

Association of M2 macrophages in the development of fibrovascular membranes in diabetic retinopathy

Yoshiyuki Kobayashi1, Shigeo Yoshiida1, Shintaro Nakao1, Takashi Tachibana1, Takahito Nakama1, Keijiro Ishikawa1, Yukio Sassa1–2, Hiroshi Enaida1, Yugi Oshima1, Tatsuro Ishibashi1. 1Ophthalmology, Kyushu University, Fukuoka, Japan; 2Ophthalmology, Fukuoka University Chikuushi Hospital, Fukuoka, Japan.

**Purpose:** It was recently reported that M2 macrophages play an important role in wound healing, fibrosis and cancer metastasis. However, their role in diabetic retinopathy remains elusive. The purpose of this study was to determine whether M2 macrophages can be detected in patients with proliferative diabetic retinopathy (PDR).

**Methods:** We measured the levels of VEGF, peristin and, CD163, a

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marker for M2-polarization, by sandwich enzyme linked immunosorbent assay in vitreous samples collected from patients with macular hole, epiretinal membrane, diabetic macular edema, PDR, and proliferative vitreoretinopathy (PVR). The location of CD163 and periostin was also determined by immunohistochemistry. Results: The mean vitreous levels of CD163 were significantly higher in patients with PDR and PVR than in macular hole patients (P <0.001). There was a significant correlation between the vitreous concentrations of CD163 and periostin in patients with PDR (P <0.001). Immunohistochemical analysis showed colocalization of CD163 and periostin in fibrovascular membranes (FVMs) obtained from patients with PDR.

Conclusions: These findings indicate that M2 macrophages may be involved in the development of FVMs possibly through induction of periostin.

Commercial Relationships: Yoshiyuki Kobayashi, None; Shigeo Yoshida, None; Shintaro Nakao, None; Takashi Tachibana, None; Takahito Nakama, None; Keijiro Ishikawa, None; Yukio Sassa, None; Hiroshi Enaida, None; Yuji Oshima, None; Tatsuro Ishihashi, None

Program Number: 5781 Poster Board Number: D0028
Presentation Time: 8:30 AM - 10:15 AM
Quantitative assessment of Differences in Macular Visibility through a Variety of Intraocular Lenses during Vitrectomy: an Eye Model Experimental Study
Hirokazu Sakaguchi,1 Jiro Hidaka,2 Yusuke Oshima,1 Naoyuki Maeda,1 Kohji Nishida,2; 1Ophthalmology, Osaka University Graduate School of Medicine, Suita, Japan; 2HOYA Corporation Medical Division, Itabashi, Japan.

Purpose: Magnification of the macular area is sometimes required during vitrectomy. Using a model eye, we determined if the observable range of the macular area changes with the intraocular lens (IOL) type or dioptic power and determined the degree of the change.

Methods: A 10-, 15-, 20-, 25-, or 30-diopter (D) spherical IOL (VA-60BBR) or aspheric IOL (NY-60, HOYA Corporation) was inserted into a model eye. Two chandelier light pipes were inserted and a meniscus contact lens was placed on the cornea of the model eye to view the magnified macular area. A stripe chart (line width, 0.1 mm; space, 0.1 mm) placed on the macular area was photographed with a digital camera through a surgical microscope. The diameter of the clearly observable range was measured and the relationship between the diameter versus the IOL type and dioptic power were analyzed by two-way analysis of variance.

Results: The diameter of the observable range changed from 4.4 to 2.6 mm and from 3.8 to 2.2 mm, while the dioptic powers of the spherical and aspheric IOLs changed from 10 to 30 D, respectively. The range was significantly less when the IOL dioptic power was greater and after insertion of the aspheric IOL (each p<0.0001). The ratio of the range between the IOL types was 1:0.82-0.94, while the maximal ratio of the range for the difference in the lens dioptic power was 1:0.58.

Conclusions: The observable macular range changed with the IOL type and dioptic power. It is important to recognize these characteristics when using magnification for surgical procedures in the macular area.

Commercial Relationships: Hirokazu Sakaguchi, HOYA Corporation (R); Jiro Hidaka, HOYA Corporation Medical Division (E); Yusuke Oshima, Synergies (C), Topcon Medical Laser Systems (C), DORC (R), Baush & Lomb (R); Naoyuki Maeda, Topcon (F), Santen (R), Otsuka (R), Oculus (R), HOYA (R); Kohji Nishida, Alcon (C), Alcon (F), HOYA (F), Senju (F), Pfizer (F), Santen (F), Osaka University (P)

Program Number: 5782 Poster Board Number: D0029
Presentation Time: 8:30 AM - 10:15 AM
Risk factors for development of full thickness macular holes following pars plana vitrectomy for myopic foveoschisis
Yasushi Ikuno, Xinxia Gao, Satoko Fujimoto, Kohji Nishida; Department of Ophthalmology, Osaka Univ Medical School, Suita, Japan.

Purpose: To explore the risk factors of secondary full thickness macular holes following pars plana vitrectomy with inner limiting membrane (ILM) peeling for myopic foveoschisis

Methods: The medical records of all patients who underwent pars plana vitrectomy with ILM peeling for myopic foveoschisis with or without retinal detachment from January 2002 to June 2012 were retrospectively reviewed. The factors for developing of postoperative full thickness macular holes were investigated.

Results: Forty-two eyes with myopic foveoschisis but without macular hole before surgery were included in this study and 8 cases (19.0%) of them were identified to develop a postoperative full thickness macular hole by optical coherence tomography (OCT) during the follow-up period. No significant association of age (P =.369), axial length (P =.113), visual acuity (P =.859), status of fovea (P =.331), posterior staphyloma (P =.1000) or chorioretinal atrophy (P =.837) were found between patients with and without secondary macular holes. Among the characteristics on OCT images, the percentage of eyes with the inner segment/outner segment junction (IS/OS) defect was significantly higher in the patients with macular hole than in those without macular hole (P =.013, Fisher exact test). IS/OS defect (P =.018) was the only significant risk factor for development of secondary macular holes by logistic regression analysis.

Conclusions: Development of secondary macular holes may occur in myopic foveoschisis following pars plana vitrectomy with ILM peeling. Preoperative IS/OS defect can be a risk factor.

Commercial Relationships: Yasushi Ikuno, Topcon (F), TOMEY (F); Xinxia Gao, None; Satoko Fujimoto, None; Kohji Nishida, Alcon (C), Alcon (F), HOYA (F), Senju (F), Pfizer (F), Santen (F), Osaka University (P)

Program Number: 5783 Poster Board Number: D0030
Presentation Time: 8:30 AM - 10:15 AM
Clinical Efficacy and Safety of Dexamethasone/Netilmicin Gel in the Management of Ocular Inflammation After Vitreoretinal Surgery
Vincenzo Papa1, Daria Rasà1, Claudio Iannaccone2, Cristina Cannatella1, Antonio Rapisarda2, 1Medical Affairs, SIFI SpA, Catania, Italy; 2Ophthalmology Unit, Garibaldi Hospital, Catania, Italy; 3Department of Statistics, Sparc Consulting Srl, Milano, Italy.

Purpose: To evaluate the efficacy and safety of a new hydrogel formulation of Netilidex (SIFI SpA, Italy), a preservative-free steroid/antibiotic fixed combination containing 0.1% dexamethasone and 0.3% netilmicin plus 1% xanthan gum (as vehicle), in the treatment of ocular inflammation after microincisional vitreoretinal surgery.

Methods: The study was a multicentre, randomized, open, active-controlled clinical trial. After sutureless 23-25 gauge vitreoretinal surgery, patients received Netilidex eye gel (n=50) or Tobradex eye ointment (n=53) qid for 3 days; treatment continued until day 14 after surgery with a combination of eye-drops tid, during daytime, and eye gel or ointment sid at bed time. Efficacy parameters evaluated were: conjunctival hyperemia, anterior chamber flare and
cells, symptoms of ocular discomfort (pain, photophobia, itching) and presence of ocular infection. All parameters were graded on a scale of 0 (none) to 3 (severe) with the exception of symptoms that were evaluated by a VARS scale. The primary outcome was the percentage of patients showing a resolution of bulbar conjunctival hyperemia at postoperative day 14. Safety variables examined were: symptoms of local tolerance, adverse events and IOP.

**Results:** In the full analysis 92.9% and 75.0% of patients in the Netilidex and Tobradex groups, respectively, had a complete resolution of bulbar conjunctiva hyperemia at day 14 (p=0.02, Fisher's exact test). No differences were found for all other efficacy parameters evaluated. Neither ocular infections nor increase in IOP were observed during the study. Statistically significant differences in favor of Netilidex (p< 0.0001, ANOVA) were found for most of subjective tolerance variables examined (blurred vision, foreign body sensation, stickiness and burning).

**Conclusions:** Netilidex is safe and effective in the treatment of postoperative ocular inflammation. The new Netilidex hydrogel formulation is characterized by a better tolerability profile than Tobradex eye ointments. In addition it does not contain preservative thus providing an additional benefit to patients.

**Commercial Relationships:** Vincenzo Papa, SIFI SpA (E); Daria Rasà, SIFI SpA (E); Claudio Iannacone, None; Cristina Cannatella, SIFI S.p.A. (E); Antonio Rapisarda, None

**Clinical Trial:** 2008-005082-64

**Program Number:** 5784 **Poster Board Number:** D0031
**Presentation Time:** 8:30 AM - 10:15 AM

**Cones implicit time as a predictor for visual outcome in Macular Hole Surgery**


**Purpose:** To investigate whether preoperative retinal function as measured by full field ERG and mfERG correlates to postoperative visual acuity after macular hole surgery

**Methods:** 19 consecutive patients underwent macular hole surgery. Standard pars plana vitrectomy with removal of the ILM was performed and intraocular gas tamponade with (C2F6) gas-air mixture followed by a face-down position for at least 5 days. All patients were examined with ETDRS chart, full-field electroretinography (Espin), multifocal electroretinography (mfERG Veris 6) and optical coherence tomography (OCT) preoperatively, at 6 weeks and at 6 months after surgery.

**Results:** In all patients longstanding alteration of cone and rod function reflected by mfERG and full field ERG were verified 6 months after surgery. A prolonged cone 30Hz flicker implicit time in the full field ERG and the cone implicit time in the sum mfERG before surgery was significantly correlated to the ETDRS visual acuity 6 months postoperatively p > 0.05; (Wilcoxon signed rank test nonparametric test).

**Conclusions:** Preoperative evaluation of retinal function with mfERG and fullfield ERG enhances understanding of the retinal recovery process after macular hole surgery. The cone implicit time in the fullfield 30Hz flicker ERG and the sum mfERG are valid predictors for long-term visual outcome, which may be useful for patient selection prior to surgery.

**Commercial Relationships:** Sten Andreasson, None; Sten Kjellstrom, None; Henrik Barth, None; Fredrik K. Ghosh, None

**Support:** The Swedish Research Council, The Princess Margaretas Foundation for Blind Children, Marianne and Marcus Wallenberg's Foundation and Olle Engkvist Foundation

**Program Number:** 5785 **Poster Board Number:** D0032
**Presentation Time:** 8:30 AM - 10:15 AM

**One Year Clinical Outcomes Of A Randomized Clinical Trial Investigating Pre-operative Adjunctive Bevacizumab For Tractional Retinal Detachment (TRD) Due To Proliferative Diabetic Retinopathy (PDR)**


1. Department of Ophthalmology and Visual Sciences, University of Iowa, Iowa City, IA; 2. Doheny Eye Institute, University of Southern California and Los Angeles County Hospitals, Los Angeles, CA; 3. Departments of Pathology and Ophthalmology, Keck School of Medicine, University of Southern California, Los Angeles, CA; 4. Massachusetts Eye and Ear Infirmary, Boston, MA; 5. Atlantis Retina Institute, Huntington Beach, CA.

**Purpose:** Utility of pre-operative bevacizumab for TRD due to PDR remains contested due to the risk of TRD progression versus benefit of attenuation of neovascularization. Preliminary three month post-operative data of this reverse translational, double-masked study has been published. In this study, we detail one-year clinical follow-up of this now completed study.

**Methods:** 20 eyes of 19 patients were randomized to receive intravitreal bevacizumab injection or sham injection 3-7 days prior to vitrectomy for TRD repair and definitive PDR treatment in a large urban, public hospital. Best-corrected visual acuity (BCVA), need for additional procedures, and postoperative complications were compared in the two groups at 6 and 12 month post-operative follow-up.

**Results:** Median BCVA at the control group was 20/400 at baseline, 20/400 at post-op month 3 (POM3), 20/170 at POM6, and 20/150 at POM12. The median BCVA in the treated group was 20/630 at baseline, 20/100 at POM3, 20/400 at POM6, and 20/150 at POM12. Four of seven eyes (57%) randomized to bevacizumab had the same or improved VA at POM12 compared to five of eight eyes (62.5%) in the control group.

All retinas were attached at POM12, but 6 eyes had decreased VA compared to baseline. In the treatment arm, 1 patient had persistent cystoid macular edema, 1 had ischemic changes postoperatively, and 1 had a visually significant cataract awaiting surgery. In the control arm, 1 patient had recurrent epiretinal membrane and 2 developed NLP vision despite retinal attachment: one from glaucoma and another from severe ischemia. During 12 month follow-up, 1 eye in each group needed repeat surgery for recurrent retinal detachment. No eye required enucleation.

**Conclusions:** Most eyes in this study experienced at least stable VA at one year follow-up. Need for additional surgical procedures for recurrent detachment is uncommon. However, a relatively high risk of poor visual outcomes despite pre-operative bevacizumab still exist in severe TRD due to end-stage PDR.

**Commercial Relationships:** Elizabeth O. Tegins, None; Michael Javaheri, None; Dean Elliott, Geneetnec (C), Regeneron (C), Ophthotech (C), Alcon (C), Bausch & Lomb (C), Allergan (C), Alimera (C), Acucela (C), Arctic (C), Salutaris (C); Leo A. Kim, None; Hani Salehi-Hadi, None; David R. Hinton, RPT (I), RPT (P); Elliott H. Sohn, None

**Clinical Trial:** NCT01270542
In the clinical study, a retrospective review of 20 consecutive patients with idiopathic macular hole and/or macular pucker who underwent surgery with pars plana vitrectomy and TA-assisted internal limiting membrane peeling was performed. Non-diluted and balanced salt solution (BSS) diluted (1:4 and 1:9) and TA-assisted ILM stainings were performed and their staining morphology were assessed. The distribution patterns of the TA crystals of various concentrations were also assessed microscopically. In the in vitro study, cytotoxicities of various concentrations of preserved TA diluted in BSS on cultured human RPE cells (ARPE-19) and retinal ganglion cells (RGC5) were evaluated. Cells were treated with BSS, 4, 8, and 40mg/ml concentration of triamcinolone acetonide for 20 minutes. Toxicity was determined by WST-1 mitochondrial dehydrogenase assays.

**Results:** Clinically, a 1:4 dilution of commercially-available preserved TA demonstrated the best consistency and particle aggregate size for ILM viewing in ILM peeling surgery. Cultured human RPE cells and retinal ganglion cells did not show decrease of mitochondrial dehydrogenase activity in 1:4 (8mg/ml) and 1:9 (4mg/ml) dilutions of preserved TA for 20 minutes.

**Conclusions:** Diluted preserved TA (≥8mg/ml) demonstrated no toxicity in cultured RPE cells and retinal ganglion cells. A 1:4 dilution (8mg/ml) of preserved TA appears to be a safe and cost-effective alternative for staining the ILM in ILM peeling surgery.

**Commercial Relationships:** Jerry Huang, None; Ling Yeung, None; Nan-Kai Wang, None; Yen-Po Chen, None; Yih-Shiou Hwang, None; Kuan-Jen Chen, None; Wei-Chi Wu, None; Tun-Lu Chen, None; Chi-Chun Lai, None.

**Program Number:** 5787 Poster Board Number: D0034
**Presentation Time:** 8:30 AM - 10:15 AM

**A computational study of the pressure burden on localized retina during vitrectomy**

Jerry Huang1, Ling Yeung1, Nan-Kai Wang2, Yen-Po Chen2, Yih-Shiou Hwang2, Kuan-Jen Chen2, Wei-Chi Wu2, Tun-Lu Chen2, Chi-Chun Lai2.

1Chang-Gung Memorial Hospital, Keelung, Taiwan; Keelung City, Taiwan; 2Chang-Gung Memorial Hospital, Taoyuan, Taiwan, Guishan Township, Taoyuan County, Taiwan.

**Purpose:** To determine the proper concentration of preserved triamcinolone acetonide (TA) suitable for internal limiting membrane (ILM) staining and peeling, and to evaluate the toxicity of various concentrations of preserved TA on in vitro retinal pigment epithelium (RPE) and retinal ganglion cells.

**Methods:** In the clinical study, a retrospective review of 20 consecutive patients with idiopathic macular hole and/or macular pucker who underwent surgery with pars plana vitrectomy and TA-assisted internal limiting membrane peeling was performed. Non-diluted and balanced salt solution (BSS) diluted (1:4 and 1:9) TA-assisted ILM stainings were performed and their staining morphology were assessed. The distribution patterns of the TA crystals of various concentrations were also assessed microscopically. In the in vitro study, cytotoxicities of various concentrations of preserved TA diluted in BSS on cultured human RPE cells (ARPE-19) and retinal ganglion cells (RGC5) were evaluated. Cells were treated with BSS, 4, 8, and 40mg/ml concentration of triamcinolone acetonide for 20 minutes. Toxicity was determined by WST-1 mitochondrial dehydrogenase assays.

**Results:** In situation of short intrusion of instrument and small gauge system, high pressure gradient was revealed. When aspiration instrument deeply inserted into vitreous cavity, fluid flows seems to be interfered with instrument. But the point of retina which opposite to infusion cannula revealed highest dynamic and static pressure, consistently. When aspiration instrument extracted from vitreous cavity, sudden decreasing of IOP was observed. After 2 seconds, overall IOP became lower than infusion pressure and stably maintained. In this condition, intraocular pressure-gradient was increased up to 2 mmHg with the various infusion pressure and gauge of instrument during fluid-fluid exchange, and higher during fluid-air and air-gas exchange.

**Conclusions:** Using computer simulations, we could quantify the pressure burden on each point of retina in various conditions. Although the computational model is somewhat different from real clinical situation, our study provided the conceptual information about pressure-burden induced mechanical damage on retina. In our simulations, high pressure-gradients which can damage the localized retina were noticed during fluid-air and air-gas exchange with small gauge system and high infusion pressure. Although fluid-fluid exchange seems to be relative safe procedure than fluid-air or air-gas exchange, caution is always needed in performing vitrectomy with small gauge system and high infusion pressure.

**Commercial Relationships:** Yong Joon Kim, None; Kyung-Seek Choi, None; Sungkil Jo, None; Youngcheol Joo, None.

**Program Number:** 5788 Poster Board Number: D0035
**Presentation Time:** 8:30 AM - 10:15 AM

**Iatrogenic retinal breaks in 25-gauge air vitrectomy compared with the standard 25-gauge system for macular diseases**

Cesare Mariotti1, Francesca Viti1, Teresio Avitabile1, Mario D. Toro2, Andrea Saitta1, Alfonso Giovanni1, Antonio Longo2, Vittorio De Grande2, Santo Stella2, Michele Reibaldi2.

1Clinica Oculistica, Universita Politecnica delle Marche, Ancona, Italy; 2Ophthalmology, University of Catania, Catania, Italy.

**Purpose:** To compare the incidence rates of iatrogenic retinal breaks in eyes that underwent 25-gauge air vitrectomy and 25-gauge standard vitrectomy for macular diseases.

**Methods:** Retrospective, comparative, interventional study. We compared the incidence of iatrogenic retinal breaks in 197 eyes of 197 consecutive patients undergoing 25-gauge air vitrectomy (air-group) and 238 eyes of 238 consecutive patients undergoing 25-gauge standard vitrectomy (standard-group) for either idiopathic macular holes (MH) or idiopathic epiretinal membranes (ERM). All surgeries were performed by one surgeon at a single hospital. Main outcome measure was the incidence rate of iatrogenic peripheral retinal breaks discovered intraoperatively and postoperatively.

**Results:** The incidence rate of iatrogenic retinal breaks was significantly higher in the standard-group than in air-group (8% and 2% respectively; P = 0.005). The percentage of intraoperative retinal breaks was 6% in eyes undergoing standard vitrectomy and 2% in eyes undergoing air vitrectomy (P = 0.034). Retinal breaks were identified postoperatively in 5 eyes (2%) in the standard-group and no eyes (0%) in the air-group (P = 0.066). A postoperative rhegmatogenous retinal detachment developed in 2 eyes (1%) in the standard-group, whereas none in the air-group (0%). The incidence rate of retinal breaks in eyes that underwent vitrectomy for MH was higher in eyes that underwent standard vitrectomy compared with eyes treated by air vitrectomy (17% and 3%, respectively, P = 0.010). In ERM cases, the number of iatrogenic retinal breaks was higher in the standard-group than in the air-group (5% and 1%, respectively), with not quite statistically significant difference (P = NS). A statistically significant relation between posterior vitreous...
detachment induction and presence of retinal breaks was identified in the standard-group.

**Conclusions:** 25-gauge air vitrectomy is associated with a low incidence rates of iatrogenic retinal breaks compared to standard 25-gauge vitrectomy.

**Commercial Relationships:** Cesare Mariotti, None; Francesca Viti, None; Teresio Avitabile, None; Mario D. Toro, None; Andrea Saitta, None; Alfonso Giovannini, None; Antonio Longo, None; Vittorio De Grande, None; Santo Stella, None; Michele Reibaldi, None

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**Program Number:** 5789 Poster Board Number: D0036

**Presentation Time:** 8:30 AM - 10:15 AM

**Dynamic Contour Tonometry versus Goldmann Applanation Tonometry after vitrectomy**

Nikolaos Mamas, Matthias Fuest, Gernot Roessler, Babac A. Mazinani, Niklas Plange. Ophthalmology, RWTH Aachen University, Aachen, Germany.

**Purpose:** To investigate the agreement of intraocular pressure (IOP) measurement using Dynamic Contour Tonometry (DCT) and Goldmann Applanation Tonometry (GAT) in eyes after vitrectomy with intraocular tamponade of gas, eyes after vitrectomy with no tamponade, and controls.

**Methods:** In this prospective comparative study IOP was measured with GAT and DCT in 74 control eyes with no history of glaucoma or intraocular surgery, 20 gas-filled eyes one to three days after vitrectomy and 24 water-filled eyes with a history of vitrectomy. DCT measurements were accepted with a quality score of 3 or better. GAT and DCT measurements lower than 6mmHg were excluded.

**Results:** The mean difference between GAT and DCT (GAT-DCT) in control eyes was -0.17 ± 3.4, in eyes after vitrectomy with no tamponade -0.36 ± 4.9, and in gas-filled eyes 4.08 ± 5.9 (p<0.001). IOP obtained by both instruments correlated significantly in the control group (r=0.30, p=0.0099), and in the group with gas-filled eyes (r=0.78, p<0.0001). There was no significant correlation in the water-filled eyes (r=0.24, p=0.25). No significant correlation was found between the differences of GAT and DCT (GAT-DCT) to the mean IOP of GAT and DCT in control eyes (r=-0.01, p=0.92) and water-filled eyes (r=-0.21, p=0.33). A significant correlation was found in the gas-filled eyes (r=0.87, p<0.0001).

**Conclusions:** IOP as determined by DCT underestimates IOP in gas-filled eyes compared to GAT. GAT values were on average 4mmHg higher compared to DCT. The extent of IOP underestimation using DCT increases in higher IOP values. IOP evaluation after vitrectomy with gas endotamponade remains a difficult challenge.

**Commercial Relationships:** Nikolaos Mamas, None; Matthias Fuest, None; Gernot Roessler, None; Babac A. Mazinani, None; Niklas Plange, Implantdata Ophthalmic Products (F)

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**Program Number:** 5790 Poster Board Number: D0037

**Presentation Time:** 8:30 AM - 10:15 AM

**Macular hole repair closure rates in phakic and non-phakic patients with nonsupine positioning and sulfur hexafluoride endotamponade**

Jaafar El Annan1, Jordan Heffez2, Joshua D. Udoetuk1, Menka M. Sanghvi3, Petros E. Carnounis1. Ophthalmology, Baylor College of Medicine, Houston, TX; 2George Washington University School of Medicine and Health Sciences, Washington, DC; 3Retina Consultants P.C., Washington, DC.

**Purpose:** To compare macular hole closure rates between phakic and non-phakic patients following sulfur hexafluoride (SF6) endotamponade and nonsupine positioning.

**Methods:** Retrospective interventional case series of consecutive patients who underwent vitrectomy with internal limiting membrane peel for macular hole repair using SF6 and non-supine positioning postoperatively between August 2007 and December 2011.

**Results:** The overall macular hole closure rate was 95.6% in the 45 eyes of the 41 patients included. There was no significant difference in anatomic success between phakic (26/27) and non-phakic (17/18; 16/17 pseudophakic eyes and 1/1 aphakic eye) eyes (p=0.99).

**Conclusions:** Macular hole closure rates are not significantly different in phakic and non-phakic patients following vitrectomy with ILM peel, sulfur hexafluoride endotamponade and non-supine positioning.

**Commercial Relationships:** Jaafar El Annan, None; Jordan Heffez, None; Joshua D. Udoetuk, None; Menka M. Sanghvi, None; Petros E. Carnounis, Allergan (C)

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Pre-operative (top picture) and 3 months post-operative (bottom picture) colour fundus photograph of the left eye of a patient with sub retinal haemorrhage treated with intravitreal SF6 and Lucentis injections

Commercial Relationships: Indu Kumar, None; Thomas Papathomas, None; Ahmed Kamal, None

Program Number: 5792 Poster Board Number: D0039
Presentation Time: 8:30 AM - 10:15 AM
Movement of fovea toward optic disc after macular hole surgery with internal limiting membrane peeling
Kenichi Kawano, Yasuki Ito, Mineo Kondo, Hiroko Terasaki, 1, 2 Ophthalmology, Nagoya University, Nagoya, Japan; 2 Ophthalmology, Mie University, Tsu, Japan.
Purpose: To determine whether there is a movement of the fovea after successful macular hole (MH) surgery with internal limiting membrane (ILM) peeling.
Methods: Spectral-domain optical coherence tomography (SD-OCT) was performed before and >3 months after the surgery. The preoperative distances between the center of the MH and optic disc (MH-OD), center of macular hole and bifurcation of retinal vessels (MH-RV), and postoperative distance between the center of the fovea and optic disc (F-OD) were measured in the OCT images.
Results: The OD was 2.67±0.33 diameters (DD) which was significantly longer than that of the MH-OD of 2.77±0.33 DD (P<0.001). The RV was also significantly shorter than the MH-RV on the inner nasal area (from 0.85±0.16 DD to 0.79±0.15 DD; P<0.001), the inner temporal area (from 0.82±0.15 DD to 0.77±0.14 DD; P<0.001), and outer nasal area (from 1.70±0.31 DD to 1.65±0.32 DD; P<0.001), but was significantly longer than the MH-RV in the outer temporal area (from 1.65±0.29 DD to 1.68±0.29 DD; P=0.006). In eyes with a spontaneous closure of the MH, the “MH-OD and F-OD” and “MH-RV and F-RV” were not significantly different.
Conclusions: Our results showed that successful closure of a MH by vitrectomy with ILM peeling and gas tamponade results in a movement of the center of the macula toward the optic disc.

Commercial Relationships: Kenichi Kawano, None; Yasuki Ito, Mineo Kondo, Hiroko Terasaki, None
Support: Grant-in Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology of Japan (Dr Ito, C2159225).

Program Number: 5793 Poster Board Number: D0040
Presentation Time: 8:30 AM - 10:15 AM
COARSE OF INTRA-OCULAR PRESSURE AFTER VITREORETINAL SURGERY WITH SILICONE OIL INJECTION: A FOLLOW-UP OF 5 YEARS
Elyse Jabbour, George Azar, Joelle Antoun, Alexandre Jalkh, 1 Ophthalmology, Eye & Ear University Hospital, Beirut, Lebanon; 2 Department of Medicine, Université Saint Esprit Kaslik (USEK), Beirut, Lebanon.
Purpose: To assess and evaluate the course and medical treatment of intra-ocular pressure (IOP) after pars plan vitrectomy (PPV) with silicone oil injection (SOI) for different vitreoretinal conditions.
Methods: This is a 5-year prospective study. A total of 260 eyes operated for different vitreoretinal conditions and who had completed a minimum of 6 months follow-up were included in this study. Main outcomes were anterior segment examination, IOP measurement by aplanation, fundus exam, number and duration of glaucoma medications needed. Preoperative, intraoperative, postoperative and demographic parameters were also evaluated to determine their predictive value in the increase of IOP.
Results: The indications for PPV with SOI were rhegmatogenous retinal detachment (RDR) (70.8%; 184 of 260), proliferative diabetic retinopathy (PDR) (15.8%; 41 of 260), trauma (5.8%; 15 of 260), macular hole (6.5%; 17 of 260) and others (1.1%; 3 of 260). Overall, 122 of 260 eyes (47%) developed elevated IOP (defined as IOP > 21 mmHg) after PPV with SOI at 5 days (range 1 day-3 years), whereas 138 eyes (53%) did not have any. The onset of increased IOP was early (≤ 1 week), intermediate (1 week-6 months) and late (> 6 months) in 74 (60.7%), 37 (30.3%) and 11 (9.0%) of eyes respectively. By stratifying our results according to the different vitreoretinal conditions, 97 (52 %) of the RDR group, 11 (27%) of the PDR group, 7 (47%) of the trauma group and 7 (41%) of the macular hole group raised their IOP postoperatively. IOP was controlled in 104 (85%) of 122 eyes with medical treatment alone within a median duration of 5 months (range 4 days-4 years). Medical therapy reduced the IOP from a mean ± SD of 26.35 ± 6.55 mmHg before treatment to 18.15±5.92, 3 months following treatment (p=0.001). 18 (9%) needed chronic use of medical treatment to control their IOP after removal of SOI.
Conclusions: Our study provides summary data on IOP course after vitreoretinal surgery for different etiologies. The group RDR seems to have the highest rate of IOP elevation, but without reaching a statistically significant difference. High myopia was the only predictive factor for high IOP, while diabetes was found to be a protective factor against IOP elevation.
Commercial Relationships: Elyse Jabbour, None; George Azar, None; Joelle Antoun, None; Alexandre Jalkh, None

Program Number: 5794 Poster Board Number: D0041
Presentation Time: 8:30 AM - 10:15 AM
27-gauge sutureless microincision vitrectomy surgery for various retinal pathologies
Stanislao Rizzo, Federica Genovesi-Ebert, Francesco Barca, Emanuele Di Bartolo, UO Chirurgia Oftalmica, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy.
Purpose: To evaluate the efficiency, preliminary safety, and feasibility of a 27-gauge instrument system for transconjunctival microincision vitrectomy surgery (MIVS) in a variety of vitreoretinal diseases.
Methods: Interventional case series twenty-one eyes (21 patients) underwent a variety of vitreoretinal procedures using the 27-gauge transconjunctival MIVS Alcon CONSTELLATION® system to treat...
epiretinal membrane (n = 7), idiopathic macular holes (n = 5), diabeti
c vitreous hemorrhage (n = 3), vitreous opacity (n = 3), focal
diabetic traction retinal detachment (n = 2), macular traction
syndrome (n = 1). Surgical outcomes, including anatomic success,
visual outcomes, operating times, and intraoperative and
postoperative complications, were evaluated. Main outcome
measure was the sclerotomy closure.

**Results:** Anatomic success was achieved in all study eyes (100%); 17
eyes (80%) had visual improvement of 3 lines or more. No eyes
required conversion to larger gauge instrument. All sclerotomies self-
sealed without hypotony (IOP < or = 7 mmHg) from 1 day
postoperatively. No sutures was required. Mean operative times was
36,3 minutes (range 24,5-91,4 minutes). No surgical related
complication occurred.

**Conclusions:** The most serious criticisms regarding the current 23-
and 25-g systems have focused on complications related to wound
sealing, such as leakage, hypotony, and postoperative infectious
endophthalmitis. Although the recent refinement of trocar-cannula
systems has ergonomically improved their self-sealing architectures,
special techniques are still required. Complete self-sealing wounds are
not yet achievable in every case, even with 25-g systems. Indeed
by using the 27-g system , opening and closing procedures are
simplified compared to 23- and 25-g systems. Although the fluid
dynamics and cutting efficiency of 27-gauge instruments are lower
compared with 25-gauge MIVS, the 27-gauge system is feasible and
may reduce concerns about wound-sealing-related complications in
selected cases.

**Commercial Relationships:** Stanislao Rizzo, None; Federica
Genovesi-Ebert, None; Francesco Barca, None; Emanuele Di
Bartolo, None

**Program Number:** 5795 Poster Board Number: D0042
**Presentation Time:** 8:30 AM - 10:15 AM
**Anatomic and functional follow-up of patients with an idiopathic
epiretinal membrane and a preserved visual acuity**
**Arnaud Bonnabel, Rodica Isaico, Alain M. Bron, Catherine Creuzot-
Garcher,** Ophthalmology, General Hospital, Dijon, France.
**Purpose:** To determine the anatomic and functional retinal
modifications in patients with an idiopathic epiretinal membrane
(ERM) and a preserved visual acuity (VA).

**Methods:** Monocentric, prospective study in 24 eyes of 24 patients
with an ERM and a VA better than 20/25. Recorded data were best
corrected VA on ETDRS scale, retinal anatomic lesions on spectral-
domain OCT, retinal sensitivities on microperimetry and macular and
foveal thicknesses at 0 and 6 months.

**Results:** At inclusion, mean VA was 84 ± 5 letters, mean macular
sensitivity was 14.0 ± 1.4 decibels (dB) and mean foveal sensitivity
was 14.4 ± 1.5 dB. Mean macular thickness was 351 ± 34 µm and
mean foveal thickness was 348 ± 66 µm. At six months, one patient
was operated on ERM. For the other patients, fixation within the 2
central degrees was significantly lower than at baseline (p=0.04)
whereas retinal thicknesses and retinal sensitivities were unchanged.
At inclusion, no patient had an interruption of the external limiting
membrane and only two of them had an interruption of the inner and
the outer segments junction. At six months, the retinal status in OCT
was similar.

**Conclusions:** Retinal thickening is the first anatomic change on OCT
in patients with an ERM. A central fixation loss could be an early
sign of retinal impairment in these patients. Microperimetry
combined with spectral domain OCT could improve the detection of
early anatomic and functional retinal changes in patients with an
ERM and a preserved VA.

**Commercial Relationships:** Arnaud Bonnabel, None; Rodica
Isaico, None; Alain M. Bron, Allergan (C), Bausch Lomb (C),
Horus (F), Théa (C); Catherine Creuzot-Garcher, None

**Program Number:** 5796 Poster Board Number: D0043
**Presentation Time:** 8:30 AM - 10:15 AM
To develop a new surgical strategy for removing emulsified
droplets in the eye to reduce the complications associated the use of
silicone oil (SO)
**Yau Kei J. Chan**, Ho Cheung Shum**, Sai Hung David Wong**
1Department of Ophthalmology, University of Hong Kong,
Pokfulam, Hong Kong; 2Department of Mechanical Engineering,
University of Hong Kong, Hong Kong, Hong Kong.
**Purpose:** Emulsification is an inherent problem with the use of SO as
a substitute for the vitreous; the emulsified droplets can cause
postoperative complications, such as glaucoma, cataract and
proliferative vitreoretinopathy. This study aims to reduce the
complications associated with the emulsification of SO by developing
a rinsing agent for removing any emulsified oil droplets formed.
The current treatment approach of rinsing the eye cavity using balanced
salt solution is found to be ineffective and there is currently no viable
rinsing agent in use.

**Methods:** The proposed rinsing agent consists of
hexamethylsiloxane, the monomer of polydimethylsiloxane
(PDMS) as the major component with a small portion of a silicone-
based hydrophobic surfactant Dow Corning 749 fluid. Silicone oil
1300cSt was stained with BODIPY 493/503 and then dispersed in 4%
Pluronic F68 in 1X phosphate buffer saline (PBS) to form an oil-in-
water (O-W) emulsion. This emulsion was then added to and kept in
an eye model chamber for 24 hours. The chamber was subsequently
washed with the proposed rinsing agent or 1XPBS in the control
experiment. The washout was collected and observed under an
optical microscope. The chamber after rinsing was then filled with
1XPBS. After 24 hours, the number of emulsified oil droplets was
quantified using a particle counter Coulter counter Multiziser 4.
**Results:** In the in-vitro washing model, rinsing by the proposed
washing agent led to a reduction of oil droplets; the amount of oil
droplets remaining is only one-third of that after washing by 1XPBS.
Moreover, an oil-in-water-in-oil (O-W-O) double emulsion was
observed in the washout of the proposed rinsing agents. Fluorescence
signals due to BODIPY were detected within the larger water
droplets; this confirms that the initial SO droplets were encapsulated
by an aqueous shell phase. The resultant O-W-O double emulsion
could be washed away easily, while the remaining washing agent can
be easily removed by evaporation.

**Conclusions:** Emulsified SO droplets can be encapsulated within
water droplets with the use of the proposed rinsing agent and the
resultant O-W-O double emulsion can be easily washed away.
Therefore, this proposed rinsing agent demonstrates an excellent
potential in reducing the postoperative complications associated with
emulsification after the removal of silicone oil.

**Commercial Relationships:** Yau Kei J. Chan, None; Ho Cheung
Shum, None; Sai Hung David Wong, None
**Support:** Development Fund from The University of Hong Kong

**Program Number:** 5797 Poster Board Number: D0044
**Presentation Time:** 8:30 AM - 10:15 AM
**Blood flow changes of the retina and choroid after vitrectomy for
epiretinal membrane measured by laser speckle flowgraphy**
Eiko Tsuiki, Kiyoshi Suzuma, Yuki Muekawa, Takashi Kitaoka.
Department of Ophthalmology and Visual Sciences, Graduate School
of Biomedical Sciences, Nagasaki University, Nagasaki, Japan.
Purpose: To investigate the changes of chorioretinal blood flow using laser speckle flowgraphy (LSFG) before and after vitrectomy in patients with epiretinal membrane (ERM).

Methods: A retrospective analysis was performed for consecutive patients with ERM at the Department of Ophthalmology of the Nagasaki University from June 2011 through May 2012. Forty-four eyes of patients (21 men and 23 women, mean age 68.1±8.2) were examined for the best corrected visual acuity (BCVA), the retinal blood flow at the optic disc and the chorioretinal blood flow at the macula using LSFG before, approximately 1 week, 1 month and 3 months after surgery. The relative blood velocity was measured as the mean blur rate (MBR).

Results: The mean BCVA (logMAR±SD) significantly improved from baseline (0.44±0.28) to 1 month (0.28±0.19) and 3 months (0.20±0.20) after surgery (P<0.01). The average MBR of the blood flow in the main retinal vessels at the disc area was 46.5±14.4 and the average MBR of chorioretinal blood flow at the macula was 8.8±2.7 before surgery. Compared to before surgery (before; 100%), MBR at both of the disc (105.2±29.6%, 96.6±23.1%, 105.2±26.5%) and macula (96.5±17.1%, 101.1±13.9%, 96.4±22.5%) exhibited no statistically significant difference at 1 week, 1 month and 3 months respectively. (repeated measures ANOVA).

Conclusions: Vitrectomy for ERM indicated no significant difference in the retinal blood flow at the disc area and the chorioretinal blood flow at the macula. Blood flow of the retina and choroid were not affected by vitrectomy in patients with ERM.

Commercial Relationships: Eiko Tsuiki, None; Kiyoshi Suzuma, None; Yuki Maekawa, None; Takashi Kitaoka, None

Program Number: 5798 Poster Board Number: D0045
Presentation Time: 8:30 AM - 10:15 AM
Vitreous oxygenation bio-implant for central retina artery occlusion
Raul Velez-Montoya, Jeffrey Olson, Ophthalmology, University of Colorado, Aurora, CO.

Purpose: Central retina artery occlusion (CRAO) is a rare but devastating eye emergency, characterized by a sudden stop of the oxygen supply to the retina due to a decrease in retinal perfusion. The damage to the ocular tissue due to severe hypoxemia may be reversible if the oxygen supply is restored during the first 90 minutes to up to the first 8 to 24 hours if the occlusion is not total. After this time, the damage is rendered irreversible, even though the blood supply is restored. To try to solve this problem, a membrane encapsulated bio-implant was designed, aimed to deliver high concentration of oxygen to the retinal tissue during the window period in which damage can be prevented. The objective of this study is to assess the feasibility and oxygen delivery capabilities of the prototypes as well as to assess its effects on retinal tissue in an animal model of CRAO.

Methods: Sixteen animals (rabbits) were divided into three groups (control 4, sham 5 and active 7). A CRAO were induced by increasing the intraocular pressure up to 90mmHg through the insertion of a needle in the anterior chamber attached to a water column. The occlusion was sustained for 90 minutes. The vitreous oxygen content was measured before the occlusion and 1 hour after the event. During the recovery time the sham group received an active implant while the active group received the oxycell implant. There was no implant for the control group. An electroretinogram (ERG) was done in all animals at baseline and at 15 days of follow up.

Results: There was no difference in vitreous oxygenation at baseline. There was a statistical significant (p<0.01) increase in the vitreous oxygenation among the rabbits on the active group, 1 hour after the CRAO. However the oxygen levels decreased fast, reaching the same as in the control and sham group at day 3 of follow-up. The ERG showed no improvement on retinal function of the active group.

Conclusions: The membrane encapsulated bio-implant seems to be a viable option for increasing vitreous oxygenation during a CRAO. Further studies are needed in order to understand the best way to use this capability in order to prevent retinal damage.

Commercial Relationships: Raul Velez-Montoya, None; Jeffrey Olson, University of Colorado (P)

Program Number: 5799 Poster Board Number: D0046
Presentation Time: 8:30 AM - 10:15 AM
Epiretinal Membrane Peeling Following Uncomplicated Primary Retinal Detachment Repair
Kyle Godfrey1, Tanuj Banker2, Eric Weichel3, 2, 1Georgetown University School of Medicine, Washington, DC; 2Ophthalmology, Georgetown University Hospital, Washington, DC; 3Retina Group of Washington, Washington, DC.

Purpose: To evaluate the incidence and outcome of epiretinal membrane (ERM) peeling with pars plana vitrectomy (PPV/MP) following uncomplicated small gauge PPV repair of primary rhegmatogenous retinal detachments (RD).

Methods: A consecutive interventional case series from 2002 to 2012 by one group of retina surgeons performing PPV/MP after uncomplicated primary RD repair using either 23 or 25 gauge PPV instrumentation with or without scleral buckle (SB). Exclusion criteria included preoperative proliferative vitreoretinopathy, pre-existing ERM, pre-existing macular disease, previous PPV or SB, and documented follow-up of less than 3 months. Primary outcome measures included: 1) rate of PPV/MP, and 2) pre/postoperative central macular thickness (CSMT) and central foveal thickness (CFT), as measured by optical coherence tomography (OCT). Secondary outcome measures included: 1) pre/postoperative visual outcomes, 2) rates of cystoid macular edema (CME) confirmed by OCT/fluorescein angiography, and 3) identifying risk factors associated with post-operative CME development.

Results: 204 eyes with post operative ERM and a mean age 60.0 years ± 17.6 years were identified following uncomplicated RD repair. The mean visual acuity was 20/40 (logMAR .32 ± .38). 32 eyes (15.7%) underwent PPV/MP. In this group, the mean preoperative visual acuity was 20/100 (logMAR .86 ± .65) improving to 20/50 (logMAR .43 ± .43) postoperatively (p<0.006). The mean preoperative CSMT was 397.5µ ± 127.3 improving to 282.6µ ± 73.3 postoperatively (p<0.0001). There were 9 (28.1%) cases of chronic postoperative CME. The mean time from RD repair to PPV/MP was 326.1 +/- 299.1 days. There was not a statistically significant difference in PPV/MP or CME rates with regards to lens status.

Conclusions: PPV/MP is common following uncomplicated RD repair. PPV/MP can significantly improve visual acuity and decrease CSMT. Eyes that have undergone PPV/MP require close follow-up to rule out chronic CME.

Commercial Relationships: Kyle Godfrey, None; Tanuj Banker, None; Eric Weichel, None

Program Number: 5800 Poster Board Number: D0047
Presentation Time: 8:30 AM - 10:15 AM
Vitreous levels of MCP-1 and CD163 in vitreoretinal diseases
Takashi Tachibana, Shigeko Yoshida, Yoshiyuki Kobayashi, Takahito Nakama, Keijiro Ishikawa, Shintaro Nakao, Yukio Sassa, Hiroshi Enaida, Yuji Oshima, Tatsuro Ishibashi, Kyushu University, Fukuoka, Japan.
**Purpose:** MCP-1 is a chemokine associated with wound healing and fibrosis. Roles of MCP-1 and M2 macrophage in ocular disease are not fully understood. The purpose of this study was to determine the vitreous levels of MCP-1 and CD163, a specific M2 macrophage marker, and the correlation of these molecules in vitreoretinal diseases.

**Methods:** Vitreous samples were obtained from 377 eyes of 317 patients with macular hole (MH; n = 62), diabetic macular edema (DME; n = 40), proliferative diabetic retinopathy (PDR; n = 253), and proliferative vitreoretinopathy (PVR; n = 22) during pars plana vitrectomy. We also obtained vitreous samples from 53 eyes of patients with PDR who underwent secondary intraocular lens implantation approximately 6 months after the initial vitrectomy. The levels of MCP-1, CD163, and periostin in vitreous samples were measured by sandwich enzyme linked immunosorbent assay. Correlation between MCP-1, CD163, and periostin levels were calculated by Pearson correlation coefficient.

**Results:** The mean vitreous MCP-1 levels in patients with PDR (482.5 pg/ml) and PVR (3203 pg/ml) were significantly higher than that in patients with MH (482.5 pg/ml, P<0.001). In patients with PDR and PVR, the vitreous level of MCP-1 was correlated with that of CD163 (ρ=0.594, p=0.0001, r=0.7564, p=0.0003). The changes in the vitreous level of MCP-1 were not significant after vitrectomy.

**Conclusions:** Our data suggest that MCP-1 may play an important role in epiretinal fibrous proliferation, by possibly recruiting M2 macrophages.

**Commercial Relationships:** Takashi Tachibana, None; Shigeo Yoshida, None; Yoshiyuki Kobayashi, None; Takahito Nakama, None; Keijiro Ishikawa, None; Shintaro Nakao, None; Yukio Sassa, None; Hiroshi Enaida, None; Yuji Oshima, None; Tatsuro Ishibashi, None

**Program Number:** 5801 Poster Board Number: D0048
**Presentation Time:** 8:30 AM - 10:15 AM

**Vitrectomy for macular hole secondary to blunt ocular trauma satomi ohta, Takayuki Baba, Shuichi Yamamoto. chiba university, Chiba, Japan.**

**Purpose:** To determine the anatomical and functional outcomes after pars plana vitrectomy (PPV) for eyes with a macular hole secondary to blunt ocular trauma.

**Methods:** We reviewed the medical charts of 7 patients with a unilateral macular hole due to blunt trauma who underwent PPV at the Chiba University Hospital. The surgical procedures included peeling of the internal limiting membrane made visible by indocyanine green and brilliant blue G and intraocular tamponade with sulphur hexafluoride. The lens was removed and an intraocular lens implanted in one eye. The main outcome measures were the closure of macular hole confirmed by OCT and the best-corrected visual acuity (BCVA).

**Results:** The average age of the patients ranged from 9-55 years (median, 19 years). The causes of the unilateral blunt trauma were the eye hit by a tennis racket, a bat, a fist, an air-bag, and fireworks. In addition, one eye developed a macular hole after laser in situ keratomileusis, and it was also studied. The time from the injury to PPV ranged from two to eleven months (median, 6 months), and the median follow-up time was 12 months (range: 3-24 months). The macular hole of five patients was closed after the first operation and one patient required a second surgery. The decimal BCVA improved from 0.76±0.56 to 0.21±0.37 at the final visit (P=0.046). There were no intra- or postoperative complications. One patient had chorioretal atrophy at the macular and underwent PPV two months after the injury. In this case, the macular hole was not closed after the initial surgery and the patient did not want further treatment. The BCVA in this case remained 20/200 at the final visit.

**Conclusions:** A macular hole after blunt trauma can be successfully closed by PPV in most cases. The absence of chorioretal atrophy and the closure of macular hole appeared to be important for the recovery of the BCVA in cases of a traumatic macular hole.

**Commercial Relationships:** satomi ohta, None; Takayuki Baba, None; Shuichi Yamamoto, None

**Support:** None in the Support

**Program Number:** 5802 Poster Board Number: D0049
**Presentation Time:** 8:30 AM - 10:15 AM

**Rate of Elevated Intraocular Pressure Post Primary Vitrectomy Surgery Milad Hakimbashih, 1, 2, Kourous A. Rezaeia, 1, 3. Ophthalmology, Rush University, Chicago, IL; 3Ophthalmology, Illinois Retina Associates, Chicago, IL.**

**Purpose:** To evaluate the rate of immediate post-operative intraocular pressure (IOP) elevation in patients who have undergone primary vitrectomy surgery.

**Methods:** Retrospective chart review of primary vitrectomies performed between 1/2010-10/2012 in a multi-surgeon retina practice. Patients with previous history of glaucoma, vitreo-retinal surgery, combination of vitrectomy and scleral buckling procedure, or trauma were excluded. IOP of 26 mmHg or above within the first week after surgery was considered elevated IOP.

**Results:** Charts of 138 patients were reviewed and 102 eyes were included in the study. 10 eyes of 10 patients experienced IOP elevation within the first week after surgery. The average age of these patients was 65 years. 6 eyes were pseudophakic. The pre-operative diagnosis for surgery was retinal detachment (3 eyes), vitreous hemorrhage (3 eyes), epiretinal membrane (2 eyes), and macular hole (2 eyes). One eye had undergone 20-gauge vitrectomy surgery and rest had undergone 23-gauge vitrectomy surgery. 5 eyes required intraocular non-expansible gas tamponade (4 with C3F8, and 1 with SF6). None of the eyes had history of previous steroid exposure. The average post-op IOP was 32 mmHg with a range of 27-42 mmHg. All patients required topical pressure reducing drops. 2 patients required additional oral dorzolamide to lower the IOP. The average duration of the IOP elevation was 11.2 days with a range of 1-30 days. The patients were followed for an average of 13 months. 2 eyes were referred to glaucoma specialists for further management and required long term topical pressure reducing drops.

**Conclusions:** The rate of immediate IOP elevation post vitrectomy surgery in patients with no previous history of glaucoma or retinal surgery was 9.8%. In all patients the IOP elevation was treated with topical or oral therapy and no glaucoma surgery was necessary. In most patients the IOP increase was transient and only 2 patients were ultimately diagnosed with glaucoma and needed long term topical treatment. Intraocular pressure needs to be monitored post vitrectomy surgery.

**Commercial Relationships:** Milad Hakimbashih, None; Kourous A. Rezaeia, Alcon (C), Alcon (F), Genentech (F), BMC (C), Alimera Sciences (C), Regeneron (F), Thrombogenics (C)

**Program Number:** 5803 Poster Board Number: D0050
**Presentation Time:** 8:30 AM - 10:15 AM

**An Experimental Proliferative Vitreoretinopathy (PVR) Model in Pigmented Rabbits for Testing of New Treatment Lichian Zhong. Ocular Science Department, Toxikon Corporation, Bedford, MA.**

**Purpose:** The study is to create an experimental proliferative vitreoretinopathy (PVR) model induced by injecting rabbit conjunctival fibroblast cells (RCFs) into the vitreous cavity for...
Methods: One male New Zealand Red pigmented rabbit was used to generate RCFs. The concentration of the RCFs was 5.0 x 100000 /100uL in balance salt solution (BSS) per eye and the RCF viability was identified by Trypan Blue Exclusion Test. Eight male and eight female rabbits were injected intravitreally with RCFs. The day of the RCF injection was designated as Day 1 and the last day of the study was Day 28. The eye of the RCF injection was designated as the PVR eye and the contralateral eye as the non-PVR eye. All animals were received ocular examinations (OE) for signs of PVR at pre-study, Day 1 and 3, weekly and at pre-sacrifice. Classification of PVR is divided into six stages (0 - 5) using the clinical grading criteria. Intraocular pressure (IOP) and photography (OP) in all animals was measured and taken at pre-study, Day 1 and 3, weekly and at pre-sacrifice. All animals were weighed at pre-study, weekly and at pre-sacrifice. All animals were monitored daily for signs of distress. Any additional gross ocular observations were recorded. All animals were observed for clinical observation daily and moribund/mortality twice daily. All animals were sacrificed at the end of study and all eyes were enucleated and processed for histopathological evaluation.

Results: All animals exhibited the PVR in the vitreous body of the PVR eyes and scored stage 4 or 5 by Day 28. The non-PVR eyes of animals were scored stage 0 as normal. IOP measurements in the PVR eyes showed no difference compared to those in the non-PVR eyes (p>0.05). None of the animals had any change their body weight during the course of the study. No significant clinical signs were observed. Histopathological report shows that fibrosis/fibroblast cells were noted and scored minimal to moderate in vitreous body and/or choroid and/or retinas/optic disc in all animals and retinal detachments were found in 11 animals in the PVR eyes, based on the microscopic observations.

Conclusions: The PVR model was 100% successfully induced and the pigmented rabbit PVR model may provide a stable, effective and reliable method for testing of new treatment for patients.

Commercial Relationships: Lichun Zhong, None

Program Number: 5804 Poster Board Number: D0051
Presentation Time: 8:30 AM - 10:15 AM
Light Microscopy Features of Epiretinal Membranes
Laura N. Distefano, None; Marco Dutra Medeiros, None; Anna Salas Torras, None; Andrea R. Carvalho, None; M Carme Dinàrës i Fernàndez, None; Francesc Tresserra, None; Miguel A. Zapata, None; Jose Garcia-Arumi, None

Purpose: The first aim of this study was to assess a possible correlation between etiologic and histological types of epiretinal membranes. Furthermore the second objective was to analyse a correlation between evolution and etiology or histological type.

Methods: 64 eyes which went under pars plana vitrectomy by the same surgeon between January 2010 and December 2011 were studied. Patients were split up into three main groups according to clinical features that led to surgical indication: idiopathic epiretinal membranes, fibrovascular membranes of proliferative diabetic retinopathy, and proliferative vitreoretinopathy (PVR) membranes. Removed tissue during surgery was fixated and evaluated by light microscopy under hematoxylin eosin staining. 19 eyes were excluded because of insufficient material. The remaining 45 samples were then divided into three groups according to the amount of pigment presented and grade of cellularity: A, no pigment present and scarce cellularity; B, scarce pigment and moderate cellularity; C, abundant pigment and cellularity. Evolution was recorded considering onset of symptoms and time of surgery.

Results: 20 eyes (44%) were classified as PVR, 16 were idiopathic (36%) and 9 were diabetic retinopathy membranes (20%). Among the PVR etiology, 9 tissue samples (45%) were labeled as histological type B, 7 (35%) as type A, and 4 (20%) as type C; in the idiopathic group, 13 samples (81%) were included in type A group, 2 (13%) in type B, and 1 (6%) in group C; while in PVR patients 4 (44%) were type A, 4 (44%) were type B, and 1 (11%) was type C. No statistical significant correlation was found between etiologic and histologic types of epiretinal membranes.

Conclusions: No significant correlation was found between histological type of membranes and etiology. Idiopathic and diabetic membranes had more frequently symptoms longer than 4 months until surgery was applied, while PVR patients were operated up to 4 months from onset of symptoms in the majority of cases. There was a positive correlation between samples with long evolution and its less amount of pigment and cellularity.

Commercial Relationships: Laura N. Distefano, None; Marco Dutra Medeiros, None; Anna Salas Torras, None; Andrea R. Carvalho, None; M Carme Dinàrës i Fernàndez, None; Francesc Tresserra, None; Miguel A. Zapata, None; Jose Garcia-Arumi, None

Program Number: 5805 Poster Board Number: D0052
Presentation Time: 8:30 AM - 10:15 AM
Treatment Of Surgically Induced Cystoid Macular Edema By Intravitreal Implant Of Dexamethasone
Rino Frisina, ophthalmology, Sant’Anna Hospital, Brescia, Italy.

Purpose: Surgically induced cystoid macular edema (SICME) is a post-operative complication that can occur after cataract surgery, commonly known as Irvine Gass syndrome. However, SICME can occur after pars plana vitrectomy (PPV) with or without cataract surgery. The pathogenesis of SICME is attributed to the breakdown of the blood-aqueous barrier due to an exaggerated inflammatory reaction and to the release of cytokines. The purpose of this study was to evaluate the efficacy and safety of the implant of Dexamethasone 0.7 mg (Ozurdex, Allergan, Irvine, Calif, USA) (IVO injection) for the treatment of SICME refractory to the most common topical anti-inflammatory therapy.

Methods: Prospective, non-comparative, open-label study. Six eyes of 5 patients affected by SICME for at least 3 months, had undergone treatment with IVO injection. The mean time of SICME was 19,3±20,1 months. Best corrected visual acuity (BCVA), intraocular pressure (IOP), fundus examination were performed at baseline and every month after IVO injection. Fluorescein angiography (FA) was performed in all patients, prior to IVO injection, to exclude neovascular diseases. Central foveal thickness (CFT) and macular morphology (reduction or disappearance of intra-retinal cysts) were studied with optical coherence tomography (OCT) every month to the end of follow up.

Results: Six eyes of five patients had undergone PPV for epiretinal membrane (ERM). In two cases cataract surgery was also performed. SICME appeared between 1 and 3 months post-op. In the group of patients who underwent PPV without cataract surgery only one case was phakic. The pre-operative BCVA average was 0.62±0.35, range 0.70-1 (ETDRS). The pre-operative CFT average was 654,6±172,85, range 445-800, micron. The pre-operative IOP average was

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13.8±1.48, 12-16, mmHg. The post-operative BCVA average was 0.4±0.37, 1-0 and the post-operative CFT average was 279.17±78.13, 180-350 micron, at the last control (follow up 49-189 days). In all cases there was an improvement of BCVA and the intra-retinal cysts disappeared. There were no side effects such as increased IOP.

**Conclusions:** IVO injection for the treatment of SICME was effective and safe. In our study, we noticed an improvement in BCVA, the disappearance of the cysts and the CFT reduction in all patients.

**Results:**

**Closing and Opening Cutter Velocities.**

<table>
<thead>
<tr>
<th>Probe</th>
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<tr>
<td>DPD</td>
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**Table 1. Results: Closing and Opening Cutter Velocities.**

**Program Number:** 5806
**Poster Board Number:** D0053
**Presentation Time:** 8:30 AM - 10:15 AM

**Anatomic and Visual Success after Macular Hole Surgery in an Asian population**

Karen Chia, Hon Tym Wong, Ophthalmology, National Healthcare Group Eye Institute, Tan Tock Seng Hospital, Singapore, Singapore, Singapore.

**Purpose:** To identify factors associated with anatomical and visual success of macular hole surgery in an Asian population.

**Methods:** A retrospective, interventional case series of 79 consecutive eyes with idiopathic senile full thickness macular holes treated by pars plana vitrectomy (PPV) were analysed.

**Results:** The median follow-up time was 19.5 months. The mean age was 63.4 years (range 36-82 years) and there were more females (64.6%). Anatomical success was achieved in 78.5% of eyes after 1 surgery. Best corrected visual acuity (VA) improved from a median of LogMAR of 0.88 to 0.48 at last follow up. Thirty-seven eyes (46.8%) had final VA of 20/40 or better, Sixty-two (78.5%) holes were closed after 1 surgery. Internal limiting membrane (ILM) peel was performed in 70 eyes (88.6%), of which 26 had no stain and staining was used in 44 eyes (55.7%). Trypan blue was the most common stain used (35 eyes, 79.5%). Cataract, epiretinal membrane formation and high IOP were the most common complications of surgery.

Hole closure correlated well with final BCVA 20/40 or better (p=0.011, Chi-square with continuity correction, OR=7.5). Anatomical closure correlated with improvement of at least 3 lines (p=0.024) but not duration of symptoms (p=0.069).

The main factors predictive for hole closure was performing an internal limiting membrane peel (p=0.002). Pre-operative hole diameter (≤400μm) was predictive for good final VA (p=0.003), but was not correlated with anatomical closure (p=0.099). Patients with poor preoperative vision had higher likelihood of visual improvement of 3 lines or more (p=0.002) but duration of symptoms 1 year or more correlated with poor final VA (p=0.004). Final VA correlated closely with hole diameter (p=0.002) but not base diameter (p=0.253). The type of gas used, posturing technique and gauge of vitrectomy had no statistical effect on outcomes.

**Conclusions:** There was good success rates of macular hole surgery in Asians. Anatomic success was associated with ILM peel with stain. Pre-operative hole diameter (≤400μm) was predictive for good final VA.

**Commercial Relationships:** Karen Chia, None; Hon Tym Wong, None.

**Program Number:** 5807
**Poster Board Number:** D0054
**Presentation Time:** 8:30 AM - 10:15 AM

**Cutter Velocities of Two Vitrectomy Probes: Dual Pneumatic and a Single Pneumatic Drive With Spring Return**


**Purpose:** This study was conducted to compare the cutter velocities of 2 different vitrectomy probes: a dual pneumatic drive (DPD), in which a pneumatic drive pulse drives the probe both open and closed, and a single pneumatic drive with a spring return (SPDSR), in which a pulse drives the probe closed but a spring opens the port. The purpose was to determine the effect of these 2 designs on the cutter velocities.

**Methods:** Two different types of probes were compared: DPD (Constellation® UltraVit®, Alcon Laboratories, Inc.) and SPDSR (Stellaris PC, Bausch & Lomb). Six each of 23- and 25-gauge (G) probes were tested. High-speed video of the cutter movement through the probe port was captured at 25,000 frames per second. All probes were run at 1500, 2500, and 5000 cuts per minute (cpm). The cutter movement was analyzed from the captured video frames to calculate the cutter closing and opening velocities.

**Results:** See Table 1.

**Conclusions:** The SPDSR cutter closing and opening velocities were highest at 2500 cpm. The DPD cutter closing and opening velocities were highest at 5000 cpm. For all probes, the closing velocities were higher with the 25G probe compared to the 23G probe. Optimal tissue shearing may be associated with high cutter velocities. In this study, the 25G DPD cutter in the Shave mode at 5000 cpm generated the highest closing velocities Md potentially the beat shearing capabilities.

**Program Number:** 5808
**Poster Board Number:** D0055
**Presentation Time:** 8:30 AM - 10:15 AM

**Robot assistance for micrometer precision in vitreoretinal surgery**

Dina Joy K. Abulon, Alcon Labs (E).

**Commercial Relationships:** Dina Joy K. Abulon, None.
Thijs H. Meenink1,2, Gerrit Naus1,2, Marc D. de Smet3,4, Maarten Beelen1,2, Maarten Steinbuch1. 1Mechanical Engineering, Technische Universiteit Eindhoven, Eindhoven, Netherlands; 2PRECEYES Medical Robotics, Eindhoven, Netherlands; 3Ophthalmology, Clinique de Montchoisi, Lausanne, Switzerland; 4Department of Ophthalmology, University of Amsterdam, Amsterdam, Netherlands.

**Purpose:** Precision in vitreoretinal surgery is a major requirement particularly since the steadiness of the human hand is limited. Recent developments in vitreoretinal surgery such as imaging techniques based on optical coherence tomography allow for micrometer resolution diagnoses. Corresponding surgical precision, however, is not achievable by the human hand. The purpose of this study is to show the applicability of robot assistance in achieving the required precision to enable treatment of manually untreatable levels.

**Methods:** Human hand tremor is in the order of 100µm when translated to the tip of a vitreoretinal instrument [Riviere, 1997]. The size of the smallest structures that surgeons currently target for treatment is typically in the order of 30µm. To enable surgery for these structures, the surgeon needs assistance. To this end, a high-precision robotic master-slave system has been developed; the PRECEYES Surgical System [Meenink et.al., 2012]. The master-slave layout of the system facilitates motion scaling and tremor filtering, providing a high precision. This precision is validated via reproducibility tests using a laser vibrometer (Polytec OVF-5000 with OVF-552 at 500 µm/V). Furthermore, point-and-pick and cannulation experiments on the chorioallantoic membrane of 12-day fertilized chicken eggs are performed to evaluate the system in practice.

**Results:** The reproducibility tests show that the robotic system provides an intrinsic precision of 2 to 10µm, depending on the degree of freedom. This precision is calibrated at the tip of the instrument when positioned at the retina, which represents an improvement of 10 to 20 times compared to the human hand. As such, the system enables treatment of manually untreatable levels. This is supported by the cannulation experiments. In these experiments, veins down to 30 µm are penetrated and injected with air using a spiked tip glass micropipette (RI instruments). Besides the high positioning precision, the stand-by functionality of the robotic system allows this position to be held for a long time. Consequently, the injection can be prolonged over several minutes.

**Conclusions:** A robotic system has been developed to assist the surgeon during vitreoretinal surgery by improving upon human precision with a factor 10 to 20. This high precision allows for the development of procedures / treatment of challenging cases.

**Commercial Relationships:** Thijs H. Meenink, PRECEYES Medical Robotics (E); Gerrit Naus, PRECEYES Medical Robotics (E); Marc D. de Smet, Thrombogenics (P), Thrombogenics (C), Sanofi (C), Bayer (C), Regeneron (C), Preceyes (R), Allergan (C), Janssens (R), GSK (C), CRL (C); Maarten Beelen, PRECEYES Medical Robotics (E); Maarten Steinbuch, None

**Program Number:** 5809 Poster Board Number: D0056
**Presentation Time:** 8:30 AM - 10:15 AM

**Results of long-term silicone oil tamponade for more than 12 months and its complications**

Yong Sok Ji, Hyun Ho Jung, Kyung Chul Yoon, Sang Woo Park, Chonnam National University Hospital, Gwangju, Republic of Korea.

**Purpose:** To assess the anatomic and functional outcomes of long-term silicone oil (SO) tamponade and its complication rates.

**Methods:** We retrospectively reviewed 98 eyes of 97 patients with intraocular SO (Oxane 5700 Bausch & Lomb, Kingston-upon-Thames, UK) for at least 12 months. Clinical data and any SO-related complications were recorded from the notes at baseline, and at months 3, 6, 12 and last follow-up. We defined the ambulatory vision as visual acuity of 4/200 (logMAR 1.7) or better.

**Results:** Mean age was 55.2±17.4 years, and mean duration of silicone oil in the eye was 30.2±20.9 months. The main reasons for long-term SO tamponade were ocular trauma (22.4%), retinal redetachment (19.4%), uveitis (13.3%), and proliferative diabetic retinopathy (10.2%). Anatomic success (flat retina) and ambulatory vision were achieved in 65 and 36 eyes respectively at last follow-up. The common complications were optic neuropathy (13.3%), corneal decompensation (9.2%), hypotony (8.2%), and band keratopathy (5.1%). Accessed separately according to the reason for long-term SO, anatomic success rates were relatively high in retinal redetachment (79.0%) and uveitis (76.9%) and low in severe proliferative vitreoretinopathy (55.6%) and trauma (50.0%) cases. The rates of under-ambulatory vision were 100%, 66.7, and 66.7% in trauma, endophthalmitis, and severe proliferative vitreoretinopathy respectively.

**Conclusions:** The long-term SO tamponade can be a last resort option in complex cases. But the anatomic and functional success rates were low due to the various SO-related complications. The prognosis was especially poor in trauma and severe proliferative vitreoretinopathy cases.

**Commercial Relationships:** Yong Sok Ji, None; Hyun Ho Jung, None; Kyung Chul Yoon, None; Sang Woo Park, None

**Program Number:** 5810 Poster Board Number: D0057
**Presentation Time:** 8:30 AM - 10:15 AM

**Temporal pattern of macular thickness resolution and visual acuity improvement after epiretinal membrane peel surgeries**

Ashley Campbell, Demetrios Vavvas. Ophthalmology, Massachusetts Eye and Ear, Boston, MA.

**Purpose:** The aim of this study was to determine the temporal pattern of central macular thickness (CMT) improvement after epiretinal membrane peel surgeries performed at a teaching institution (Massachusetts Eye and Ear Infirmary).

**Methods:** This is a retrospective review of 23 patients who underwent vitrectomy and membrane peel for idiopathic epiretinal membrane (ERM) between 2010-2012 at the Massachusetts Eye and Ear Infirmary. Visual acuity and spectral-domain optical coherence tomography (SD-OCT) images were analyzed to compare pre-operative values from post-operative day one (POD1), and week one (POW1), and months 1-3 (POM1-3).

**Results:** Of the 23 patients reviewed, 16 had pars plana vitrectomy (PPV) with membrane peel (MP) alone and 7 had PPV/MP with...
ARVO 2013 Annual Meeting Abstracts by Scientific Section/Group – Retina

phacoemulsification of their cataract at the same time. Preoperatively, the average visual acuity (VA) was 0.65 log minimal angle of resolution (logMAR) (standard deviation ± 0.30) and the average OCT central macular thickness (CMT) was 476 μm ± 90. The average visual acuity at POD1, POW1, and POM1-3 was 1.00 logMAR ± 0.45, 0.77 logMAR ± 0.53, and 0.49 logMAR ± 0.29, respectively, demonstrating that while visual acuity initially worsened in the immediate post-operative period, it eventually improved during the POM1-3 time frame. Ultimately, 73.9% of patients enjoyed an improvement in visual acuity, with an average improvement of -0.17 logMAR (P=0.02). The average CMT at POD 1, POW1, and POM1-3 was 428 μm ± 98, 399 μm ± 106, and 349 μm ± 83, respectively. This represents a 25.1% (P=0.004), 35.2% (P=0.002), and 53.9% (P=0.001) reduction in CMT at POD1, POW1, and POM1-3, respectively, as compared to pre-operative values. The top five responders at POW1, who had an average 70% reduction in CMT, ultimately had an average improvement in VA of 0.48 logMAR, which is markedly better than the overall average. Conversely, the bottom five responders at POW1 had an average 5% increase in CMT, which were associated with an overall average -0.17 logMAR reduction in VA.

Conclusions: Our study shows that 50% of the anatomical improvement after ERM peel surgery is seen in the first day/week after the surgery. Improvement of macular thickness precedes the VA improvement and the improvement seen in the first week can be used to help predict the final visual acuity.

Commercial Relationships: Ashley Campbell, None; Demetrios Vavvas, MEEI (P), Kala pharmaceuticals (C), Roche (C), Genentech (C)

519 Retina-RPE Transplantation
Thursday, May 09, 2013 8:30 AM-10:15 AM
Exhibit Hall Poster Session
Program #/Board # Range: 5811-5818/D0071-D0078
Organizing Section: Retina

Program Number: 5811 Poster Board Number: D0071
Presentation Time: 8:30 AM - 10:15 AM

iPS-RPE implantation in the Royal College of Surgeons Rat does not lead to adverse events in a long term study of health and graft stability

Stephen Bravo1, Peter D. Westenskow1, Toshihide Kurihara1, Alison Dorsey1, Liliana Paris3, Jonathan H. Lin2, Martin Friedlander1.
1Department of Cell Biology, The Scripps Research Institute, La Jolla, CA; 2Department of Pathology, UC San Diego School of Medicine, La Jolla, CA.

Purpose: Age-related macular degeneration is one of the leading causes of incurable vision loss in industrialized countries and can be caused by retinal pigment epithelium (RPE) dysfunction or death. One exciting potential therapy involves the transplantation of stem cell-derived RPE to replace dysfunctional RPE and maintain photoreceptor function. However, concerns about the abnormal migration, tumor formation, and immunogenicity of stem cell derived treatments have been raised. Several studies, including our own, have shown RPE grafts slow photoreceptor degeneration in animal models of inherited RPE-mediated retinal degeneration, but the long-term safety and health of the animals following transplantation have yet to be examined. Here we present the results of a two-year comprehensive evaluation of the behavior and health of rats implanted with induced pluripotent stem cell (iPS)-derived RPE prepared using an alternative and potentially safer method of reprogramming.

Methods: Royal College of Surgeons (RCS) rats received a single subretinal injection of human iPS-derived RPE, PBS, or no injection at three weeks of age (n=30). The animals were continuously immunosuppressed using cyclosporine A. Photoreceptor function was monitored in vivo using optical coherence tomography and focal ERG. All animals were monitored daily and any abnormalities were catalogued. The animals were sacrificed as late as two years post-injection and necropsies and blood tests were performed at the end of the study; pathologists also examined select tissues.

Results: iPS-RPE survived in the subretinal space, and no tumors of human origin were observed. Lens and cornea opacities occurred at similar frequencies in both uninjected and injected rats. Unusual extracellular tissue masses developed in all groups, but were observed in a higher frequency in uninjected animals. Necropsies and blood tests revealed no gross abnormalities.

Conclusions: While safety concerns regarding iPS-derived grafts exist, here we show that iPS-RPE grafts are stable and the transplanted cells do not migrate from the eye. Furthermore, they provide photoreceptor rescue in the RCS rat without inducing gross abnormalities in the behavior or health of the host animals. This evidence indicates that implanted iPS-RPE cells do not lead to contraindicative adverse events in an animal model of retinal degeneration.

Commercial Relationships: Stephen Bravo, None; Peter D. Westenskow, None; Toshihide Kurihara, None; Alison Dorsey, None; Liliana Paris, None; Jonathan H. Lin, None; Martin Friedlander, None
Support: CIRM TR1-01219, The Lowy Medical Institute (MacTel)

Program Number: 5812 Poster Board Number: D0072
Presentation Time: 8:30 AM - 10:15 AM

Development of a Novel Device for Subretinal Transplantation of Human iPSC-RPE Cell-Sheet

Hiroyuki Kamao1,2, Michiko Mandai1, Osamu Mita1, Yoshihisa Harada1, Junichi Kiyu2, Masayo Takahashi1,2,3. 1Laboratory for Retinal Regeneration, RIKEN Center for Developmental Biology, Kobe, Japan; 2Ophthalmology, Kawasaki Medical School, Okayama, Japan; 3Nidek inc., Gamagori, Japan.

Purpose: To evaluate a surgical technique for human induced pluripotent stem cell-derived retinal pigment epithelium (hiPSC-RPE) cell-sheet without artificial scaffold using a novel device.

Methods: A novel device consisted of a processed flat 20-gauge cannula and a custom-made plunger. Subretinal transplantation of a 1.3 mm X 3.0 mm hiPSC-RPE cell-sheet was performed in 12 rabbits. Results were evaluated by graft condition (damaged or folded), settled side (correct or upside down), position (center, near, far), and direction (anterior, posterior, right, left) immediately after surgery and graft condition (shrunk or folded) 2 weeks after surgery with fundus photographs. The eyes were then fixed for histology. Besides, Subretinal transplantation of grafts in the medium with 50 % viscosity was performed in 8 rabbits.

Results: All grafts could be transplanted without obvious damage. Among the 12 transplanted grafts, 2 were folded, 12 were settled with correct side, 12 were center positioned, 10 were shifted in anterior direction and 2 were in right direction immediately after surgery. However, by inserting the device co-axial to the direction of flow paths corrected the grafts direction (consecutive 9 of 9 grafts). Two weeks after surgery, 2 of 12 grafts were invisible, 2 were folded, and 4 were shrunk. All the grafts in 50 % viscosity medium ended up shrunk. Nevertheless, adequate drainage of subretinal fluid during surgery to help the adhesion of graft and host prevented grafts from shrinking (consecutive 4 of 4 grafts). Histology demonstrated that outer nuclear layer above the grafts were not significantly different
from those around the grafted area.

**Conclusions:** We presented a novel device to transplant hiPSC-RPE cells-sheet safely and stably with the correct positioning into subretinal space by inserting the grafts in the coxial direction of flow paths and with adequate subretinal drainage. We will further confirm these results by transplanting hiPSC-RPE cell-sheet into monkey eyes.

**Commercial Relationships:** Hiroyuki Kamao, Nidek incorporated (P); Michiko Mandai, None; Osamu Mita, NIDEK CO., LTD. (E), NIDEK CO., LTD. (P); Yoshihisa Harada, NIDEK CO., LTD. (P), NIDEK CO., LTD. (E); Junichi Kiryu, None; Masayo Takahashi, None

**Program Number:** 5813 Poster Board Number: D0073

**Presentation Time:** 8:30 AM - 10:15 AM

**Three-dimensional imaging of developing photoreceptors transplanted in a mouse model of CEP290-Leber congenital amaurosis (LCA)**

Yi-Sheng Chang\(^1\), Robert Fariss\(^2\), Chris Lin\(^3\), Jutaro Nakamura\(^2\), Winnette McIntosh Ambrose\(^2\), Kohei Homma\(^2\), Rivka A. Rachel\(^2\), Artur V. Cideciyan\(^4\), Samuel G. Jacobson\(^4\), Anand Swaroop\(^5\)

\(^1\)Department of Ophthalmology, National Cheng Kung University, Tainan City, Taiwan; \(^2\)National Eye Institute, National Institutes of Health, Bethesda, MD; \(^3\)Scheie Eye Institute, University of Pennsylvania, Philadelphia, PA.

**Purpose:** To investigate the maturation, migration and integration of transplanted photoreceptors in rd16/Nrl-/- mouse retina using three-dimensional imaging reconstruction.

**Methods:** Immature photoreceptors from postnatal day 5 retina of Nrl-GFP mice were dissociated and injected into the sub-retinal space of rd16/Nrl-/- mice, a CEP290 mutation model of Leber congenital amaurosis (LCA). Retinas were sectioned after 1 month, stained and scanned for serial confocal imaging. Three-dimensional structure was reconstructed.

**Results:** Transplanted photoreceptors developed outer segments with polarization toward the retinal pigment epithelial layer. During cellular migration, defects of tight junctions at the outer limiting membrane created the passage for transplanted cell bodies or processes. After reaching the outer nuclear layer, transplanted photoreceptors developed synapses, interacting with host bipolar cells in three different patterns. Typically, one synapse was derived from one photoreceptor interacting to one bipolar cell. At times, we observed two synapses derived from one inner segment or two inner segments from one photoreceptor.

**Conclusions:** Three-dimensional imaging technique was applied to photoreceptor transplantation, overcoming the limitations of conventional two-dimensional imaging. This allows better evaluation of structural changes in donor cells and host tissues. Our studies are expected to contribute to broader understanding of cell-based strategies for photoreceptor replacement in mouse models of human retinal degenerative diseases.

**Commercial Relationships:** Yi-Sheng Chang, None; Robert Fariss, None; Chris Lin, None; Jutaro Nakamura, None; Winnette McIntosh Ambrose, None; Kohei Homma, None; Rivka A. Rachel, None; Artur V. Cideciyan, None; Samuel G. Jacobson, None; Anand Swaroop, None

**Support:** NHRI PS9806 from the National Health Research Institute, Taiwan.

**Program Number:** 5813 Poster Board Number: D0074

**Presentation Time:** 8:30 AM - 10:15 AM

**Retinal Pigment Epithelium - Choroid Transplantation: results up to 3 years**

Laura Bertazzi\(^1\), Antonio Peroglio Deiro\(^1\), Matteo G. Cereda\(^2\), Grazia Pertile\(^3\)

\(^1\)Ophthalmology, Ospedale Sacro Cuore Don Calabria, Negrar, Verona, Italy; \(^2\)Ophthalmology, Ospedale Sacco, Milano, Italy.

**Purpose:** To report and analyze functional and anatomical outcomes following an autologous retinal pigment epithelium (RPE) - choroid graft (PATCH) transplantation in patients with neovascular macular degeneration.

**Methods:** Retrospective analysis of 72 patients who underwent a RPE-choroid transplantation between April 2007 and November 2011. All patients had a subfoveal choroidal neovascularization (CNV) with or without haemorrhage or an RPE tear. All were either ineligible for or non-responsive to conventional therapy. SD-OCT and fluorescein angiography (FA) combined with indocyanine green angiography (ICGA) examinations were obtained using Spectralis HRA+OCT (Heidelberg Engineering, Heidelberg, Germany) before surgery and during follow-up. Preoperative and postoperative best-corrected visual acuity (BCVA) measurements were performed using ETDRS charts.

**Results:** 72 consecutive patients (38 female, 34 male) underwent RPE-choroid graft surgery. The mean age was 73 years (range: 34-88). Medium followup was 20±13 months. The mean preoperative BCVA was 1.5 logMAR. Mean postoperative BCVA was 1.2 logMAR. The BCVA remained stable or improved in 52 out of 72 eyes. Mean graft's revascularization time was 31 days. Severe complications were reported in 15 eyes (20%): 9 submacular haemorrhages, 2 macular holes, 2 retinal detachment, 2 lack of vascularization of the choroidal grafts. Three (4%) eyes developed a recurrent subfoveal choroidal neovascularization during the follow-up.

**Conclusions:** RPE-choroid graft transplantation has the potential to maintain or restore macular function in selected eyes affected by subfoveal CNV, with low recurrence rates. Retinal sensitivity, BCVA data, and fixation on the graft suggest that the graft was responsible for the preservation of the macular function. This surgery may represent an alternative for patients with exudative AMD that cannot benefit from anti-VEGF therapy.

**Commercial Relationships:** Laura Bertazzi, None; Antonio Peroglio Deiro, None; Matteo G. Cereda, None; Grazia Pertile, None

**Program Number:** 5815 Poster Board Number: D0075

**Presentation Time:** 8:30 AM - 10:15 AM

**The sodium iodate model for transplantation of hESC-derived RPE**

Madalena Carido\(^1\), Yu Zhu\(^1\), Boris Benkner\(^2\), Thomas Kurth\(^1\), Thomas A. Münch\(^2\), Elly Tanaka\(^1\), Marius Ader\(^1\)

\(^1\)Center for Regenerative Therapies Dresden, DRESDE, Germany; \(^2\)Werner Reichardt Centre for Integrative Neuroscience, Tubingen, Germany.

**Purpose:** The Royal College of Surgeons (RCS) dystrophic rats are widely used for modeling human diseases characterized by RPE cell dysfunction or degeneration, and represent the standard pre-clinical model for RPE transplantation. However, there are disadvantages associated with this model, such as the early onset and fast progression of degeneration, and the ability of diverse cell sources to delay photoreceptor degeneration. Here we describe in detail the effect of sodium iodate (SI), a strong inducer of RPE cell death, on the mouse retina, and evaluate the utility of this model for transplantation experiments.

**Methods:** SI was injected systemically in 6-8 week old C57BL/6 mice. Functional characterization was done by ERG and by measuring visual acuity with an optomotor drum, 3, 7, 14, 21 and 28 days post injection. Morphological characterization and RNA

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isolation were performed at the indicated time points. hiPSC-derived RPE cells were transplanted into the subretinal space 1 week after SI injection. 3 weeks post transplantation the retinae were isolated and analyzed.

Results: The effect of SI on RPE cells was very severe, leading to the complete loss of the RPE monolayer by day 7. The effect on photoreceptors was slower, with 10-33% reduction of ONL thickness by day 28. The ERG showed that 3 days post injection the retinas were less sensitive and that by day 14 both a- and b-waves became unrecordable. Interestingly, light seemed to enhance the effect of SI, since ERG waves were better preserved when animals were kept in the dark. A reverse transcription followed by PCR using primers specific for genes involved in the phototransduction cascade and pigment regeneration showed a reduced expression of several genes by day 3. In SI-treated retinae protein mislocalization and dendrite sprouting of bipolar cells was observed. Interestingly, transplantation into the SI-model revealed that RPE donor cells were able to form a polarized monolayer on the free Bruch’s membrane and to phagocyte shed outer segments.

Conclusions: Injection of SI is a reproducible protocol to cause RPE toxicity and, consequently, retinal degeneration. Additionally, it leads to altered gene expression and retinal remodeling. Our combined data suggests that the SI model is appropriate for analyzing the behavior of donor cells upon transplantation, but less suitable for functional studies.

Commercial Relationships: Madalena Carido, None; Yu Zhu, None; Boris Benkner, None; Thomas Kurth, None; Thomas A. Münch, None; Elly Tanaka, None; Marius Ader, None

Support: FCT, SFRH/BD/69144/2010

Program Number: 5816 Poster Board Number: D0076
Presentation Time: 8:30 AM - 10:15 AM
Transplantation of CD73-sorted photoreceptor precursors into the rat retina

Kai Postel, Tiago Santos-Ferreira, Marius Ader. DFG-Center for Regenerative Therapies Dresden, Technische Universität Dresden, Dresden, Germany.

Purpose: Photoreceptor transplantation for the treatment of retinal degenerations is discussed as a possible therapeutic strategy. In mice enrichment and transplantation of photoreceptor precursors (PRPs) lead to integration and formation of morphological mature photoreceptors as well as restoration of vision. However, the majority of grafting experiments were conducted in mice leaving other mammalian species in regard to photoreceptor replacement not well studied. Therefore, transplantation experiments in rats were performed.

Methods: Donor rats expressing GFP under an ubiquitous promoter and host dark agouti rats were used. Magnetic activated cell sorting (MACS) with CD73 antibody was established for rat PRPs. GFP expressing and CD73 enriched rat as well as mouse PRPs, isolated at postnatal day 4 (PN4), were transplanted into the subretinal space (SRS) of adult wild type (WT) rats and mice. Integration rate of donor cells into host retinas was analysed two weeks after transplantation.

Results: Transplantation of MACS enriched PRPs from GFP expressing mice into the retina of wt mice led to integration of cells into the outer nuclear layer (ONL) and the formation of morphological mature photoreceptors. MACS of PN4 rat cells with CD73 antibody was established leading to enrichment of PRPs with a purity of 88%. Enriched rat PRPs were transplanted into adult mice and rats and their integration efficiency was compared with MACS-sorted mouse photoreceptors also transplanted into mice and rats. In all conditions, the majority of transplanted cells survived in the hosts’ SRS two weeks after grafting expressing photoreceptor specific markers. Whereas a significant proportion of mouse donor cells integrated into the ONL of mouse hosts, in all other conditions only a low number of cells integrated into the ONL and formed mature photoreceptors.

Conclusions: The difference between mouse and rat tissue as donor as well as host strongly influences the integration of transplanted PRPs. Thus, assessment of photoreceptor integration in pre-clinical animal models as well as human tissue will be crucial for evaluating the potential of photoreceptor replacement strategies. Additionally, a detailed analysis of the molecular requirements that allow successful mouse to mouse grafting and evaluation of the factors hindering photoreceptor integration in rats might be highly important for the development of cell transplantation for retinopathies.

Commercial Relationships: Kai Postel, None; Tiago Santos-Ferreira, None; Marius Ader, None

Support: DFG SFB655 Gant 041296318

Program Number: 5817 Poster Board Number: D0077
Presentation Time: 8:30 AM - 10:15 AM
Cone-like photoreceptor transplantation into the mouse retina

Tiago Santos-Ferreira, Kai Postel, Marius Ader. AG Ader, DFG-Center for Regenerative Therapies Dresden, Technische Universität Dresden, Dresden, Germany.

Purpose: Vision impairment affects around 314 million people worldwide. In diurnal organisms, day vision depends on cone photoreceptors (PR) and several eye diseases including age-related macular degeneration, lead to cone PR degeneration. Several therapeutic approaches, such as gene and cell-therapy, are currently being developed mainly focusing on rod dystrophies, leaving cone-dystrophy therapies not well studied. Thus, we evaluated the feasibility of cone-like PR transplantation into wild type and diseased mouse retinas and the possibility of functional recovery.

Methods: Cone PR account for only 3% of the cells in the mouse retina. Hence, a more comprehensive source of cone PRs was developed. We crossed Nrl+/− mice, that contain no rods but only cone-(like) photoreceptors, with an actin GFP reporter line (aGFP). The resulting line tgf(Nrl-/-,aGFP) was used as a source for cone-like PRs. Cone-like cells were sorted using Magnetic Associated Cell Sorting (MACS) using CD73 as a cell surface marker. Enriched CD73+ cells were transplanted into the subretinal space of adult wild-type (WT) retinas. Integration efficiency was analyzed 2 weeks after transplantation. Cone-like PRs were then transplanted into age matched cone dystrophy model (Cpf11 mutant mice) and WT retinas. Integration rate and functional recovery (ERG measurements) were analyzed 4 weeks after transplantation.

Results: The generated reporter line showed rosette-like structures typical of a rodless retina and expressed cone-specific markers. tgf(Nrl-/-,aGFP) showed comparable ERG measurements to Nrl+/− mice. Cone-like PRs expressed CD73, which was used as a cell surface marker. MACS-CD73 sorted cone-like cells were able to integrate into WT hosts, having a peak of integration at post-natal day 4 (P4). Integrated cone-like cells are able to acquire a mature photoreceptor morphology. P4 MACS-CD73+ sorted cells were then transplanted into cpf11 hosts, showing similar integration rates as in WT retinas and an increased a- and b-wave amplitudes under mesopic and photopic conditions.

Conclusions: Cone-like cells can integrate in different types of host retinas having a peak of integration at PN4. Cone-like cells express cone specific markers, acquire mature photoreceptor morphology and partially rescue daylight vision. Hence, cone-like cell transplantation might represent a promising strategy for the restoration of vision in cone-dystrophies.

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ARVO 2013 Annual Meeting Abstracts by Scientific Section/Group – Retina

Commercial Relationships: Tiago Santos-Ferreira, None; Kai Postel, None; Marius Ader, None

Support: FCT: SFRH / BD / 60787 / 2009; DFG (CRTD-FZIII, SFB-041296318)

Program Number: 5818 Poster Board Number: D0078
Presentation Time: 8:30 AM - 10:15 AM
Development of an ex-vivo retinal explant model to assess transplantation efficiency of photoreceptor progenitor cells

Purpose: Transplantation of photoreceptor precursor cells (PPCs) derived from human embryonic stem cells (hESCs) is one of the most promising and widely applicable approaches to the treatment of retinal degenerations. However, the factors that promote PPC engraftment are largely unknown. Here we focused on developing a novel ex-vivo system to facilitate investigation and optimization of PPC transplantation.

Methods: Harvested neural retinas from adult rats were dissected into equal-sized quadrants and placed directly on i) a hydrophilic Millicell filter (with 0.4 micron pores) of tissue culture inserts, or ii) on monolayers of different retinal pigment epithelium (RPE) cell lines (RPE-J, ARPE19 and hESC derived RPE) growing on the same filter. These explants, with or without RPE, were cultured for up to three weeks in serum-free medium. Tissue microstructure was assessed and outer nuclear layer (ONL) thickness was measured at different time points. Immunocytochemical analysis was performed with markers for different retinal cell types, such as photoreceptors (e.g. CRX and S-Opsin), to validate explants’ viability. To mimic PPC transplantation to the subretinal space, hESC derived PPCs were inserted between the rat neural explant and underlying RPE/filter combination and their growth and integration was assessed.

Results: Explants co-cultured with RPE maintain normal gross morphology for up to three weeks and continued to express proteins characteristic of rod and cone photoreceptors. ONL thickness and cell viability measurements demonstrate negligible changes over time. We also demonstrate the feasibility of “transplanting” PPCs into this system and assessing their integration efficiency in the presence of selected factors (e.g., isolated components from the interphotoreceptor matrix).

Conclusions: A model system that includes retinal explants, co-cultured with RPE, can be used to screen and define factors that influence integration efficiency of transplanted PPCs. Identifying factors that enhance integration of PPCs into retinal explants in an ex-vivo system can then be examined in in-vivo models of retinal degeneration.

Commercial Relationships: Anat Yanai, None; Christopher R. Laver, None; AMA E. Bashar, None; Andrew Metcalfe, None; Kevin Gregory-Evans, None

520 Imaging II, RE
Thursday, May 09, 2013 8:30 AM-10:15 AM
Exhibit Hall Poster Session
Program #/Board # Range: 5819-5873/D0130-D0184
Organizing Section: Retina

Program Number: 5819 Poster Board Number: D0130
Presentation Time: 8:30 AM - 10:15 AM
The Papillomacular Fold in Posterior Microphthalmos: New Insights Based on Novel Spectral-Domain Optical Coherence Tomography Findings

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Sawsan R. Nowilaty, Ahmed Mousa, Nicola G. Ghazl

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Purpose: To characterize spectral-domain optical coherence tomography (SD-OCT), the internal structure of the papillomacular fold in posterior microphthalmos (PM) and analyze the posterior pole curvature in PM and its relationship to the axial length (AL) and the papillomacular fold features and pathogenesis.

Methods: Forty PM eyes (20 patients) and 70 control eyes (35 subjects) underwent AL biometry (IOLMaster) and macular SD-OCT (Spectralis). SD-OCT features analyzed included the papillomacular neurosensory retinal fold’s internal structure, height and protrusion, and a novel parameter termed the “posterior pole curvature index (PPCI)” measured along the vertical and horizontal meridians. The relationship of the PPCI to the papillomacular fold height and AL, as well as to the PPCI of controls was analyzed.

Results: All papillomacular folds, regardless of their height, were horizontal and invariably partial thickness sparing the photoreceptor layer, inner segment/outer segment junction, external limiting membrane, and outer nuclear layer. The retinal stratification was preserved within the fold. There was no foveal depression. Papillomacular folds harbored clinically-invisible inner nuclear layer cysts in 50%, additional clinically-visible ganglion cell layer cysts in 35% and surface corrugations with prominent vitreous in 65% of cases. PM eyes had notably larger vertical and horizontal PPCIs than controls (vPPCI mean 173 vs. 13µ; hPPCI 118 vs. 15µ, p < 0.0001 for both). Moreover, in all PM eyes, but not in controls, the vertical PPCI was notably larger than the horizontal PPCI (mean difference of 55µ, p <0.0001) and correlated strongly with inverse AL (R= -0.71, p <0.0001) and papillomacular fold height and protrusion (R= 0.68, p <0.0001). Papillomacular fold height and protrusion also correlated strongly with inverse AL (R = -0.62, p < 0.0001).

Conclusions: The papillomacular fold in posterior microphthalmos is consistently partial thickness, horizontally oriented with predictable internal and surface anatomical features. The posterior pole curvature in PM is invariably steep, particularly along the vertical meridian, and correlates strongly with inverse AL and the papillomacular fold height and protrusion. These findings may offer novel clues for the pathogenesis and consistent horizontal orientation of the papillomacular fold.

Commercial Relationships: Sawsan R. Nowilaty, None; Ahmed Mousa, None; Nicola G. Ghazi, None

Program Number: 5820 Poster Board Number: D0131
Presentation Time: 8:30 AM - 10:15 AM
The Use of PolyChromatic Angiography for the Assessment of the Effects of VEGF and Bevacizumab on the Rabbit Retina
Samir R. Tari, C. Michael Samson, Uday B. Komppella, Robert L. Harris, Cheng-mao Lin, David A. Antonetti, Gaetano R. Barile

1PCAsso Diagnostics, North Brunswick, NJ; 2New York Eye and Ear Infirmary, New York, NY; 3Rutgers University, New Brunswick, NJ; 4University of Colorado Denver, Denver, CO; 5University of Michigan, Ann Arbor, MI; 6Manhattan Eye Ear and Throat Hospital, New York, NY.

Purpose: To determine the utility of PolyChromatic Angiography (PCA) in the assessment of the response to different doses VEGF and bevacizumab.

Methods: Twenty six eyes of twenty four Dutch Belted rabbits were injected intravitreally with 1.25 µg (group A, n=5), 4 µg (Group B, n=6) and 10 µg (Group C, n=7), 4 µg (Group D, n=4) and 4 µg (Group E, n=4) VEGF on day 0. Groups D and E were also injected intravitreally with 1.25 µg and 12.5 µg bevacizumab, respectively, on
day 2. On days 0, 2, 4, 7, 11 and 14 PCA was performed using a contrast agent mixture composed of fluorescein sodium, Indocyanine green, PCM102 and PCM 107 and imaged by a modified TRC 50 VT fundus camera. PCA scores were given based on leaking fluorophores. **Results:** On day 7, there was a statistically significant difference between group A (0.6 ±0.89, PCA Score± st. dv.) and both groups B (2.67±1.37, p value = 0.0154) and C (3.33±0.52, p value = 0.00085). There was also a statistically significant difference between groups B and E (PCA score 0.75 ± 0.96, p value = 0.032) on day 7. On day 11, there was statistically significant difference between group C (1.80±1.1) and both groups A (0, p value=0.021) and B (0.33±0.52, p value= 0.037).

**Conclusions:** PCA is a useful tool for the assessment and grading of BRB dysfunction in the rabbit retina. PCA may become a useful diagnostic tool for grading disease severity in patients with similar pathologies.

**Figures:**

1. **PCA scores before, 2, 4 7 11 and 14 days after intravitreal VEGF± bevacizumab injection in rabbits.** Mean ± Standard deviation. * p≤0.05, **p≤0.001.

2. **PCA scores before, 2, 4 7 11 and 14 days after intravitreal VEGF± injection in rabbits.** Mean ± Standard deviation. * p=0.05, **p=0.001.

**Commercial Relationships:** Samir R. Tari, PCAsso Diagnostics LLC (I), PCAsso Diagnostics LLC (E), PCAsso Diagnostics LLC (P); C. Michael Samson, CLS Pharmaceuticals (I), PCAsso (I); Uday B. Kompella, University of Colorado Denver (P), PCAsso Diagnostics (C), NanoTrans Technologies, Inc. (F), University of Nebraska Medical Center (P); Robert L. Harris, PCAsso Diagnostics (F); Cheng-mao Lin, None; David A. Antonetti, None; Gaetano R. Barile, PCAsso Diagnostics LLC (P), PCAsso Diagnostics LLC (I)

**Support:** JDRF Grant 17-2011-518

**Program Number:** 5821 **Poster Board Number:** D0132

**Presentation Time:** 8:30 AM - 10:15 AM

**In-vivo Imaging and Measurement of the Bursa Premacularis using 1,050nm Swept-Source Deep Range Imaging Optical Coherence Tomography (DRI-OCT1 Atlantis®)**

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Silvestro Caputo1, Anna Sala-Puigdollers1, Hojr Jaberansari2, Jane Gray1, Yvonne D’Souza1, Stephen J. Charles3, Susmito Biswas4, David B. Henson1, David McLeod1, Paulo E. Stanga1, 2, 3

1Vitreoreal Unit, Manchester Royal Eye Hospital, Manchester, United Kingdom; 2School of Medicine, University of Manchester, Manchester, United Kingdom; 3Manchester Academic Health Science Centre and Centre for Ophthalmology and Vision Research, Institute of Human Development, University of Manchester, Manchester, United Kingdom.

**Purpose:** To image in-vivo the posterior cortical vitreous, the Bursa Premacularis (BPM) and Space of Martegiani and to measure the BPM using a new 1,050nm Swept-Source optical coherence tomography (OCT) scanner (Topcon® Deep Range Imaging, DRI-OCT1 Atlantis®).

To determine the relationship between the prevalence and dimensions of the BPM and patient age.

**Methods:** Pilot and retrospective study. One hundred and seventeen consecutive patients (234 eyes, including normal eyes and eyes with various retinal pathologies) underwent DRI-OCT1 Atlantis® scans. Patient age ranged from 5-90 years (mean: 52.4 years). Single-Line 12 mm long horizontal scans passing through the fovea and optic disc were assessed. The BPM was measured manually using the system’s software caliper function. The horizontal (width) and the anteroposterior (depth) dimensions of the BPM, as well as the distance between the anterior wall of the BPM and the deepest foveal point, were recorded. Presence of the SM was also recorded.

**Results:** The BPM and the SM were detected in the posterior cortical vitreous of 54 patients (84 of 234 eyes, 35.9%). All eyes (100%) with a BPM also showed a SM; no eyes (0%) with SM showed absence of BPM. Twenty-four of the 54 patients (44%) showed a unilateral BPM and thirty (56%) showed a bilateral BPM. Bilateral BPM tended to be symmetrical in width but less so in depth (Correlation coefficient: width 0.66 p<0.005; depth 0.45 p=0.013). The BPM was detected more frequently over the age of 20 and up to the age of 76 years. The mean age of patients showing a BPM was 43 years (range: 5 - 76 years). The mean width of the BPM was 7,714 microns (range: 11,312 - 4,339 microns, SD: 1,431) and the mean depth was 501 microns (range: 1,340- 73 microns, SD: 272). Variation in width and depth of the BPM did not correlate with age (Correlation coefficient: width 0.09, p=0.44; depth 0.076, p=0.49).

**Conclusions:** The utilisation of Swept-Source OCT with 1,050nm wavelength, 100,000 A-line scans/sec and 12mm long scans allows for improved in-vivo anatomical characterisation of the BPM and, for the first time, demonstration of a positive correlation between the presence of BPM and SM.

This could be the cohort of patients with the widest range of patient age in whom the cortical vitreous has been assessed in-vivo.

**Figures:**

1. **Bursa Premacularis measurement and Space of Martegiani.

2. **Commercial Relationships:** Silvestro Caputo, None; Anna Sala-Puigdollers, None; Hojr Jaberansari, None; Jane Gray, None; Yvonne D’Souza, None; Stephen J. Charles, None; Susmito Biswas, None; David B. Henson, None; David McLeod, None; Paulo E. Stanga, OPTOS PLC (F), OPTOS PLC (C), OPTOS PLC (P).

**Support:** JDRF Grant 17-2011-518

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Choroidal Thickness in Pseudoxanthoma Elasticum Measured by Enhanced Depth Imaging Optical Coherence Tomography

Martin Gliem, Christian K. Brinkmann, Frank G. Holz, Peter Charbel Issa. Department of Ophthalmology, University of Bonn, Bonn, Germany.

**Purpose:** Pseudoxanthoma elasticum (PXE) is a rare multisystem disorder associated with characteristic fundus alterations including angiod streaks, peau d’orange, peripheral chorioretinal atrophy and secondary choroidal neovascularisations (CNV) in the macular region. So far little is known on alterations of the choroid in this disease. The purpose of this study was to determine and quantify changes of the choroid in patients with PXE.

**Methods:** We investigated 70 eyes from 35 patients in whom the diagnosis of PXE was based on ophthalmologic examination, skin biopsy and/or genetic testing. 22 eyes of 11 probands without any eye disease served as a control group. Eyes with PXE were subdivided into 4 groups: Eyes with angioid streaks only (group 1), eyes with secondary CNV (group 2), eyes with subretinal fluid without CNV (group 3) and eyes with progressive chorioretinal atrophy without CNV (group 4). Choroidal thickness was measured using enhanced depth imaging (EDI) optical coherence tomography (OCT) (Spectralis, Heidelberg Engineering).

**Results:** All 5 groups showed no significant differences with regard to age and refractive error. Compared to the control group (315.2µm ± 12.3; mean ± SEM), mean subfoveal choroidal thickness in eyes with PXE was significantly reduced within all groups (group 1: 224.4µm ± 23.4, p<0.001; group 2: 177.7µm ± 17.3, p<0.001; group 3: 211.3µm ± 19.2, p<0.001; group 4: 113.8µm ± 12.6, p<0.001). The difference between control eyes and eyes of PXE patients was most pronounced within the nasal half of horizontal scans. To the temporal half all groups showed an approximation to the level of the control eyes, which is in line with the characteristic centrifugal disease spread at the macular fundus. Within the PXE groups eyes with angioid streaks only (group 1) showed the least reduction of choroidal thickness, while it was most pronounced within group 4.

**Conclusions:** Choroidal thickness in eyes affected by PXE was significantly thinner compared to control eyes. Complications such as CNV, subretinal fluid or progressive chorioretinal atrophy were associated with an increased thinning of the choroid indicating a potential important pathogenetic and prognostic role for patients suffering from PXE. Choroidal thickness measurement might serve as an easily noninvasively obtainable parameter to monitor disease progression as well as the effect of potential future therapies.

**Commercial Relationships:** Martin Gliem, Heidelberg Engineering, Germany (F), Carl Zeiss Meditec, Germany (F), Optos, UK (F); Christian K. Brinkmann, Heidelberg Engineering, Germany (F), Carl Zeiss Meditec, Germany (F), Optos, UK (F); Frank G. Holz, Accucl (C), Allergan (C), Genentech (F), Heidelberg Engineering (F), Zeiss (F), Novartis (F), Novartis (C), Optos (F), Merz (C), Bayer (F), Bayer (C), Boehringer Ingelheim (C); Peter Charbel Issa, Heidelberg Engineering (F)

Program Number: 5823 Poster Board Number: D0134
Presentation Time: 8:30 AM - 10:15 AM
Pigment Migration Distribution in Eyes with Non-neovascular Age-Related Macular Degeneration

Yanling Ouyang1,2, Florian M. Heussen1,2, Alexander C. Walsh1, Antonia M. Joussen1, Srinivas R. Sadda1. Ophthalmology, Charité-Universitätsmedizin Berlin, Berlin, Germany; 1Ophthalmology, Doheny Eye Institute, Los Angeles, CA.

**Purpose:** Intraretinal hyperreflective foci evident on OCT in eyes with non-neovascular age-related macular degeneration (NNVAMD) are know to represent pigment migration (PM). The purpose of this study is to utilize three-dimensional OCT to assess the prevalence of PM and its distributional characteristics in eyes with early NNVAMD.

**Methods:** Patients with the clinical diagnosis of NNVAMD who underwent digital Color Fundus (Topcon 50IX, Topcon Co) and OCT (512x128 volumes) imaging (3D-OCT-2000, Topcon Corp, Tokyo, Japan) in both eyes, on the same day, between September 2006 and July 2009 at a retina subspecialty clinic were retrospectively reviewed. Eyes with evidence of atrophy, choroidal neovascularization (CNV), other retinal diseases or history of retinal surgery, and/or ungradable images (OCT or color) were excluded. Foci of PM were assessed by OCT as definitely present, questionably present, absent for each individual B-scan. If definite PM was observed, the number of individual PM foci on the B-scan, as well as the retinal layers involved by the migration, were also documented. Findings were tabulated across all B-scans for each eye, and the presence and frequency of PM in each retinal layer were computed for each ETDRS grid subfield.

**Results:** A total of 153 visits of 153 eyes from 111 patients met the inclusion criteria. The mean age of patients was 78.4 (range, 53-97) years. 43.8% eyes (67/153) with definite PM, and an additional 0.7% eyes (1/153) with questionable PM were observed by OCT and confirmed by color photos. For eyes with definite migration, 50.7% (34/67) of eyes with showed pigment migration in the photoreceptor cell layer (PR), 76.1% in the outer nuclear layer (ONL), 67.2% in the outer plexiform layer (OPL) and 40.3% in the inner nuclear layer (INL). When looking at the frequency (number of B-scans involved) we observed: 113 for PR, 522 for ONL, 353 for OPL, and 140 for the INL. When analyzing the topographical distribution of pigment in accordance with the ETDRS grid, PM was most frequent in superior inner macula (SIM). However, the density of PM was greatest in the central subfield (2.58 foci/eye*mm²).

**Conclusions:** Three-dimensional OCT scanning can permit the study of the distribution of pigment migration in eyes with NNVAMD. These findings may provide new insights into the pathogenesis and progression of this disease.

**Commercial Relationships:** Yanling Ouyang, Bayer healthcare Pharmaceuticals Inc (R); Florian M. Heussen, Novartis (C); Alexander C. Walsh, Envision Diagnostics, Inc (I), Envision Diagnostics, Inc (E), Doheny Eye Institute (P); Antonia M. Joussen, None; Srinivas R. Sadda, Regeneron (C), Genentech (C), Allergan (C), Carl Zeiss Meditec (C), Optos (C), Carl Zeiss Meditec (F), Optovue (F), Optos (F)

Program Number: 5824 Poster Board Number: D0135
Presentation Time: 8:30 AM - 10:15 AM
Acute zonal occult outer retinopathy: A new classification based on multimodal imaging

Samira Khan, Lee M. Jampol. Ophthalmology, Northwestern University, Chicago, IL.

**Purpose:** To classify acute zonal occult outer retinopathy (AZOOR) based on clinical course, funduscopy exam, autofluorescence (FAF) and spectral domain optical coherence tomography (SD-OCT) characteristics.

**Methods:** Thirty two eyes of 22 patients with AZOOR were identified based on clinical course and funduscopy examination. 12
eyes had FAF and SD-OCT studies done.

**Results:** Based on multimodal imaging, AZOOR can be classified as three types. Type 1 or primary AZOOR typically shows a peripapillary hypoautofluorescence with a ring of hyperautofluorescence surrounding the lesion. SD-OCT demonstrates loss of outer layers of the retina and typically spares the fovea. These features may stabilize over many years. Type 2 or secondary AZOOR clinically presents as a multifocal choroiditis with localized or diffuse photoreceptor loss demonstrated on SD-OCT. Type 3 AZOOR initially shows a normal funduscopic exam with normal fovea with depressed photopic response on electroretinogram. This can progress to show pigmentary changes in the fovea and corresponding outer retinal abnormalities on SD-OCT.

**Conclusions:** AZOOR can be classified as 3 types. FAF and SD-OCT may show altered fluorescence of the retinal pigment epithelium and a specific pattern of loss of photoreceptors in Type 1 AZOOR. Type 2 AZOOR is characterized by clinical evidence of multifocal choroiditis with secondary diffuse loss of photoreceptors. Type 3 AZOOR demonstrates clinical features of AZOOR with normal funduscopic examination and FAF. With progression, alteration of outer retinal layers may be noted on SD-OCT.

**Commercial Relationships:** Samira Khan, None; Lee M. Jampol, Pfizer (C), Baxter International (C), Stem Cell Organization/Quintiles (C)

**Program Number:** 5825 Poster Board Number: D0136
**Presentation Time:** 8:30 AM - 10:15 AM

**Retinal Morphology Changes After Epiretinal Membrane Peeling**

**Purpose:** To determine whether the morphologic appearance of the foveal contour and the continuity of the IS/OS junction as assessed with optical coherence tomography (OCT) of patients presenting with epiretinal membrane (ERM) correlate with changes in best corrected visual acuity (BCVA), central retinal thickness (CRT), central subfield thickness (CST) and volume (CSV) following pars plana vitrectomy (PPV) for ERM removal with internal limiting membrane (ILM) peel.

**Methods:** Images from consecutive forty-seven subjects were analyzed retrospectively. Foveal contour grades were determined by 2 independent graders using radial line scans at 30° intervals. Grades were classified as 0 (fovea thinner than surrounding macula), 1 (flat), and 2 (fovea thicker than surrounding macula). In cases of observer disagreement, OCT-derived thickness values of the retina at the fovea and 1 mm radially from the fovea were used to generate quantitative thickness profiles and applied as tiebreakers. The continuity of the IS/OS junction was assessed on 6 radial line scans. CST and CSV data were collected from OCT-generated map.

**Results:** 40 of the 47 subjects had both preoperative and 3 month follow-up OCT. 29 of these 40 were Grade 2 preoperatively, 11 were Grade 1, and none were Grade 0. 14 of the 29 Grade 2 subjects resolved to Grade 0/1, while 3 of the preoperative Grade 0/1 subjects were Grade 2 at 3 months (McNemar test, P=0.013). Preoperative CRT, CST, and CSV values were negatively correlated with the changes in CRT (P<0.001), CST (P<0.001), and CSV (P<0.001), respectively, at 90 days. Foveal contour grade was not significantly correlated to the change in these outcome values (P>0.05).

BCVA was not found to improve significantly in preoperative Grade 0/1 patients (-0.11 LogMar units, P=0.122), nor in preoperative Grade 2 patients (-0.04, P=0.380), at 3 months. No significant difference in BCVA changes between groups was found (P=0.42).

However, linear mixed model analysis with random subject effect demonstrated a statistically significant improvement in BCVA (regression coefficient = 0.01 LogMar units, P=0.048) when controlling for the confounding effects of lens status (0.18, P=0.001) and baseline IS/OS junction disruption (0.15, P=0.012).

**Conclusions:** Preoperative IS/OS junction disruption and postoperative cataract progression, but not preoperative foveal contour grade, significantly affect BCVA following PPV for ERM removal with ILM peel.

**Commercial Relationships:** Judy E. Kim, None; Nathan R. Mathews, None; Sergey Tarima, None

**Support:** Unrestricted Grant from Research to Prevent Blindness; Grant U1LRR031973 from the Clinical and Translational Science Award (CTSI) program of the National Center for Research Resources, National Institutes of Health

**Program Number:** 5826 Poster Board Number: D0137
**Presentation Time:** 8:30 AM - 10:15 AM

**Comparison of a widefield Polarization-sensitive OCT with standard imaging of Geographic atrophy**

**Purpose:** To image geographic atrophy (GA) with Polarization-sensitive OCT (PS-OCT) and evaluate the data in comparison to standard-imaging methods.

**Methods:** 51 eyes of 29 patients with unilateral or bilateral GA were imaged with a new widefield PS-OCT system and compared to standard imaging methods like fundus autofluorescence (FAF), red-free imaging (RF) or infrared imaging (IR).

The device used in this study is capable of recording 3D datasets of the human retina at a scanning speed of 70,000 A scans/s. Different scanning angles were used ranging from 20x20° up to 40x40°.

**Results:** Using the widefield PS-OCT, it was possible to reliably demarcate regions of GA. In 33 out of 51 eyes a thickening of the depolarizing area at the retinal pigment epithelium (RPE) was noticed at the GA margins, which corresponded well to regions of hyperautofluorescence in FAF in 26 out of these 33 eyes. An advantage of PS-OCT over AF was that there was no shadowing effect at the fovea, which is caused by the accumulation of pigment in the central macula. Another advantage of PS-OCT over AF-images was the three-dimensional information, making it possible to rule out artefactual lesions of the retina or the RPE. In the depolarizing material thickness maps not only were the atrophic areas clearly demarcated as hypointense zones (comparable to AF), but also could be observed as hyperintense specks, the signal intensity of which being in contrast to normal RPE (comparable to RF).

The absence of RPE in the GA allows a deeper penetration of the imaging beam into the choroid. Therefore choroidal structures can be visualized within the GA comparable to IR-imaging.

Additionally, three dimensional intensity-OCT scans provided information of the retinal morphology.

**Conclusions:** In eyes with GA, PS-OCT provided comprehensive information of all layers of the ocular fundus (retina, RPE, choroid) in great detail and all locations. Thus, a single three-dimensional PS-OCT dataset provides superior multimodal information as combined AF, IR, RF and standard spectral domain-OCT performed separately.

**Commercial Relationships:** Philipp K. Roberts, Canon Inc. (F); Stefan Zetter, Canon Inc. (F); Bernhard Baumann, Canon Inc. (F);
Matthias Bolz, None; Christopher G. Kiss, None; Ramzi G. Sayegh, None; Magdalena Baratsits, None; Michael Pircher, Canon Inc. (F), Canon Inc. (C); Christoph K. Hitzenberger, Canon Inc. (F), Canon Inc. (C); Ursula Schmidt-Erfurth, Alcon (C), Bayer Healthcare (C), Novartis (C)

Program Number: 5827 Poster Board Number: D0138
Presentation Time: 8:30 AM - 10:15 AM

Detection of Fundus Abnormalities in Diabetic Retinopathy using Spectral Domain OCT versus Mydriatic Color Fundus Imaging

Qing Shao1, Yanling Ouyang2,3, Florian M. Heussem4,5, Alexander C. Walsh6, Antonia M. Joussen2, Srinivasa R. Sadda2,6, Ophthalmology, Charité-Universitätsmedizin, Berlin, Germany; 2Ophthalmology, Doheny Eye Institute - USC, Los Angeles, CA.

Purpose: To determine the sensitivity for detection of retinal abnormalities using volume Spectral Domain OCT versus single field fundus imaging in eyes of patients with diabetes.

Methods: Images from consecutive patients in a retina clinic undergoing simultaneous volume spectral domain OCT scanning (512x128) and single field, fovea-centered mydriatic 45 degree color fundus imaging with a 3D-OCT-1000 (Topcon Corp, Tokyo, Japan) over a 29 month period were retrospectively collected. Findings for each modality (Table 1) were graded independently by two graders as being present, questionable or absent. Findings from both modalities were combined to form the gold standard for comparison for each modality.

Results: A total of 312 volume OCT scans and fundus images from 312 eyes of 167 patients were included in this study. 234 eyes were clinically diagnosed with diabetic retinopathy (DR) with varying severities. In this cohort (Table 1), OCT was more sensitive than color photos for most features, in particular the detection of cystoid macular edema and vitreous hemorrhage. Vascular abnormalities such as venous beading were not detectable by OCT.

Conclusions: In this study, OCT was more sensitive than a color fundus photograph for detection of many abnormalities in eyes of patients with diabetes. The prospect of OCT as a potential adjunctive tool in screening applications warrants further study.

Table 1:

<table>
<thead>
<tr>
<th>Feature</th>
<th>Sensitivity</th>
<th>OCT Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous hemorrhage</td>
<td>5.77%</td>
<td>98.3%</td>
</tr>
<tr>
<td>Epiretinal neovascularization</td>
<td>50.49%</td>
<td>95.6%</td>
</tr>
<tr>
<td>Epiretinal membrane</td>
<td>46.49%</td>
<td>95.6%</td>
</tr>
<tr>
<td>Epiretinal edema</td>
<td>17.39%</td>
<td>95.6%</td>
</tr>
<tr>
<td>Intraretinal microvascular</td>
<td>2.2%</td>
<td>95.6%</td>
</tr>
<tr>
<td>abnormalities/venous</td>
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<td></td>
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<tr>
<td>beading/vascular tortuosity/Fundus</td>
<td>92.3%</td>
<td></td>
</tr>
</tbody>
</table>

Commercial Relationships: Qing Shao, None; Yanling Ouyang, Bayer healthcare Pharmaceuticals Inc (R); Florian M. Heussem, Novartis (C); Alexander C. Walsh, Envision Diagnostics, Inc (I); Florian M. Heussem, Envision Diagnostics, Inc (E); Antonia M. Joussen, None; Srinivasa R. Sadda, Regeneron (C), Genentech (C), Allergan (C), Carl Zeiss Meditec (C), Optos (C), Carl Zeiss Meditec (F), Optovue (F), Optos (F)

Program Number: 5828 Poster Board Number: D0139
Presentation Time: 8:30 AM - 10:15 AM

Efficacy of NIR and SW-FAR in resolved central serous chorioretinopathy: Detecting outer retinal layer abnormality

Seong-Woo Kim1, Jaeryung Oh2, Sang-Kyoon Kim1, Jong-Hyun Oh3, Cheolmin Yun1, Kuhl Huh2,3, None; 1Ophthalmology, Korea University, College of Medicine, Seoul, Republic of Korea; 2Ophthalmology, Dongguk University, Ilsan Hospital, Goyang, Republic of Korea.

Purpose: To evaluate the correlation of short wave length fundus autofluorescence (SW-FAF) and near-infrared FAF (NIR-FAF) changes with spectral domain-optical coherence tomography (SD-OCT), and FA changes in resolved central serous chorioretinopathy (CSC).

Methods: Design is retrospective, observational case study. Patients with a history of resolved CSC and abnormal FAFs imaging were assessed by means of SD-OCT and FA. The outer retinal layer alteration in the OCT image and abnormality in FA were analyzed and correlated with corresponding FAF.

Results: Ninety-one eyes from 86 patients were analyzed. All of abnormal NIR-FAF showed hyper-fluorescent FA window defect in corresponding area. There was a significant association between OCT findings and the SW-FAF findings. Presence of the abnormal SW-FAF was significantly associated with the loss of the photoreceptor inner and outer segment junction (IS/OS) on SD-OCT. (chi-square test; P < 0.0001) NIR-FAF could not predict the status of IS/OS without the SW-FAF image.

Conclusions: Outer retinal layer change in OCT image could be expected by combining both SW-FAF and NIR FAF images together. When abnormal changes were manifested in SW-FAF image, IS/OS damage could be predicted.

Commercial Relationships: Seong-Woo Kim, None; Jaeryung Oh, None; Sang-Kyoon Kim, None; Jong-Hyun Oh, None; Cheolmin Yun, None; Kuhl Huh, None

Support: the Korean Health Technology R&D Project, Ministry for Health, Welfare & Family Affairs, Republic of Korea (A102024)

Program Number: 5829 Poster Board Number: D0140
Presentation Time: 8:30 AM - 10:15 AM

A Comparison of Heidelberg and Zeiss OCT Imaging in Common Laboratory Animals: Retinal Cell Layer Definition and Correlation to Histopathology

Margaret E. Collins4, William S. Culp4, Kelly Tenneson5, Sylvie Wise1,2, Mark Vezina1,2, 4Toxicology, Charles River, Reno, NV; 5Ocular and Neuroscience, Charles River, Montreal, QC, Canada; 6Technical Operations, Charles River, Reno, NV

Purpose: The use of OCT is gaining popularity as a non-invasive tool for retinal evaluation in preclinical studies, both for ocular therapeutics as well as non-ocular indications where adverse ocular side effects may be a concern. This poster presents OCT images of normal eyes from the Heidelberg Spectralis and Zeiss Cirrus systems in 4 laboratory animal species, with an evaluation of quality of retinal cell layer definition and histopathology correlates.

Methods: Retina images were collected for non-human primate, dog, rat and rabbit on each system. Animals were sedated for all imaging sessions; a mydriatic was used to dilate the pupil. For the Cirrus system, macular cube was used as the scan type. For the Spectralis system, volume scans or individual scans were used. Images were compared for clarity of retinal layers and correlation with H&E stained histopathology sections.

Results: Both systems provided high resolution retinal cross sections in all 4 species with the ability to measure overall retinal thickness or the thickness of individual retinal layers. The anatomical orientation of the retinal layers correlated well with histopathology and published literature on human eyes. The significant size difference between human eyes and the animal eyes images did not impede obtaining high quality, interpretable images in eyes as small as rats with these clinical instruments.

Conclusions: Each platform provides the ability to image and analyze retinal layers in NHP, dogs, rabbits and rats that is...
Long-term progression, cystoid macular edema and secondary epiretinal membranes in severe chloroquine retinopathy

Simone Kellner1,2, Silke Weinitz3, Gazaleh Farmand1, Ulrich Kelner2,3. Rare Retinal Disease Center, Augenzentrum Sieburg, MVZ ADTC Siegburg GmbH, Siegburg, Germany; RetinaScience, Bonn, Germany.

Purpose: To investigate the long-term course of chloroquine retinopathy after drug cessation in eyes with marked photoreceptor/retinal pigment epithelial (RPE) damage.

Methods: Nine female patients (age range at first examination: 46-78 years) were examined between 1.5 - 6 years after cessation of chloroquine use due to severe retinopathy. In addition to clinical examination they underwent high resolution OCT (SD-OCT; Spectralis OCT, Heidelberg Engineering, Germany), wide-angle fundus and near-infrared autofluorescence (FAF, NIA; HRA2, Heidelberg Engineering, Germany) and wide-angle peripheral fundus autofluorescence (Optos 200Tx; Optos PLC, UK). Follow-up examinations were available in 6/9 patients.

Results: All 9 patients complained about progressive loss of visual function after cessation of the drug (treatment duration: 6-20 years). Progression of retinal degeneration could be documented either by increased changes in FAF, NIA or SD-OCT. FAF and NIA changes included an increase of affected area or a regional increase or decrease of FAF or NIA intensity. SD-OCT changes included reduction of retinal thickness, an increased area of photoreceptor or retinal pigment epithelial loss, development or increase of cystoid macular edema or development of secondary epiretinal membranes. Wide-angle imaging indicated retinal degeneration extended beyond the vascular arcades. Topical or systemic therapy of cystoid macular edema with dorzolamide/acetazolamide was of limited benefit.

Conclusions: Progression of chloroquine retinopathy has to be expected over a long period of time after cessation of drug treatment, and patients need to be counseled accordingly. The course of disease progression may be complicated by cystoid macular edema and epiretinal membrane formation. The present findings underline the necessity for early detection of chloroquine retinopathy.

Commercial Relationships: Simone Kellner. None; Silke Weinitz. None; Gazaleh Farmand. None; Ulrich Kelner. None

Program Number: 5832 Poster Board Number: D0143
Presentation Time: 8:30 AM - 10:15 AM

Reading Center Evaluation of Retinal Vein Occlusion Using Wide-field Angiography

Eric Brinton1, Amitha Domalapally2, Barbara A. Blodi1,2.

1Ophthalmology, University of Wisconsin, Madison, WI; 2Ophthalmology, Fundus Photograph Reading Center, Madison, WI.

Purpose: To develop a grading protocol to evaluate wide-field fluorescein angiography using the Optos grid in patients with retinal vein occlusions. The Optos widefield retinal imaging device is able to simultaneously image the far retinal periphery and the posterior pole. In addition, the expanded field detects peripheral retinal pathology that would otherwise not be seen on standard fluorescein angiography. This peripheral pathology may be significant in understanding the natural history and response to treatment of macular edema due to retinal vein occlusions. Studies to explore this link would require a standardized protocol to quantify areas of retinal pathology.

Methods: Using an Optos imaging device (OPTOS 200Tx SLO camera), fluorescein angiograms of branch and central retinal vein occlusions were taken on 8 patients (12 eyes) from one institution. The angiograms were analyzed using the wide-field grid used in color fundus photography and autofluorescence imaging in the Reykjavik Eye Study on macular degeneration. The wide-field grid was comparable in quality to the human imaging. Applications for preclinical drug development include the ability to detect retinal thinning or detachment without having to euthanize the animal and to potentially detect retinal lesions before they are apparent clinically. Changes in the vitreous (e.g. deposits, vitreous detachment) can also be imaged.

Commercial Relationships: Margaret E. Collins, Chalres River Laboratories (E); William S. Culp, Charles River Labs (E); Kelly Tenneson, Charles River (E); Eleven Biotherapeutics (E); Sylvie Wise, Charles River (E); Mark Vezina, Charles River Laboratories (E)

Program Number: 5830 Poster Board Number: D0141
Presentation Time: 8:30 AM - 10:15 AM

Retinal Arteriolar Dilation to Flicker Light is Reduced with Repeated Stimulation

Jonathan E. Noonan1, Ryan Man1, Thanh T. Nguyen1, Jie Jin Wang2 2, Ecosse L. Lamoureux1,3. 1Centre for Eye Research Australia, East Melbourne, VIC, Australia; 2Centre for Vision Research, Sydney, NSW, Australia; 3Singapore Eye Research Institute, Singapore, Singapore.

Purpose: Flicker light-induced retinal vasodilation, a marker of dynamic retinal function that is impaired in patients with diabetes or diabetic retinopathy, is reproducible when repeated at one hour but the effect of short-term repeated stimulation is unknown. We investigated the impact of restimulation after five and thirty minutes on the reproducibility of retinal arteriolar and venular dilations.

Methods: The flicker light response was measured in non-smokers without any chronic medical conditions using the Dynamic Vessel Analyzer (DVA, IMEDOS, Germany). A temporal arteriole and venule segment was selected while the fundus was examined under red-free light. Baseline diameters were recorded for 50 seconds, followed by 20 seconds of flickering light and an 80 second recovery period. The 100-second flicker cycle was repeated twice per test. The flicker light response test was repeated after 5 and 30 minutes rest. Maximum vessel dilation was calculated as the average maximum percentage increase in vessel diameter during flicker stimulation compared to that before stimulation. Within-subject differences were assessed using repeated measure analysis of variance.

Results: 19 participants were recruited (74% female; mean ± SD age 33 ± 5.9 years). Mean ± SD maximum arteriolar dilations during stimulation were at baseline: 3.27 ± 2.10%; after five minutes: 2.68 ± 1.89%; and after a further thirty minutes: 3.28 ± 2.09%. Maximum arteriolar dilation was significantly reduced when repeated after five minutes (p = 0.048) but not after thirty minutes (p = 0.958) compared to the baseline test. Corresponding mean ± SD maximum venule dilations were 4.56 ± 1.48%, 4.16 ± 1.61% and 4.61 ± 1.66%, respectively, without statistically significant differences (p > 0.05 for all). Arteriole and venule diameters before flicker stimulation were not significantly different between baseline and repeated tests.

Conclusions: Repeated flicker light stimulation within five minutes, but not thirty minutes, appears to reduce retinal arteriolar vasodilations in healthy humans. This temporal effect, probably due to a bleaching of photoreceptors or exhaustion of dilatory molecules, suggests that sufficient recovery time is needed to ensure reliable measurements in repeated measure designs.

Commercial Relationships: Jonathan E. Noonan. None; Ryan Man. None; Thanh T. Nguyen. None; Jie Jin Wang. None; Ecosse L. Lamoureux. None

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The functional and prognostic significance of these abnormalities is identified in a large percentage of patients with retinal dystrophies.

Conclusions:

Patients with vision worse than 20/60 had an average central subfield FAF abnormalities with focal areas of hyperfluorescence and hypofluorescence. Although the peripheral zones can be difficult to grade, our wide-field grading protocol uses a simple method of assessing leakage and non-perfusion by percent involvement of a subfield. This protocol allows for correlation of leakage and non-perfusion of the mid-peripheral and central retina. Change over time in percentage involvement of a subfield can also be assessed. These measurements may be of benefit in future trials of macular edema due to retinal vein occlusion.

Commercial Relationships: Eric Brinton, None; Amitha Domalpally, None; Barbara A. Blodi, None

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Presentation Time: 8:30 AM - 10:15 AM

Characterization of Ultra-widefield Fundus Autofluorescence Patterns in Retinal Dystrophies

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Purpose: Retinal dystrophies are commonly characterized by abnormalities in lipofuscin metabolism and accumulation. Although many are considered macular diseases, they are in fact panretinal diseases and may have FAF abnormalities throughout the retinal periphery. Ultra-widefield fundus autofluorescence (FAF) is an emerging technology that allows for the characterization of the peripheral retinal features of vitreoretinal diseases. In this study, we describe the FAF patterns of several retinal dystrophies and their genotypic/phenotypic associations.

Methods: An IRB-approved retrospective consecutive case series was performed of retinal dystrophy patients who underwent ultra-widefield FAF imaging. Patients were imaged with the Optos 200Tx system. Spectral domain OCT was used to measure macular thickness. Visual acuity was measured using a standard Snellen chart. Clinical variables, genotypes, and phenotypic characteristics were reviewed.

Results: Thirty-two patients were identified. The diseases included in this study were Retinitis Pigmentosa (n = 11), Stargardt disease (n = 7), Leber Congenital Amaurosis (n = 4), Rod-Cone Dystrophy (n = 3), Congenital Stationary Night Blindness (n = 2), Pattern Dystrophy (n = 2), North Carolina Macular dystrophy (n = 1), Doyne honeycomb macular dystrophy (n = 1), and Goldman-Favre enhanced S cone syndrome (n = 1). Macular FAF abnormalities were noted in 100% of cases. 48% of cases had peripheral FAF abnormalities. All patients with Retinitis Pigmentosa 100% demonstrated peripheral FAF abnormalities with focal areas of hyper- and hypofluorescence. Patients with vision worse than 20/60 had an average central subfield thickness (CST) of 170 um whereas patients with vision better than 20/60 had CST of 245 um. (p<0.001)

Conclusions: Distinctive macular and peripheral FAF patterns are identified in a large percentage of patients with retinal dystrophies. The functional and prognostic significance of these abnormalities is not completely understood and deserves further research. Ultra-widefield imaging may provide important information to facilitate diagnosis and follow-up of these challenging cases.
thinner subfoveal choroidal thickness in the treated eye compared to the contralateral, untreated eye. This is consistent with previous studies that show reduction in choroidal thickness in other diseases with compromised vasculature such as diabetes. Patients with radiation retinopathy tended to have a thicker choroid compared to patients who did not develop this complication after brachytherapy. This may be a consequence of increased vascular permeability in both the retina and choroid, but further studies are needed to elucidate the mechanism behind this phenomenon.

**Commercial Relationships:** Kavitha R. Sivaraman, None; Clement C. Chow, None; William F. Mieler, Genentech (C), Alcon (C), Allergan (C)

**Program Number:** 5836 Poster Board Number: D0147

**Presentation Time:** 8:30 AM - 10:15 AM

**Choroidal and Retinal Thickness in Patients Affected by Chronic Posterior Uveitis**

Luisa Pierro, Marco Gagliardi, Elisabetta Misericocchi, Lorenzo Iuliano, Ingrid Bianchi, Claudia Del Turco, Giuseppe Parrinello, Giulio Modorati, Maurizio B. Parodi, Francesco Bandello.

Department of Ophthalmology, Vita-Salute University, San Raffaele Scientific Institute, Milan, Italy.

**Purpose:** To evaluate macular choroidal and retinal thicknesses in patients affected by chronic posterior uveitis treated with systemic anti-inflammatory drugs.

**Methods:** 71 eyes of 40 consecutive patients with chronic treated posterior uveitis were enrolled. 30 healthy eyes were the control group. Eyes with uveitis were divided into active and non-active groups. Choroidal thickness (CT) was assessed using the Heidelberg Engineering® Spectral domain optical coherence tomography (SDOCT) with the Enhanced Depth Imaging (EDI) scan system at the fovea and up to 1 mm at intervals of 0.5 mm from the fovea in the superior, inferior, nasal and temporal choroid. Central foveal thickness (CFT) was also measured.

**Results:** Average CT was 240±76μm in the active group, and 250±66μm in the non-active group. No significant statistical difference in CT was found between pathological eyes with active or non-active uveitis (p=0.0043 and p=0.0256 respectively). No statistically significant difference was found between active-uveitis eyes CFT (320±120μm) and controls CFT (280±20μm; p=0.7189), while in non-active eyes it was found to be thinner (250±88μm; p=0.0001) compared to controls. Macular/choroid ratio in active-uveitis eyes (1.5±0.76) was significantly higher than in controls (0.99±0.29; p=0.007), while no statistical differences were found in non-active eyes (0.88±0.38; p=0.2124).

**Conclusions:** In eyes with chronic active uveitis, the retina appears to be more involved in the inflammatory process than the choroid. In eyes with non-active uveitis, both the retina and the choroid are involved in a similar way.

**Commercial Relationships:** Luisa Pierro, None; Marco Gagliardi, None; Elisabetta Misericocchi, None; Lorenzo Iuliano, None; Ingrid Bianchi, None; Claudia Del Turco, None; Giuseppe Parrinello, None; Giulio Modorati, None; Maurizio B. Parodi, None; Francesco Bandello, ALLERGAN Inc. (S), NOVARTIS PHARMACEUTICALS CORPORATION (S), FARMILA-THEA (S), BAYER SCHERING PHARMA (S), PFIZER Inc. (S), ALCON Inc. (S), BAUSCH AND LOMB (S), GENENTECH Inc. (S), ALIMERA SCIENCES Inc. (S), SANOFI AVENTIS (S), THROMBOGENICS (S)
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**ARVO 2013 Annual Meeting Abstracts by Scientific Section/Group – Retina**

**Program Number: 5837 Poster Board Number: D0148**  
**Presentation Time:** 8:30 AM - 10:15 AM  
**Loss of GCL in HIV positive patients with low (< 100) nadir CD4 counts**  
Frank D. Verbraak, Nacli Demirkaya, Michael D. Abramoff.  
*Ophthalmology, Univ of Amsterdam Acad Med Ctr, Amsterdam, Netherlands; Biomedical Engineering & Physics, Academic Medical Center, Amsterdam, Netherlands; University of Iowa, Iowa City, IA.*  
**Purpose:** In HIV positive patients neurodegeneration is part of the overall co-morbidity. Structural loss of neuro-retinal tissue has been described in these patients. We measured the individual retinal layers in search of possible neuro-retinal degeneration.  
**Methods:** Seventy-two HIV-positive patients were enrolled in this study. All underwent a complete ophthalmological examination. Patients with a history of retinitis or any other disease known to influence the retina were excluded (n=10). Patients were divided in two groups; patients with a nadir CD4 count > 100 (n=40), and patients with a nadir CD4 count less than 100 (n=22). Macular 3D volume OCT scans were made with SD-OCT (Topcon, MarkII), and segmented with custom-build software developed at the University of Iowa. Mean thickness of each individual layer was measured, and compared between both groups.  
**Results:** Of all layers measured the Ganglion Cell Layer (GCL) was the only statistically significant thinner layer in the group of patients with a low nadir CD4 count compared to patients with higher nadir CD4 counts: 31.6 micrometer (+/- 3.4), versus 33.8 micrometer (+/-3.6), p = 0.03 (Man-Whitney U-test).  
**Conclusions:** HIV-positive patients with a low nadir CD4 count (<100) have a thinner macular GCL compared to HIV positive patients with higher nadir CD4 counts (>100), demonstrating structural neuro-retinal degeneration, which could be part of a more degeneralized neurodegeneration.  
**Commercial Relationships:** Frank D. Verbraak. None; Nacli Demirkaya. None; Michael D. Abramoff. IDx LLC (E), IDx LLC (I), University of Iowa (P)  
**Support:** AIDS Fonds , nummer 2012023

**Program Number: 5838 Poster Board Number: D0149**  
**Presentation Time:** 8:30 AM - 10:15 AM  
**Long-term follow-up of fundus autofluorescence and multispectral reflectance imaging using ultra-widefield scanning laser ophthalmoscopy in patients with different retinal pathologies**  
**Purpose:** To evaluate peripheral changes in retinal pathologies over a period of three years by using an ultra-widefield scanning laser ophthalmoscopy (SLO) for fundus autofluorescence (FAF) and color fundus imaging.  
**Methods:** Longitudinal FAF and multi-spectral reflectance ultra-widefield imaging were performed in 14 eyes from 7 patients with different retinal pathologies (mean age 60 years, range 22-81). In 2009, we used an Optos P200CAF prototype and in 2012 an Optos 200Tx (Optos Ltd, Scotland). Images were evaluated for quality and changes in signal distribution of central and peripheral retinal lesions. Retinal pathologies included age-related macular degeneration (AMD), Stargardt disease, angiod streaks and other hereditary retinal dystrophies.  
**Results:** In AMD, progression of existing and development of novo peripheral atrophic spots beyond the vascular arcades were observed in addition to central lesion evolution. In rod-cone dystrophy and angiod streaks secondary to Pseudoxanthoma elasticum, increase in area involvement of mid-peripheral decreased FAF signal alterations were visible. In a patient with advanced Stargardt disease, both increase in atrophic lesion size and focally increased FAF abnormalities beyond the vascular arcades were detected. In a patient with unilateral unknown peripheral atrophy, no changes in lesion size were visible.  
**Conclusions:** Ultra-widefield scanning laser ophthalmoscopy imaging allows for the visualization of the evolution of both central and peripheral lesions in one image. Changes in levels of peripheral decreased FAF may be helpful to predict localized retinal dysfunction. This may be helpful for the assessment and long-term follow-up of patients with retinal lesions which extend into the periphery.  
**Commercial Relationships:** Viola Graham, Heidelberg Engineering, Germany (F), Carl Zeiss Meditec AG, Germany (F), Optos, UK (F); Monika Fleckenstein, Heidelberg Engineering, Germany (F), Heidelberg Engineering, Germany (C), Heidelberg Engineering, Germany (R), Carl Zeiss Meditec, Germany (F), Optos, UK (F), Optos, UK (C); Katharina Zilkens, Heidelberg Engineering, Germany (F), Optos, UK (F), Carl Zeiss Meditec, Germany (F); Steffen Schmitz-Valckenberg, Heidelberg Engineering (F), Optos (F), Carl Zeiss Meditec (F), Heidelberg Engineering (R), Genentech (C), Novartis (C), Novartis (R), Roche (R), Novartis (F); Frank G. Holz, Acucela (C), Allergan (C), Genentech (F), Heidelberg Engineering (F), Zeiss (F), Novartis (F), Novartis (C), Optos (F), Merz (C), Bayer (F), Bayer (C), Boehringer Ingelheim (C)

**Program Number: 5839 Poster Board Number: D0150**  
**Presentation Time:** 8:30 AM - 10:15 AM  
**Measuring drusen over time: OCT vs. Fundus Photography**  
Giovanni Gregori, Carlos Alexandre A. Garcia Filho, Zohar Yehoshua, Renata Portella Nunes, William J. Feuer, Srinivas R. Sadaru, Philip J. Rosenfeld.  
*Ophthalmology, Bascom Palmer Eye Institute, Miami, FL; Ophthalmology, Doheny Eye Institute - USC, Los Angeles, FL.*  
**Purpose:** To compare measurements of drusen area from digital color fundus photography and optical coherence tomography (SDOCT) prospectively in a population of patients with non-exudative age-related macular degeneration (AMD).  
**Methods:** Patients with drusen with an SDOCT volume of at least 0.03 mm³ in the absence of geographic atrophy were recruited into a prospective study. Digital color fundus images (CFIs) and SDOCT images (Cirrus™ HD-OCT, Carl Zeiss Meditec Inc., Dublin, CA), were obtained at baseline and at follow-up visits at months 3, 6, 9, and 12. CFIs were registered to the corresponding OCT datasets using the OCT Fundus Images and an automated registration algorithm. Matched circles centered on the fovea with diameters of 3 mm and 5 mm were identified on both the CFIs and the SDOCT images. SDOCT drusen measurements within the circles were obtained using a proprietary algorithm. Experienced graders at the Doheny Image Reading Center (DIRC) manually traced drusen boundaries on color fundus images. Based on our previous work showing that the square root of drusen area is a better parameter for statistical analysis than the actual drusen area, results are reported in terms of the square root of the drusen area (SQDA).  
**Results:** Thirty patients were enrolled and 42 eyes met inclusion criteria. The SDOCT mean SQDA in the central 3 mm was 1.451 mm at baseline and 1.464 mm at 26 weeks. The CFIs mean SQDA in the central 3 mm was 1.555 mm at baseline and 1.583 mm at 26 weeks. The differences between SDOCT and CFI measurements are statistically significant (p=0.004 at baseline, p=0.003 at 26 weeks). Excluding two eyes with very pronounced drusen loss, both modalities showed a statistically significant mean growth in SQDA.

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over 26 weeks. The difference between the changes in SQDA over 26 weeks measured with SD-OCT and CFI was not significantly different from 0 (mean 0.014 mm, p=0.5).

Conclusions: The SD-OCT drusen area measurements are more reproducible and systematically smaller than the ones obtained from digital fundus photography. However, when considering the changes in drusen area over time, we found no bias between the two modalities. While SD-OCT measurements differ somewhat from the classical interpretation of drusen area, our results support the conclusion that the results are similar and both approaches are very useful for studying drusen dynamics.

Commercial Relationships: Giovanni Gregori, Carl Zeiss Meditec (F), Carl Zeiss Meditec (P); Carlos Alexandre A. Garcia Filho, None; Zohar Yehoshua, None; Renata Portella Nunes, Carl Zeiss Meditec Inc. (F); William J. Feuer, Abbott Medical optics (F), New World Medical (F); Srinivas R. Sadda, Regeneron (C), Genentech (C), Allergan (C), Carl Zeiss Meditec (C), Optos (C), Carl Zeiss Meditec (F), Optovue (F), Optos (F); Philip J. Rosenfeld, Acucela (C), Advanced Cell Technology (F), Alexion Pharmaceuticals (F), Bayer Healthcare Pharmaceuticals (C), Boehringer Ingelheim (C), Chengdu Kanghong Biotech (C), GlaxoSmithKline (F), Oraya (C), Sanofi/Genzyme (C), ThromboGenics (C), Carl Zeiss Meditec (F)

Support: NIH center core grant P30EY014801; Research to Prevent Blindness; Department of Defense (W81XWH-09-1-0675); Grant from Carl Zeiss Meditec Inc

Program Number: 5840 Poster Board Number: D0151
Presentation Time: 8:30 AM - 10:15 AM

Varicella Zoster virus and Central serous retinopathy
Lukán P. Mishev, Aneta Misheva, Ioanna Misheva, Yanita Cankova, Anton Angelov
Ophthalmology, Focus Eye Center, Sofia, Bulgaria.

Purpose: To find a causal connection between Varicella zoster virus and CSR and a possible rationale for treatment with Aciclovir.

Methods: A group of 25 patients with CSR diagnosed with SD-OCT (line scan, en-face and Lumbroro report) was treated with Aciclovir (2 grams per day, for 20 days) based on the high IGG antibodies in the serum, found by ELISA method. We have OCT exams on the 1-st week, 2-nd week and after 30 days. The second ELISA blood serum testing was performed after a 60 days period. Patients with pigment epithelial detachments along with the serous detachment were excluded.

Results: In 23 patients we have observed a rapid resolution of the serous detachment (in the first 2 weeks period) which was OCT monitored at every week. The treatment was with Aciclovir 2g. per day, with no additional medication or laser treatment. Two of the patients were with chronic recidive CSR and the resolution of the serous detachment took more then two week period (1 month)

Conclusions: In this study we have observed clinical connection between high serum IGG antibodies for Varicella zoster virus and the presence of active CSR. When this patients were treated with the specific drug (Aciclovir) which target the Varicella zoster virus (VCV), there was complete resolution of the CSR in very rapid manner which may prove that this is a effect of a treatment and not a spontaneous improvement.

One of the proposed pathogenesis of the CSR is that there is a pigment epithelium impairment leading to disturbed metabolism as a major cause for accumulation of fluid between neurosensory retina and the pigment epithelium. In histopathological studies was proven that there can be a replication of Varicella zoster virus in the pigment epithelium of the retina. This can cause the impairment of the PE and we base our hypothesis for treatment and cause of CSR on that assumption.

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Spherical equivalent of the subjects were also obtained.

**Results:** The mean age of participants was 30.8 ± 8.8 years, with 20 (44.4%) men. The average of SE was -3.97 ± 2.76 diopter. The average CPT was 226.5 ±17.4 μm (Zeiss) and 228.1 ± 15.8 μm (Heidelberg), there was no significant difference between the two groups (p=0.119, paired t test), and there was very strong positive relationship (r=0.917, p<0.01, Pearson's correlation coefficient). Male gender was associated with a slightly thicker CPT, but there was no significant difference between males and females (p=0.344-0.579, independent samples t-test). There was negative relationship between spherical equivalent and CPT without reaching statistical significance (r=-0.162~0.125, p>0.05, Pearson's correlation coefficient). There would be no relationship between age and CPT (r=0.124~0.166, p>0.05, Pearson's correlation coefficient).

**Conclusions:** There was no significant difference in CPT manually between by Zeiss machine or Heidelberg machine, indicating that these two machines are interchangeable. In normal subjects, SD-OCT showed that CPT was not related to age or spherical equivalent.

**Commercial Relationships:** Makoto Shirasawa, None; Hiroto Terasaki, None; Hiroki Kawano, None; Takehiro Yamashita, None; Shozo Sonoda, None; Taiji Sakamoto, None

**Program Number:** 5842 Poster Board Number: D0153
**Presentation Time:** 8:30 AM - 10:15 AM

**Optical coherence tomography findings in uveitic macular edema**

Breno R. Lima, Sankaranarayana Mahesh, H Nida Sen. 1 National Eye Institute, National Institutes of Health, Bethesda, MD; 2Wills Eye Institute, Philadelphia, PA.

**Purpose:** To characterize features of macular edema using spectral-domain optical coherence tomography (OCT) in patients with uveitis in a tertiary referral clinic.

**Methods:** Retrospective, cross-sectional study of uveitis patients with macular edema imaged with spectral-domain OCT between September 2007 through May 2011. The first OCT scan of each patient (baseline) was used in the study. Measurements of central subfield thickness (CST), macular cube volume and presence/absence of epiretinal membrane were obtained for all eyes with macular edema. Pattern of edema was classified in four groups (diffuse; intraretinal cysts; subretinal fluid; and mixed pattern with both intraretinal cysts and subretinal fluid). Photoreceptor layer was classified as disrupted or intact. Information on visual acuity, etiology of uveitis and anatomic location (anterior, intermediate, posterior or panuveitis) was obtained and correlated with OCT findings.

**Results:** A total of 86 uveitic eyes (66 patients) with macular edema were evaluated by OCT. Mean patient age was 46.42 years ± 19.01. Mean central subfield thickness (CST) was 389.3 μm ± 175.2. Most common pattern of edema was intraretinal cysts (46.51%), followed by a mixed pattern with both intraretinal cysts and subretinal fluid (36.05%). The mean logMAR visual acuity was 0.54 ± 0.34 (Snellen equivalent 20/69). Most prevalent anatomic location of uveitis was panuveitis (36.05%), followed by intermediate uveitis (24.42%). The etiology of uveitis was idiopathic in the majority of cases (50 eyes, 38 patients), followed by sarcoidosis (9 eyes, 7 patients). No pattern of edema was pathognomonic of a specific site of inflammation or etiology of uveitis. Linear regression analysis evaluating the relationship of logMAR visual acuity and CST showed a statistically significant positive correlation between poorer logMAR visual acuity and increased CST (r squared=0.121, p=0.001). Comparison of eyes with or without epiretinal membrane did not show a statistically significant difference in visual acuity (p=0.32). Eyes with disruption of the photoreceptor (PR) layer had worse visual acuities compared to eyes with intact PR layer (p=0.0002).

**Conclusions:** Macular edema may complicate the course of uveitis regardless of the anatomic location of inflammation or etiology. Certain architectural OCT features such as severe disruption of the photoreceptor layer are indicators of poor visual acuity.

**Commercial Relationships:** Breno R. Lima, None; Sankaranarayana Mahesh, None; H Nida Sen, None

**Program Number:** 5843 Poster Board Number: D0154
**Presentation Time:** 8:30 AM - 10:15 AM

**Posterior Eye Wall Radius of Curvature as a Measure of Staphylopaia Progression in Myopic Foveoschisis Patients as Gauged by Optical Coherence Tomography**

Pamela Sherwood, Jamie Leong, Stanley Chang, Gemmy C. Cheung, Quan V. Hoang. 1 Ophthalmology, Columbia University Medical Center, New York, NY; 2Singapore National Eye Centre, Singapore, Singapore.

**Purpose:** Myopic progression occurs in up to 50% of myopic patients. In such eyes, the development of posterior staphyloma may be associated with vision-threatening myopic maculopathy such as foveoschisis, atrophy or choroidal neovascularization. We evaluate the utility of optical coherence tomography (OCT) in assessing the posterior eye wall in patients with myopic posterior staphyloma and determine if a change in staphyloma radius of curvature immediately precedes progression of myopic foveoschisis.

**Methods:** Spectral Domain OCT images (Cirrus, macular cube) obtained from 8 eyes of 8 myopic foveoschisis patients before and during progression were retrospectively reviewed. Central horizontal and vertical images through the fovea were exported and manually segmented to focus on the retinal pigment epithelial (RPE) layer. RPE radius of curvature and root mean square deviation were calculated by curve-fitting in MatLab, and horizontal and vertical values were averaged.

**Results:** Among pathologic myopia patients who experienced progression of myopic foveoschisis, the results show that a change in radius (within a patient) is not associated with progression. On average, patients experienced a decrease in RPE radius of curvature of 0.06 mm, which is associated with a 2.6% point increase in the likelihood of experiencing myopic foveoschisis progression. Specifically, our linear regression yielded a coefficient of -0.42 and standard error of 0.97. Given the average decrease in RPE radius of curvature of -0.06 mm (+0.7 to -0.8, n = 8), this translates to an increased likelihood of foveoschisis progression of 2.6% points, which is a large effect, but not statistically significant (p = 0.68).

**Conclusions:** RPE radius of curvature is a valid and readily available tool for assessing and tracking myopic staphyloma. Initial studies do not suggest that a change in RPE radius of curvature immediately precedes foveoschisis progression.

**Commercial Relationships:** Pamela Sherwood, None; Jamie Leong, None; Stanley Chang, Alcon Laboratories (C), Alimera Sciences (C); Gemmy C. Cheung, Bayer (C), Bayer (R), Novartis (C), Novartis (S), Glaxo Smith Kline (F), Roche (F); Quan V. Hoang, None

**Program Number:** 5844 Poster Board Number: D0155
**Presentation Time:** 8:30 AM - 10:15 AM

**Evaluation of the Digital Light Projector Camera (DLP-Cam) for Low-Cost Diabetic Retinopathy Screening**

Taras V. Litvin, Glen Y. Ozawa, Jorge A. Cuadros, Matthew S. Muller, Ann E. Elsner, Thomas Gast, Jeff Clendenon, Lisa Ensmann, Tuinh Roy, Danny Ll. 1 School of Optometry, UC Berkeley, Berkeley, CA; 2School of Optometry, Indiana University, Bloomington, IN; 3Aeon Imaging, LLC, Bloomington, IN.

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Purpose: To provide low-cost, nonmydriatic screening for diabetic retinopathy (DR) with a novel retinal imaging system that captures sufficient retinal detail to generate referrals with high sensitivity and specificity.

Methods: The DLP-Cam is a low-cost non-mydriatic camera that obtains confocal retinal images at 17 frames per second. It obtains 33x25 degree images over a wide refractive error (±10 diopter) with low intensity red or green illumination (42 uW). The DLP-Cam uses a small 1.6mm entrance/exit pupil and is easily transported to different sites (8”x6”x3”; 2.2 lbs). To evaluate the DLP-Cam’s ability to detect DR, a study comparing cameras was performed. The Canon CR6 fundus camera, iVue OCT, and DLP-Cam were used to image adult diabetic patients at Eastmont Wellness Center, Oakland, CA. Three overlapping 45 degree images of the posterior pole were obtained with the Canon. Three matching images were obtained using the DLP-Cam. Macular map scans were performed with the iVue. An EyePACS-certified diabetic retinopathy grader compared the Canon, iVue, and DLP-Cam images side-by-side for the presence and appearance of DR.

Results: 45 diabetic patients (average age of 53 years) were enrolled. 46% were females. 44% were Latin American, 24% were African American, 23% were Asian, and 9% were Caucasian. 33% of patients had no DR, 22% had mild non-proliferative DR (NPDR), 26% had moderate NPDR, and 13% had proliferative DR. Clinically significant macular edema was diagnosed in 6%. Compared to Canon images, the DLP-Cam showed matching hard exudates and hemorrhages (Figure 1). In addition, the DLP-Cam images provided clearer visualization of optic nerve cup-to-disc boundaries and retinal nerve fiber defects, useful for the detection of glaucoma (Figure 2). The ability to acquire images separately with red-free and red illumination channels provides visualization of the superficial retina and the choroid, respectively.

Conclusions: Preliminary testing of DLP-Cam shows potential for the DLP-Cam to be used as a low-cost, portable retinal screening camera.

Figure 1: Fovea of undilated 56 year old Caucasian male. A. Cropped color DLP-Cam image; B. Cropped Canon photo.

Figure 2: Dilated 54 year old Hispanic female. A. DLP-Cam cropped averaged red-free image. B. Canon cropped red-free comparison image. The superior nerve fiber defect (arrows) and absence of inferior nerve fiber is suggestive of glaucoma.

Commercial Relationships: Taras V. Litvin, None; Glen Y. Ozawa, None; Jorge A. Cuadros, EyePACS LLC (I); Matthew S. Muller, Aeon Imaging, LLC (I), Aeon Imaging, LLC (P), Aeon Imaging, LLC (R), Aeon Imaging, LLC (S), Indiana University Research and Technology Corporation (P); Ann E. Elsner, Aeon Imaging, LLC (I), Aeon Imaging, LLC (F), Aeon Imaging, LLC (P); Thomas Gast, None; Jeff Cledenon, Aeon Imaging, LLC (E); Lisa Ensmann, None; Tuinh Roy, None; Danny Li, None

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Program Number: 5845 Poster Board Number: D0156
Presentation Time: 8:30 AM - 10:15 AM

Ultra-widefield retinal imaging documentation and analysis of peripheral retinal disease in Marfan syndrome: From the Marfan Eye Consortium of Chicago

Safa Rahman1, Amani A. Fawzi2, Alice T. Lyon1,2, Irene H. Maumenee1, Marilyn Mits2. 1Northwestern University, Chicago, IL; 2Lurie Children’s Hospital of Chicago, Chicago, IL; University of Illinois at Chicago, Chicago, IL.

Purpose: Patients with Marfan syndrome are at high risk of significant retinal pathology including retinal detachments. Examination of these patients is often difficult due to poorly dilating pupils, subluxated lens and young age. This study aimed to report the prevalence of peripheral retinal disease, using the Optos 200Tx imaging device, in a group of Marfan patients.

Methods: 72 patients were seen on August 2nd as a part of 2012 Marfan Eye Consortium of Chicago. Of the 61 consented patients, posterior color ultra-widefield retinal images were obtained using the Optos 200Tx (age range of tested patients 3-68yrs) on 54 patients (108 eyes). The ability to view the fundus was divided into 2 groups for analysis. Post-equator category: Eyes in which we were able to view posterior pole up to equator) and anterior to equator: eyes where the examiner had sufficient retina view anterior to equator of the peripheral retina. The ultra-widefield color images were analyzed by vitreo-retinal sub-specialist, masked to the clinical exam. Each eye had several images captured, and all images for each eye were used to evaluate the categories. The color composite images were analyzed by separating the red (633 nm) and green channels (532 nm), in the Optos imaging review software, V2 Vantage.

Results: Analysis of the eyes using peripheral ultra-widefield images demonstrated the following findings: pre equatorial retina view in 95% of eyes, pre and post equatorial retina view in 57% of eyes. Retinal pathology (e.g.: peripheral scars, white without pressure) was...
evident in 24% of eyes analyzed using color, red, and green channels of V2 Vantage. Subluxated lens was evident in 25% of the eyes. The youngest patient photographed was 3 years old at time of study. Young patients (3-12yrs) tolerated the imaging well.

**Conclusions:** The peripheral retinal anatomy in the Marfan Eye Consortium of Chicago was documented and analyzed using Optos 200Tx. The ultra-widefield imaging documentation by Optos 200Tx ultra-widefield retinal images can be used to assist in fundus examination of Marfan patients that are difficult to evaluate due to their young age, inadequate dilation of pupil or lens subluxation.

**Commercial Relationships:** None; Moe Mita, None; Rieko Higashida, None; Yorihisa Tsutsumi, None; Yoshikazu Ichikawa, None; Masahiro Ishida, None

**Support:** Research to Prevent Blindness grant and Children’s Surgical Foundation grant (Lurie Children’s Hospital of Chicago)

**Program Number:** 5846 Poster Board Number: D0157

**Presentation Time:** 8:30 AM - 10:15 AM

**Intravitreal Injection of Bevacizumab for Macula Edema Secondary to Central Retinal Vein Occlusion: Efficacy at 1 Day after Injection**

**Purpose:** To evaluate the visual and anatomical outcome in eyes with macular edema secondary to central retinal vein occlusion (CRVO) at 1 day after injection of intravitreal bevacizumab.

**Methods:** A retrospective, consecutive case series identified 20 consecutive patients with CRVO undergoing intravitreal injection of bevacizumab. Optical coherence tomography images were taken at the day of injection and 1-day after injection. Retinal thickness at fovea, height of serous retinal detachment and visual acuity were monitored before and after injection.

**Results:** The mean age of patients was 67.8 years old (6 females). Retinal thickness at fovea was 726 ± 281 µm before injection and was 440 ± 264 µm at 1 day after injection. (Student t test, P=0.0020) Height of retinal detachment was 221±215 µm before injection and was 440 ± 264 µm at 1 day after injection. (Student t test, P=0.0020) Visual acuity (logMAR) was 0.762±0.477 before injection and 0.71±0.436 at 1 day after injection. (P=0.732)

**Conclusions:** Rapid resolution of intraretinal fluids was observed in CRVO, however significant improvement of vision was not observed at 1 day after injection.

- Program Number: 5847 Poster Board Number: D0158

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**Fundus Autofluorescence of Exudative Age-Related Macular Degeneration with Intraretinal Cystoid Lesion**

**Purpose:** Eyes with exudative age-related macular degeneration (AMD) often demonstrate an intraretinal cystoid lesion at the macula on optical coherence tomography (OCT) images. This lesion is either cystoid macular edema (CME) as active exudation, or cystoid macular degeneration (CMD) as fibroatrophic scar. However, fluorescein angiography (FA) is required for a definitive diagnosis. The purpose of this study was to investigate fundus autofluorescence (FAF) findings in eyes with exudative AMD and an intraretinal cystoid lesion.

**Methods:** This study included 37 eyes of 36 patients (9 eyes of 9 females and 28 eyes of 27 males; mean age: 77.3 years) with exudative AMD which were shown via an OCT image to have cystoid lesion traversing the macula. FAF (excitation: 488 nm, barrier: 500 nm) photography and FA were performed with a confocal scanning ophthalmoscope (Heidelberg Retina Angiograph 2; Heidelberg Engineering, Dossenheim, Germany). The 37 eyes were divided into the following 2 groups according to the FA findings: 1) the CME group (eyes with active leakage of fluorescein dye at the cystoid lesion), and 2) the CMD group (eyes showing staining without active leakage). The differences in FAF findings between these 2 groups were retrospectively evaluated.

**Results:** Of the total 37 eyes, the CME group and the CMD group included 26 eyes and 11 eyes, respectively. In the CME group, 23 eyes (88.5%) presented well-distinguished hyperautofluorescence corresponding to the cystoid lesion. In contrast, only 1 eye (9.1%) in the CMD group showed hyperautofluorescence at the cystoid lesion. These hyperautofluorescence findings were observed more frequently in the CME group than in the CMD group (P < 0.0001).

**Conclusions:** FAF with the 488 nm excitation reportedly displays analogous hyperautofluorescence at the cystoid lesion of CME. In this present study, the difference of the FAF findings between the CME and CMD groups may reflect the viability or damage of retinal pigment epithelial (RPE) cells below the cystoid lesion. In the CMD-group eyes, we assume that not only the sensory retina but also the RPE cell layer had been severely damaged by the long-term exudative change to date. FAF photography may become the adjunctive diagnostic tool used for distinguishing CMD from CME in the clinical setting.

**Commercial Relationships:** Tetsuya Yamagishi, None; Hideki Koizumi, None; Taizo Yamazaki, None; Nobuhiro Terao, None; Kotomi Nakayama, None; Shigeru Kinoshita, Senju Pharmaceutical Co (P), Santen Pharmaceutical Co (P), Otsuka Pharmaceutical Co (C), Alcon (R), AMO (R), HOYA (R)

**Program Number:** 5848 Poster Board Number: D0159

**Presentation Time:** 8:30 AM - 10:15 AM

**Retinal vascular abnormalities in the far periphery of pathologic myopic eyes imaged by ultra-wide-field fluorescein angiography**

**Purpose:** To evaluate the effectiveness of ultra-widefield fluorescein angiography (UWF-FA) for imaging the far peripheral retinal vasculature in highly myopic eyes.

**Methods:** A total of 11 highly myopic eyes (7 males, 4 females; mean age: 77.3 years) with retinal vascular abnormalities in the far periphery were included in this study. Digital images were captured using the Heidelberg Spectralis. Images were analyzed for the presence of retinal vascular abnormalities such as avascular zones, vasospasm, dilated vessels, microaneurysms, and exudates. The findings were compared with the clinical features and visual acuity of the patients.

**Results:** Of the 11 eyes, 9 eyes (81.8%) showed significant retinal vascular abnormalities in the far periphery, including 7 eyes (63.6%) with avascular zones and 4 eyes (36.4%) with dilated retinal vessels. No statistical correlation was found between the presence of these abnormalities and visual acuity or age of the patients.

**Conclusions:** The use of UWF-FA provides valuable insights into the retinal vascular structure in highly myopic eyes, which can aid in the diagnosis and management of vascular abnormalities. Further studies are needed to correlate these findings with clinical outcomes.

**Commercial Relationships:** Yuichiro Kaneko, None; Muka Moriyama, None; Noriaki Shimada, None; Natsuko Nagaoka, Kosei Shinhara, Yuichiro Tanaka, Kyoko Ohno-Matsui, Takashi Tokoro, Shuichiro Hirahara, Yuichiro Ogura.

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**Program Number:** 5849 Poster Board Number: D0160

**Presentation Time:** 8:30 AM - 10:15 AM

**Retinal vascular abnormalities in the far periphery of pathologic myopic eyes imaged by ultra-wide-field fluorescein angiography**

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**Program Number:** 5850 Poster Board Number: D0161

**Presentation Time:** 8:30 AM - 10:15 AM

**Retinal vascular abnormalities in the far periphery of pathologic myopic eyes imaged by ultra-wide-field fluorescein angiography**

**Purpose:** To evaluate the effectiveness of ultra-widefield fluorescein angiography (UWF-FA) for imaging the far peripheral retinal vasculature in highly myopic eyes.

**Methods:** A total of 11 highly myopic eyes (7 males, 4 females; mean age: 77.3 years) with retinal vascular abnormalities in the far periphery were included in this study. Digital images were captured using the Heidelberg Spectralis. Images were analyzed for the presence of retinal vascular abnormalities such as avascular zones, vasospasm, dilated vessels, microaneurysms, and exudates. The findings were compared with the clinical features and visual acuity of the patients.

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**Conclusions:** The use of UWF-FA provides valuable insights into the retinal vascular structure in highly myopic eyes, which can aid in the diagnosis and management of vascular abnormalities. Further studies are needed to correlate these findings with clinical outcomes.

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1Ophthalmology & Visual Science, Tokyo Medical and Dental University Graduate School of Medicine and Dental Sciences, Bunkyo-ku, Japan; 2Ophthalmology & Visual Science, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan.

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Purpose: We have previously found that the retinal vasculature in the posterior fundus showed various abnormalities due to mechanical stretching, and have called this condition as myopic retinal vasculopathy. Recently, the imaging of far-peripheral retina is possible by using Optos 200Tx. In the present study, we examined the retinal vasculature in far periphery by using Optos in a large number of highly myopic eyes.

Methods: One hundred and forty-eight eyes (79 patients) with bilateral high myopia (myopic refractive error ≥8.00 diopters (D) or axial length >26.5 mm) were studied. For the control, 42 emmetropic eyes which were the fellow eyes of aged-related macular degeneration or central serous chorioretinopathy were examined. The patients who had systemic conditions, such as diabetes of hypertension were excluded. Venous phase of the fluorescein angiographic images taken by Optos 200Tx were analyzed. To exclude the influence of eyelid, we evaluated the nasal and temporal peripheral retina.

Results: High myopic eyes showed various abnormalities in retinal vasculature in the far periphery by Optos. Retinal capillary telangiectasia was seen in 86.1%, the microaneurysms were seen in 55.4%, the dye leakage from microaneurysms or retinal capillaries was seen in 30.4%, and the avascular area was seen in 83.8%. Telangiectasia and the microaneurysms were also seen in far-peripheral retina in emmetropic eyes (80.0%, 35.6%). However, the avascular area or the dye leakage was never seen in emmetropic eyes. Even in highly myopic eyes, the avascular area was seen significantly more frequently in eyes whose axial length were > 30 mm than the eyes whose axial length was ≤ 30 mm (P < 0.05).

Conclusions: Various retinal vascular abnormalities are observed in the far periphery by using Optos. These changes were more severe and exaggerated in eyes with pathologic myopia compared to emmetropic eyes, and retinal avascular area was seen only in highly myopic eyes. Mechanical expansion of the equator of the eye might be a cause for retinal vascular alterations in eyes with pathologic myopia.

Commercial Relationships: Yuichiro Kaneko, None; Muka Moriyama, None; Noriaki Shimada, None; Natsuko Nagaoka, None; Kosei Shinohara, None; Yuichiro Tanaka, None; Kyoko Ohno-Matsui, None; Takashi Tokoro, None; Shuichiro Hirahara, None; Yuichiro Ogura, None

Program Number: 5849 Poster Board Number: D0160
Presentation Time: 8:30 AM - 10:15 AM
Retinal-choroidal changes after loading phase of ranibizumab in diabetic macular edema

Purpose: Subfoveal choroidal thickness (CT) has been reported to be reduced in diabetic macular edema eyes (DME) and that intravitreal injections of ranibizumab reduce retinal thickness (RT) by reducing vascular permeability with significant functional improvement although no information is still available regarding possible influence on CT. The purpose of this study was to explore CT changes and their relationship with functional changes in DME eyes after three injections 1 month apart (loading phase) of ranibizumab 0.5 mg in comparison with the fellow eye.

Methods: BCVA measurement with ETDRS charts, biomicroscopy, IOP measurement, ophthalmoscopy and RT measurement were performed at baseline and then monthly until 1 month after the loading phase. In addition CT measurement using enhanced depth imaging optical coherence tomography (EDI-OCT, Spectralis; Heidelberg Engineering GmbH, Heidelberg, Germany) and MP1 microperimetry (Nidek Technologies, Padova, Italy) were performed at baseline and 1 month after the loading phase, as systolic and diastolic pressure and heart rate measurement.

Results: 23 DME eyes of 23 patients with diabetes (14 males, 9 females, mean age 66.2±8.3 years) were included. Mean diabetes and macular edema duration was 16.1±8.5 and 3±1.7 years, respectively. After the loading phase mean BCVA significantly improved from 60.6±12.3 to 66.4±12.4 letters (p<0.0001) and central RT significantly reduced from 583.4±141.5 to 434.4±136.3 μm (p<0.0001). No significant changes were found in mean retinal sensitivity throughout the follow-up (10.9±4.3 vs 11.5±5.3 dB, p=0.83).

CT was found to be different between treated and fellow eye at baseline (185.4±49.9 vs 210.04±41.03, respectively) and while after the loading phase an increase of 21.2±56 μm (11.4%, from 185.4±49.9 to 206.6±60.6 μm) was found in the treated eye, no changes were found in the fellow eye. BCVA changes from baseline were found not to be related to either central RT (R2 0.11, p=0.1) or CT changes (R2 0.05, p=0.28).

No significant relationship was also found between central RT and CT at any visit as between their changes from baseline. No relationship was found between refraction, IOP, systemic pressure and CT changes.

Conclusions: Loading phase of ranibizumab in DME eyes determines an increase of choroidal thickness associated with an improvement of visual acuity and a reduction of retinal thickness.

Commercial Relationships: Paola Giorno, None; Mariacristina Parravano, None; Andrea Cacciamani, None; Francesco Oddone, None; Fabio Scarinci, None; Antonluca Boninfante, None; Monica Varano, None

Program Number: 5850 Poster Board Number: D0161
Presentation Time: 8:30 AM - 10:15 AM
Refractive Impact on the Espion Multifocal ERG in Clinical Practice
John Hamilton, Antony M. Theogene, Rejean Mungur, Stuart G. Coupland. Ophthalmology, University of Ottawa Eye Institute, Ottawa, ON, Canada.

Purpose: The multifocal electroretinogram (mERG) enables simultaneous recording of central, localized electroretinal function. A significant difference in the response density of the mERG has been suggested for every 2 diopter change in refraction, which may be attributable to changes in the retinal image size induced by the corrective lens used. There is currently no clear consensus in regards to the importance of correction during mERG testing, and no study has ever investigated the refractive impact on the Diagnosys Espion mERG. The purpose of this project is to investigate the influence of refraction, or defocus, on Espion mERG response.

Methods: The refractive impact on mERG results was studied monocularly in 30 healthy volunteers. Multifocal ERGs were recorded according to ISCEV standards using a 61 hexagonal elements stimulus projected on the central 30 degrees surrounding the fovea. Recordings were obtained using DTL electrodes with a corrective lens in front of a cycloplegic eye. Reference ear clip and ground forehead electrodes were used. Magnification caused by the trial lens was counteracted through software by changing the stimulus elements stimulus projected on the central 30 degrees surrounding the fovea. Reference ear clip and ground forehead electrodes were used. Magnification caused by the trial lens was counteracted through software by changing the stimulus.

No significant difference was found between conditions 2&3 were a result of optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&3 were attributable to optical defocus, whereas the difference between conditions 1&
Each subject's ring average results were analyzed for P1 response density amplitude and timing differences between each refractive condition.  

**Results:** There was a significant effect of defocus on mERG P1 amplitude but not timing (p<0.01). Magnification induced by the corrective lens used also significantly affected mERG P1 amplitude but not peak latency (p<0.05). The effects of image blur and magnification were greatest in ring 1 and decreased peripherally.  

**Conclusions:** Both image blur and magnification significantly affect Espion mERG P1 amplitude but not peak latency. The Espion mERG stimulus must be focused and scaled accordingly to accurately assess central retinal function. This study demonstrates the importance of refraction towards standardizing testing conditions and optimizing mERG response in clinical practice.  

**Commercial Relationships:** John Hamilton, Diagnosys LLC (C); Antony M. Theogene, None; Rejean Munger, None; Stuart G. Coupland, Diagnosys LLC (C)  

**Support:** Internal Department Funding  

**Program Number:** 5851 **Poster Board Number:** D0162  

**Macular and Optic Nerve Optical Coherence Tomography in Marfan Patients: from the Marfan Eye Consortium of Chicago  

WanWan Xu1, Sudhi Kurup2, Amani A. Fawzi1, Mary K. Durbin2, Irene H. Maumenee3, Marilyn Mets2, 4  

1Ophthalmology, Northwestern University, Chicago, IL; 2Ophthalmology, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL; 3Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL; 4Carl Zeiss Meditec, Inc, Dublin, CA.  

**Purpose:** To report the distribution of macular and optic nerve topography in the eyes of individuals with Marfan syndrome aged 2 to 56 years using optical coherence tomography (OCT) measurements.  

**Methods:** 72 patients were seen on 8/2/2012 at the Ann & Robert H. Lurie Children's Hospital Ophthalmology Clinic as part of the Annual National Marfan Foundation Conference. 60 patients consented to the study and underwent a full eye examination including evaluation with slit-lamp, indirect ophthalmoscopy, axial length measurement using the IOL Master (Carl Zeiss Meditec, Dublin, CA), and OCT measurements using the Macular Cube 512x128 and Optic Disc Cube 200x200 of the Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA). OCT data included right eyes that had signal strength ≥6 out of 10 without artifacts. If the right eye was excluded, the left eye was used.  

**Results:** 17/60 patients were excluded for having scans of insufficient signal strength. For patients between the ages of 7 to 12, the average retinal nerve fiber layer (RNFL) thickness is 90 ± 15 um, vertical cup to disc (C:D) ratio is 0.46 ± 0.17, central subfield thickness (CST) is 269 ± 43 um, and macular volume is 10.3 ± 0.55 mm³. For patients between the ages of 13 to 17, average RNFL is 83 ± 16 um, vertical C:D ratio is 0.34 ± 0.18, CST is 241 ± 63 um, and macular volume is 9.7 ± 1.6 mm³. For patients 18 years or older, average RNFL is 87.5 ± 13 um, vertical C:D ratio is 0.47 ± 0.18, CST is 358 ± 23 um, and macular volume is 10.1 ± 0.5 mm³. When the average RNFL data is compared to a normative database adjusted for age, overall, 28 of 43 eyes (65%) were greater than the 5% limit; 5 of 43 (12%) were between the 1% and 5% limits; and 10 out of 43 eyes (23%) were thinner than the 1% limit. For vertical C:D ratio, 36 of 43 eyes (83%) were >5% limit; 4 of 43 eyes (9%) were between 1-5%; and 3 of 43 eyes (7%) were <1%. For CST, 39 of 43 eyes (90%) were >5% limit; 2 of 43 eyes (5%) were between 1-5%; and 2 of 43 eyes (5%) were <1%. For macular volume, 39 out of 43 (91%) were >5% limit, while 4 out of 43 eyes (9%) were <1%.  

**Conclusions:** This study reports distribution of OCT data for patients with Marfan syndrome. Compared to normative database, 23% of eyes with Marfan syndrome had RNFL <1 % of population, suggestive of RNFL loss, with overall less significant macular changes. We are currently comparing this data to clinical exam findings.  

**Commercial Relationships:** WanWan Xu, None; Sudhi Kurup, None; Amani A. Fawzi, None; Mary K. Durbin, Carl Zeiss Meditec, Inc. (E); Irene H. Maumenee, None; Marilyn Mets, None  

**Support:** Research to Prevent Blindness, New York.  

**Program Number:** 5852 **Poster Board Number:** D0163  

**Presentation Time:** 8:30 AM - 10:15 AM  

**Multimodal imaging in Persistent Placoid Maculopathy**  

Mohamed G. Gendy1, Amani A. Fawzi2, Robert T. Wendel2, Dante J. Pieramici3, Joel A. Miller2, David M. Brown4, Lee M. Jampol5  

1Ophthalmology, Northwestern University, Chicago, IL; 2Retina Consultants, Sacramento, CA; 3California Retina Consultants, Bakersfield, CA; 4Retina Consultants of Michigan, Southfield, MI; 5Retina Consultants of Houston, Houston, TX.  

**Purpose:** To describe the acute and long term retinal changes in Persistent Placoid Maculopathy (PPM) on Spectral Domain Optical Coherence Tomography (SD-OCT), indocyanine green angiography (ICG-A), Fluorescein angiography (FA) and fundus autofluorescence (FAF).  

**Methods:** A retrospective review of medical records of twelve eyes of six patients, aged 50 to 60 years, diagnosed with PPM at four different centers.  

**Results:** All patients presented within one week of subjective symptoms. All patients presented with bilateral macular lesions except one patient, who initially presented with unilateral lesions. Six eyes had extra-macular lesions in the course of follow-up. On SD-OCT, the acute placoid lesions showed hypereflectivity in the outer nuclear layer (ONL), disruption of the external limiting membrane (ELM) and inner segments with a sliver of hyporeflectivity at the level of the outer segments in some cases. Over the course of follow-up, most lesions showed complete restoration of the outer retinal architecture, while some showed partial restoration or progression to atrophy. On FA, all placoid lesions were hypofluorescent in early frames and hyperfluorescent in late frames. ICG-A showed sharply delineated dense early hypofluorescent lesions, which persisted on late ICG-A in all patients. Hypofluorescent lesions faded completely or partially after resolution of the placoid lesions on SD-OCT and clinical examination. Three different patterns were observed on FAF. Acute placoid lesions showed hyperautofluorescence, which became hypo-autofluorescence as the disease progressed to atrophy. Acute lesions were hypo-autofluorescent in one patient. Meanwhile, in one case, lesions were not seen on FAF initially, and showed minimal hyperautofluorescence later when lesions were atrophied. Choroidal neovascularization (CNV) developed in one patient who was treated with photodynamic therapy, intravitreal Bevacizumab and sub-Tenon’s capsule Triamcinolone acetate injections. Two patients received treatment with oral immunosuppression. The mean follow-up time was 25 (range, 2-92) weeks.  

**Conclusions:** On SD-OCT, acute retinal changes in PPM involve the ONL, ELM and inner segments. Retinal pigment epithelium (RPE) and choroid are involved in severely affected cases. Choroidal hypofluorescence is secondary to a blockage effect, hypoperfusion or mixed mechanisms. Variable extent of RPE involvement in this condition is reflected in highly variable FAF findings.  

**Commercial Relationships:** Mohamed G. Gendy, None; Amani A. Fawzi, None; Robert T. Wendel, None; Dante J. Pieramici, Genentech (C), alimera (C), thrombogenics (C), allergan (C), Santen (C); Joel A. Miller, None; David M. Brown, Regeneron  

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Commercial Relationships: Priyanka Kumar, None; Robert J. Courtney, None; Kimberly Baynes, None; Careen Y. Lowder, None; Justis P. Ehlers, Provisional patents filed related to intraoperative OCT technology. No company relationships (P); Robert Rennebohm, None; Sunil K. Srivastava, Bausch and Lomb (F), Bausch and Lomb (C), Novartis (F), Allergan (F)

Program Number: 5854 Poster Board Number: D0165
Presentation Time: 8:30 AM - 10:15 AM

Development of a Premacular Vitreous Pocket
Tadashi Yokoi, Noriyuki Azuma. Ophthalmology, National center for child health and development, Tokyo, Japan.

Purpose: The premacular vitreous pocket (PVP) is important structure that is related to various macular diseases, including macular holes and diabetic maculopathy. However, it has been unknown how the pocket develops.

Methods: We analyzed the posterior vitreous, retinas, and optic discs of 56 healthy eyes (39 patients; age range, 1-54 years) using swept-source OCT (Topcon, Tokyo, Japan), which provides the detailed images of the fine structures. Eyes that appeared healthy were excluded if the patient had a family history of a hereditary vitreoretinal disease.

Results: A PVP was detected in all eyes of patients older than 10 years and in no eyes of patients younger than 2 years. A vitreous laceration, considered to be a primitive structure of the premacular vitreous pocket, develops first in eyes around 2 years of age. Between 3 and 9 years, a PVP was present in 49% of eyes and a vitreous laceration in 61%. Fifty-five percent of eyes with a PVP also had a vitreous laceration, and 80% had a liquefied cavity connected to the PVP and Cloquet’s cana. The connection to Cloquet’s canal was identified in the PVP and the vitreous laceration. In younger eyes, the PVP was wider horizontally than vertically, and all detectable

Conclusions: Premacular vitreous pockets are not always associated with vitreous laceration and macular holes.
vitreous lacerations were longer horizontally than vertically. During the early phase of PVP development, several eyes had multifocal PVPs and vitreous lacerations in the premacular vitreous. A high-density structure, which appeared to be a remnant of regressed hyaloid vessels, connected to Bergmeister’s papilla, was present temporally along the laceration and wall of the PVP.

**Conclusions:** Formation of PVPs begins with a vitreous laceration, focally or multifocally, and Cloquet’s canal, a remnant of regressed hyaloid vessels and eye movement may play important role in its development.

**Commercial Relationships:** Tadashi Yokoi, None; Noriyuki Azuma, None

**Program Number:** 5855 Poster Board Number: D0166

**Presentation Time:** 8:30 AM - 10:15 AM

**Evaluation of subfoveal choroidal thickness before and after cataract surgery**

Minoru Tanigawa, Yua Shimada, Yuu Ochiai, Haruyuki Ochiai, Yoko Tsukahara, Hiromitsu Yamanaka. Shin-Nagata Eye Institute, Kobe, Japan.

**Purpose:** To evaluate the influence of the cataract surgery on the subfoveal choroidal thickness (SCT).

**Methods:** A total of 71 eyes of 54 patients were evaluated. SCT was measured prior to cataract surgery and at 1 day, 1 week, 1 month and 3 months postoperatively. Phacoemulsification with intraocular lens (IOL) implantation was performed to all 71 eyes. Spectral domain optical coherence tomography with enhanced depth imaging (EDI-OCT) was performed to measure SCT using a Cirrus® HD OCT (Carl Zeiss Meditec). EDI-OCT images were scanned by 5 trained technicians and SCT was measured by a single examiner using calipers equipped on OCT machine. SCT was defined as the distance from the posterior edge of the retinal pigment epithelium to the choroid/sclera junction.

**Results:** The average SCT was 217.2µm preoperatively, 213.9µm at 1 day post-operatively (post-op), 217.9µm at 1 week post-op, 219.4µm at 1 month post-op and 220.4µm at 3 month post-op. There were no significant differences between time points of SCT measurement.

**Conclusions:** The SCT had not significantly changed either before or after phacoemulsification with IOL implantation.

**Commercial Relationships:** Minoru Tanigawa, None; Yuu Shimada, None; Yuu Ochiai, None; Haruyuki Ochiai, None; Yoko Tsukahara, None; Hiromitsu Yamanaka, None

**Program Number:** 5856 Poster Board Number: D0167

**Presentation Time:** 8:30 AM - 10:15 AM

**Classification and Quantitative Analysis of Geographic Atrophy Lesions Using Spectral-Domain Optical Coherence Tomography Jinfeng Qu1, 2, Muneeswar Nittala1, Amirhossein Hariri1, David M. Wu1, Srinivas Sadda1, 2. Ophthalmology, People’s Hospital of Peking University, Beijing, China; 1Doheny Image Reading Center, Doheny Eye Institute, Los Angeles, CA.

**Purpose:** The junctional zone at the border of areas of geographic atrophy (GA) in eyes with age-related macular degeneration (AMD) is an important target region for future therapeutic strategies. The goal of this study was to perform a detailed classification and quantitative characterization of the junctional zone using Spectral-Domain Optical Coherence Tomography (SD-OCT).

**Methods:** SD-OCT volume cube scans (Spectralis OCT, 1024 x 37, ART=9) were obtained from 11 eyes of 8 patients with GA due to AMD. Volume OCT data were imported into previously-described validated grading software (3D-OCTOR) and manual segmentation of the retinal pigment epithelium (RPE) and photoreceptor layers was performed on all B-scans (total of 407). RPE and photoreceptor defect maps were produced for each case. In addition, all B-scans which included the atrophic lesion were individually scrutinized to classify the overlap configuration of the border zone into one of three categories (Type 0; exact correspondence between the edge of the RPE defect and photoreceptor defect; Type 1: loss of photoreceptors proximal to the edge of the RPE defect; Type 2: preservation of photoreceptors beyond the edge of the RPE defect). The relative proportion of the various border configurations was expressed as a percentage of the perimeter of RPE defect.

**Results:** 183 of the B-scans were found to pass through the GA lesion, yielding 366 individual GA borders which were separately analyzed and classified. Quantitative manual segmentation analysis demonstrated that the mean area of the RPE defect was 4.2±4.9 mm², which was significantly smaller than the mean area of the photoreceptor defect which measured 4.8±4.6 mm² (paired t-test: p=0.005). When analyzed as a percentage of the perimeter of the atrophic lesion, the Type 1 configuration (photoreceptor loss despite RPE preservation) was more prevalent (45.6±9.6%, mean 66.0±14.2%) than either the Type 2 (0.9±35.5%, mean 17.0±11.2%) or Type 0 (2.3-32.7%, mean 19.3±10.8%) configurations.

**Conclusions:** The size of the OCT-visible RPE and photoreceptor defect in GA lesions differs significantly. There were significant areas where the photoreceptors survived despite absence of visible RPE cells, and also areas of photoreceptor loss despite apparent RPE preservation. These findings have implications for development of therapeutic strategies, particularly cell-replacement approaches.

**Commercial Relationships:** Jinfeng Qu, None; Muneeswar Nittala, None; Amirhossein Hariri, None; David M. Wu, None; Srinivas Sadda, Allergan (C), Genentech (C), Regeneron (C), Optos (C), Carl Zeiss Meditec (C), Optos (F), Carl Zeiss Meditec (F), Optovue (F)
**Program Number:** 5858  
**Poster Board Number:** D0169  
**Presentation Time:** 8:30 AM - 10:15 AM  
**Assessing IOLMaster Measurement of Eye Axial Length in Pathologic Myopia Patients with Staphyloma**  
**Jamie Leong, Ronald H. Silverman, Stanley Chang, Quan V. Hoang**  
Ophthalmology, Columbia University, New York, NY.  
**Purpose:** Pathologic myopia, or extreme near-sightedness, is a leading cause of blindness worldwide. In these eyes, there is axial lengthening and eye wall thinning, allowing for focal outpouchings (staphyloma). Accurate axial length measurement is critical in gauging myopic progression. Depending on the local shape or slope at the staphylomatous area being examined, there may be unreliable measurements due to aberrant reflections of light waves. The present work compares IOLMaster-measured axial lengths and manually-measured axial lengths on B-scan ultrasonography.  
**Methods:** A prospective study was performed on 5 pathologic myopia patients clinically diagnosed with staphyloma. 5 eyes underwent measurement with both IOLMaster and B-scan ultrasonography (Quantel CineScan, 10 MHz) oriented in the anterior-posterior direction. Axial length measurement with IOLMaster was compared to that found on manual measurement by a single investigator (JL), on static frames selected from video B-scan ultrasonography captured by an experienced ultrasonographer (RS).  
**Results:** Among pathologic myopia patients with staphyloma, paired t-test analysis shows no significant difference in axial lengths measured by IOLMaster and those manually measured on B-scan ultrasonography. Axial lengths measured by the IOLMaster were greater by an average of +0.64 mm (range -0.87 to +2.58, n = 5). Although this was not statistically significant (2-tailed paired t-test, p = 0.40), the range from -0.87 to +2.58 mm is equivalent to -2.61 diopters to +7.74 diopters (a 10.35 diopter range).  
**Conclusions:** Assessment of axial length in staphylomatous eyes may be challenging, potentially influenced by staphyloma location and local slope. Initial studies suggest that axial length measured by IOLMaster is comparable to that found by manual measurement on 2-D B-scan ultrasonography, but given the wide variation, the use of both methods together is likely to provide the most accurate results in staphylomatous eyes.  
**Commercial Relationships:** None.
**Conclusions:** Cyst APD pre-combination therapy does not correlate in a linear fashion to post-combination therapy APD. All eyes with larger cyst APDs responded and had a significant mean decrease in APD as compared with the intermediate group. The best response to treatment was in the smallest cyst category. These findings suggest that, although smaller cysts may have a better prognosis, larger cyst size does not predict a poor potential response to therapy. Further studies are warranted.

**Commercial Relationships:** Gautam Kamthan, None; Ronni M. Lieberman, None.

**Program Number:** 5861 Poster Board Number: D0172
**Presentation Time:** 8:30 AM - 10:15 AM

**Photoreceptor Changes on Multi-Modal Adaptive-Optics Imaging Correlate with Transient Abnormalities on Autofluorescence and Indocyanine Green Angiography in a Patient with Multiple Evanescent White Dot Syndrome**

**Purpose:** To use multimodal imaging to identify and characterize outer retinal changes in a patient with multiple evanescent white dot syndrome (MEWDS).

**Methods:** One eye of a patient with MEWDS was imaged using a multimodal retinal imaging system with adaptive optics (Physical Sciences Inc.; Andover MA), which includes both spectral domain optical coherence tomography (AO-OCT) and confocal scanning laser ophthalmoscopy (AO-cSLO) imaging channel as well as fundus photography, indocyanine green angiography (ICG) and with blue light fundus autofluorescence (FAF). The OCT channel uses a 1050 nm super luminescent diode source with a bandwidth of 85 nanometers. All scans were obtained at baseline and then three months later.

**Results:** At baseline, the images from fundus photography showed unilateral foveal granularity typical of MEWDS. The AO-OCT and AO-cSLO showed disruption in the photoreceptor layer. The AO-OCT displayed a break in the integrity of the inner segment ellipsoid on b-scan images and the AO-cSLO confirmed the extent of the change on en-face imaging of the photoreceptor mosaic. In these scans, the abnormality was delineated by a loss of individual resolution of photoreceptors. The FAF and ICG images showed disruption in deeper structures underlying the photoreceptor changes. The FAF showed areas of increased autofluorescence signaling within the retinal pigment epithelium and the ICG images showed blocked signal of dye in the choroidal vasculature, presumably from choroidal inflammation. The follow up images confirmed complete resolution of all changes at each layer.

**Conclusions:** Multimodal imaging in this case of MEWDS displays that the pathology involves the photoreceptors as well as the retinal pigment epithelium and choroid. Each layer seems to be effected simultaneous and all changes resolve with observation which correlates with the resolution of symptoms experienced by the patient. Multimodal imaging may be used to better understand the disease pathology.

**Commercial Relationships:** John E. Legarreta, None; Andrew D. Legarreta, None; Zach Nadler, None; Leanne T. Labriola, None

**Support:** National Institutes of Health CORE Grant P30 EY008098, Eye and Ear Foundation of Pittsburgh, PA, Unrestricted Grant from Research to Prevent Blindness, New York, NY

**Program Number:** 5862 Poster Board Number: D0173
**Presentation Time:** 8:30 AM - 10:15 AM

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**Unique Features of Choroidal Vasculature In Patients with Choroidal Neovascular Membranes**

**Swetangi D. Bhaaleeya, Donald J. D’Amico, Szilard Kiss.**

Ophthalmology, Weill Cornell Medical Center, New York City, NY.

**Purpose:** High-resolution spectral domain optical coherence tomography (SD-OCT) has revolutionized the detailed imaging of retinal anatomy and has become an important clinical tool in a variety of retinal disorders. SD-OCT combined with enhanced-depth imaging (EDI) has allowed for similar level of resolution for examining the anatomy of the choroid. The purpose of this study is to evaluate the choroidal vasculature in patients with active choroidal neovascularization (CNV) and to determine possible changes in the choroid in response to anti-vascular endothelial growth factor (anti-VEGF) treatment.

**Methods:** Seventeen eyes of 14 consecutive patients with CNV who underwent SD-OCT imaging with the Heidelberg Spectralis were included in this retrospective analysis. SD-OCT images with sufficient resolution to allow for evaluation of the choroidal vasculature were analyzed. B-scans of the choroidal vascular structure immediately underneath the CNV were evaluated.

**Results:** Forty-one percent of eyes (7 of 17) included in the study had CNV secondary to myopia; in 59% of eyes (10 of 17), the CNV was due to exudative age-related macular (AMD). The mean follow-up period was 13 months. Independent analysis of choroidal vasculature by 2 masked graders revealed that in all 17 eyes, there was at least one large caliber choroidal vessel either at the border or directly underneath the CNV (see figure). There were no significant changes noted in the choroidal anatomy in response to anti-VEGF treatment.

**Conclusions:** SD-OCT demonstrates the presence of large caliber choroidal vessels in association with CNV in patients with CNV due to AMD and myopic degeneration. These vessels do not appear to change in response to anti-VEGF therapy. The clinical significance of these findings will undoubtedly require larger prospective studies.

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**Commercial Relationships:** Swetangi D. Bhaaleeya, None; Donald J. D’Amico, OptiMedica, Inc (I), Neurotech, Inc (I), Genentech, Inc (C), Lux Biosciences, Inc (C); Szilard Kiss, Alcon (F), Alimera (F), Allergan (R), Optos (F), Optos (C), Optos (R), Eytech (C), Merge/OIS (C), Merge/OIS (I)

**Program Number:** 5863 Poster Board Number: D0174
**Presentation Time:** 8:30 AM - 10:15 AM

**Choroidal thickness after treatment of chronic central serous chorioretinopathy: half-fluence photodynamic therapy versus intravitreal injection of bevacizumab**

Yong Un Shin, Byang Ro Lee, Dong Eik Lee. Ophthalmology, Hanyang University Medical Center, Seoul, Republic of Korea.

**Purpose:** There has been no report comparing the effect on choroid between intravitreal injection of bevacizumab (IVB) and half-fluence photodynamic therapy (PDT) in treating chronic central serous chorioretinopathy (CSC). We investigated the change of choroidal...
thickness obtained by enhanced depth imaging (EDI) technique between two treatments.

**Methods:** For clinical diagnosis of CSC, each subject underwent comprehensive ophthalmological examination and imaging studies including fundus photography, spectral domain optical coherence tomography (SD-OCT) with EDI-technique, fluorescein angiography (FA), and indocyanine green angiography (IA). Of enrolled eyes with chronic CSC, 11 eyes were treated with an intravitreal injection of 0.05 ml (1.25 mg) of bevacizumab (IVB group) and 8 eyes were treated with half-fluence PDT (PDT group). Subfoveal choroidal thickness (CT) was measured before, 1 month and 3 months after treatment.

**Results:** Of eyes treated with IVB, 5 eyes showed persistent serous retinal detachment (SRD), while all eyes treated with PDT showed complete resolution of SRD at 3 months follow-up visit. Before treatment, mean subfoveal CT was 382.0±66.64 and 390.1±49.60 in IVB group and PDT group respectively (p = 0.057). After treatment, subfoveal CT in both groups was decreased compared to those before treatment. Mean subfoveal CT in IVB group was 370.20±45.13 at 1 month and 355.0±57.54 at 3 months, which was not statistically significant (p=0.202, 0.160). On the other hand, PDT group showed a statistically significant decrease in CT at 1 month (325.13 ± 45.57, p = 0.028) and 3 months (326.86 ± 50.46, p=0.043). The change of choroidal thickness was more pronounced in PDT group than in IVB group.

**Conclusions:** This is the first report to compare choroidal thickness between before and after IVB or PDT for treatment of chronic CSC. Half-fluence PDT is more effective to reduce choroidal thickness than IVB in chronic CSC. Our study suggests half-fluence PDT may show better therapeutic effect than IVB because of the difference of effect on the choroid.

**Commercial Relationships:** Yong Un Shin, None; Byung Ro Lee, Nidek (C); Dong Eik Lee, None

**Program Number:** 5864 Poster Board Number: D0175
**Presentation Time:** 8:30 AM - 10:15 AM

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**Progression of Atrophy of the Retinal Pigment Epithelium in Stargardt Macular Dystrophy on Fundus Autofluorescence Imaging**

**Emily Fletcher, Yulia Wolfsön, Beatriz E. Munoz, Hendrik P. Scholl.**

1. Ophthalmology, Johns Hopkins University, Baltimore, MD; 2. Retina Division, Gloucester Royal Hospital, Gloucester, United Kingdom; 3. Ophthalmology, Medical University Graz, Graz, Austria.

**Purpose:** To characterize baseline lesions of atrophy of the retinal pigment epithelium (RPE) from fundus autofluorescence (FAF) images and to estimate the annual rate of atrophy progression in a cohort of patients with Stargardt Macular Dystrophy (STGD).

**Methods:** In this prospective longitudinal observational study, 34 eyes of 18 STGD patients were included with a minimum observation period of 5 months. FAF imaging was obtained following a standard operating procedure. For each individual FAF image, atrophic lesions within the ETDRS grid were semi-automatically detected by the RegionFinder (Spectralis®, Heidelberg Engineering) and manually corrected to adjust the borders of atrophy. The automatic numerical output for the number of lesions per image and total area of atrophy were recorded for each individual FAF scan and the annual rate of progression was estimated. The study was approved by the Institutional Review Board.

**Results:** 83 FAF images were evaluated overall. The mean size of atrophy at baseline (34 FAF images) was 4.0 (SD: 6.60; median: 1.84; range: 0.06-33.45) mm². The mean number of lesions at baseline was 7.6 (SD: 10.5; median: 5.0; range: 1-64). The mean rate of progression was 0.92 (SD: 0.87; median: 0.67; range: -0.01-3.38) mm²/year as calculated from 49 follow-up FAF images. No association was found between the rate of progression and the number of atrophic areas at baseline (p=0.72). The annual progression rate appeared to be associated with the total atrophic area at baseline: accounting for within eye and within subject correlation, and adjusted for number of atrophic areas in a single scan, the relationship was significant (p = 0.024).

**Conclusions:** The mean rate of progression of atrophy of the RPE was found to be similar to a previous study using different analysis tools (Chen et al. Eye Res. 91:143-52). Larger areas of atrophy at baseline appear to be associated with higher progression rates. The RegionFinder offers a time-efficient method for the identification and quantification of atrophic areas on FAF images and allows to estimate progression rates in STGD and thus may prove to be useful for disease monitoring in clinical practice and for the analysis of outcome measures in future clinical trials in STGD.

**Commercial Relationships:** Emily Fletcher, None; Yulia Wolfsön, None; Beatriz E. Munoz, None; Hendrik P. Scholl. None

**Support:** Wynn-Gund Translational Research Acceleration Program Enhanced Research and Clinical Training Award, Clinical Research Institute (CRI) - Foundation Fighting Blindness (FFB; NNCD-CL-0310.0049-JHU-WG); Clinical/Research Fellowship Award in Inherited Retinal Degenerations 2011 of FFB; Macular
Degeneration Research Award, American Health Assistance Foundation (AHAF; M2010042); BAYER Clinical Training Award, BAYER Global Ophthalmology Awards Program; Unrestricted grant to the Wilmer Eye Institute from Research to Prevent Blindness. Schreodering Stipend Fonds zur Foerderung der wissenschaftlichen Forschung Projekt-number J3383-B23. H.P.N.S. is the Dr. Frieda Derdeyn Bambas Professor of Ophthalmology.

Program Number: 5866 Poster Board Number: D0177
Presentation Time: 8:30 AM - 10:15 AM

Macular Choroidal Thickness Evaluation By SD OCT In Patients Affected By Retinal Vein Occlusion
Davide Borroni, Ettore Melardi, Carlo Gandolfi, Muna Al Oum, Simone Donati, Maurizio Chiaravalli, Claudio Azzolini, Department of Surgical and Morphological Sciences, University of Insubria-Circolo Hospital, Varese, Italy.

Purpose: To evaluate macular choroidal thickness in patients affected by retinal vein vascular occlusion of recent presentation.

Methods: This observational case control study included 40 eyes of 20 consecutive patients affected by Retinal Vein Occlusion (RVO) of recent presentation (less than 3 months). Patients have been divided in three groups according to the type of occlusion for a statistical subanalysis (Central, Emiretinal or Branch retinal vein occlusion). The evaluation has been performed with Spectral Domain OCT (OTI, Toronto, Canada) evaluating macular retinal and choroidal thickness. Choroidal thickness was measured by means of a manual caliper in three different points: subfoveal, 3 mm nasal to the fovea and 3 mm temporal to the fovea. Measurements were performed in the affected eye and in the fellow eye as control. Clinical systemic parameters has been considered as vascular risk factors.

Results: The measurement of choroidal thickness in eyes affected by RVO showed a mean value (mean ± standard deviation) of 316.92±71.92 µm at the subfoveal point, 280.76±64.73µm at 3 mm nasal to fovea and 320±85.14 µm at 3 mm temporal to fovea. In the control eyes SD OCT evaluation showed a mean choroidal thickness of 258.88±40.75 µm at the subfoveal point, 220±33.91 µm at 3 mm nasal to fovea and 250 ± 52.44 µm at 3 mm temporal to fovea. Differences between all affected eyes and control eyes were statistically significant in all measurements. No significative differences were showed between pathology groups.

Conclusions: Our study shows significant macular choroidal thickness increase in patients with RVO, compared to control eyes. This observation could be explained to the collateral vein circulation in the early phases to drain blood deflux, as showed in different angiography studies. At the same time, the inflammatory component related to vascular occlusion could have a important influence on vein choroidal vascular dilatation, as in showed in uveitis. Our preliminary results represents a first step for a more complete evaluation of pathological aspects of RVO and to comprehend the rational effect of different therapies, from medical to surgical approaches.

Commercial Relationships: Davide Borroni, None; Ettore Melardi, None; Carlo Gandolfi, None; Muna Al Oum, None; Simone Donati, None; Maurizio Chiaravalli, None; Claudio Azzolini, None

Program Number: 5867 Poster Board Number: D0178
Presentation Time: 8:30 AM - 10:15 AM

The Dissociation Between the Ganglion Cell Analysis/Ganglion Cell Complex and Peripapillary Retinal Nerve Fiber Layer Thickness in Hereditary Retinal Disease
Sherry J. Bass, Anna Wong, Jerome Sherman. Clinical Sciences, SUNY College of Optometry, New York, NY.

Purpose: To report the dissociation between ganglion cell analysis (GCA)/ganglion cell complex (GCC) measurements and peripapillary retinal nerve fiber layer (RNFL) measurements on SD-OCT in patients with hereditary retinal disease

Methods: A retrospective study was performed on 47 patients with symmetric hereditary retinal disease who had SD-OCT macular scans and peripapillary RNFL thickness scans. Five patients had Achromatopsia, two patients had Leber Congenital Amaurosis, 35 patients had non-syndromic Retinitis Pigmentosa, two patients had Usher’s Syndrome, and one patient had X-Linked Juvenile Retinosclerosis. Macular and RNFL scans were performed on the Cirrus SD-OCT or I-Vue SD-OCT. The macular scans were used to determine the GCA on the Cirrus SD-OCT and the GCC on the I-Vue. GCA/GCC thickness and peripapillary RNFL thickness values were classified as supernormal, normal or abnormal, based on comparison with the instruments’ normative database.

Results: For the total group (all conditions), 78.72% of eyes demonstrated abnormal GCA/GCC thickness. 31.91% of the eyes with abnormal GCA/GCC thickness demonstrated supernormal RNFL thickness and 46.81% of eyes demonstrated normal RNFL thickness. The results for the 35 patients with Retinitis Pigmentosa revealed that 85.71% of eyes had abnormal GCA/GCC thickness. 34.29% of these eyes had supernormal RNFL thickness and 51.43% had normal RNFL thickness.

Conclusions: In hereditary retinal degenerations, there appears to be a dissociation between the GCA/GCC thickness, which was abnormal and peripapillary RNFL thickness, which was either supernormal or normal in the vast majority of patients. This has implications for the use of GCA/GCC analyses, popular in the diagnosis of glaucoma, but which must be used with caution in patients with hereditary retinal degenerations who may also be glaucoma suspects. One explanation is that the two technologies do not measure the same populations: the peripapillary (RNFL) measurements reflect 100% of the axons whereas the ganglion cell measurements only reflect a reported 50% of the total ganglion cell population. The ganglion cells which are measured by the GCC/GCA correlate higher with the temporal peripapillary measurement. In addition, an algorithm failure of inner retinal measurements in patients with outer retinal pathology cannot be ruled out.

Commercial Relationships: Sherry J. Bass, None; Anna Wong, None; Jerome Sherman, Optos, Inc. (F), Optos, Inc. (C), Optos, Inc. (R), Annidis (C), Annidis (R), Zeiss (R)

Program Number: 5868 Poster Board Number: D0179
Presentation Time: 8:30 AM - 10:15 AM

Myopia Progression Accompanying with Myopic Disc Change at the Convalescent Stage of Vogt-Koyanagi-Harada Disease

Purpose: It has been reported that Vogt-Koyanagi-Harada (VKH) disease at the convalescent stage shows a marked choroidal thinning, as seen in eyes with pathologic myopia. However, it is not clear if VKH disease causes development or progression of myopia. We examined myopia progression and myopic disc changes in patients with VKH disease at its convalescent stage.

Methods: Medical records of 25 VKH patients (49 eyes) whose disease duration was more than 1 year were reviewed. The ocular manifestations at the onset of the disease, and the long-term changes of refractive error and deformation of the optic disc, i.e. tilted disc and the development of conus, were investigated. Ovality of the optic disc was expressed as the ratio of vertical / horizontal disc diameter, and the myopic disc tilting was defined as the ovality change rate.
1.2 The changes of axial length (AL) were also investigated in 14 eyes of 7 patients, including 4 phakic eyes and 10 pseudophakic eyes at the initial examination.

**Results:** The mean follow-up period was 5.0 (range: 1.1 to 11.9) years. None of them had cataract or refractive surgery during a follow-up. The mean myopic refractive error at the final examination was significantly greater than that at the initial examination (-2.58 diopter (D) vs. 1.66 D, P=0.0004; paired t test). The refractive error remained stable (<2.0 D difference) in 42 eyes, whereas the refractive error changed by >2.0 D in 7 eyes. Among the 14 eyes whose changes in AL were examined, the AL remained stable (<0.1 mm/year difference) in 9 eyes, whereas AL increased by >0.1 mm/year in 5 eyes. Tilting disc and/or conus formation occurred in 12 eyes (Figure). The incidence of papillitis, serous retinal detachment, and hypotony at onset were not different significantly between myopic progressive eyes and stable eyes.

**Conclusions:** VKH patients showed progression of myopia and myopic disc changes in the convalescent stage of the disease. Although further studies are necessary, the choroidal thinning secondary to VKH might be related to myopic progression.

Fundus photography of 42-year-old woman showing myopic disc change. Eleven years later after onset, ovality of the disc (the ratio: vertical : horizontal diameter of the disc) changed from 1.04 to 1.73 in the right eye and from 1.06 to 1.55 in the left eye.

**Commercial Relationships:** Hiroyuki Takahashi, None; Hiroshi Takase, None; Noriaki Shimada, None; Kyoko Ohno-Matsui, None; Manabu Mochizuki, Santen (F), Senju (F), Ohtsuka (F), Daiichi-Sankyo (F), Mitsubishi-Tanabe (F), AMO Japan (F), Alcon Japan (F)

**Program Number:** 5869  **Poster Board Number:** D0180  **Presentation Time:** 8:30 AM - 10:15 AM

**Novel and safe technique for smartphone fundus photography:** Application in human and animal eyes

Luis J. Haddock1, David Kim2, Francois C. Delori1, Shizuo Mukai1, 1Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, MA; 2Ophthalmology, Scheepens Eye Research Institute, Boston, MA.

**Purpose:** We describe a novel technique of smartphone fundoscopy with the application Filmic Pro (Cinegenix LLC, Seattle, WA) and a 20D lens using the coaxial light source of the phone as an indirect ophthalmoscope. The spectral distribution was limited to the 400-700 nm wavelength with 70% of light in the blue/green part of the spectrum. Light levels were measured with a radiometer (USB4000 Ocean Optics, Dunedin, FL). Similar measurements were made on a standard indirect ophthalmoscope, Keeler Vantage Plus LED (Keeler Instruments, Broomall, PA) for comparison.

**Results:** The described technique of smartphone fundoscopy captured excellent images in awake adults and children under anesthesia (Figure 1). Photodocumentation of rabbit fundus was achieved in control and experimental eyes (Figure 2). Light levels were measured with a radiometer (USB4000 Ocean Optics, Dunedin, FL). Similar measurements were made on a standard indirect ophthalmoscope, Keeler Vantage Plus LED (Keeler Instruments, Broomall, PA) for comparison.

**Conclusions:** High quality fundus images can be captured using the smartphone and light source of the iPhone 4 in combination with the application Filmic Pro and a Koeppe lens. The iPhone 4 light source when used with a condensing lens for smartphone fundoscopy with the described technique was well within the safety standards for human eyes.

Figure 1 - Human eye with retinoblastoma

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Comparing Optos OTI and Heidelberg Spectralis SD-OCT in Patients with Diabetic Macular Edema

Samia Fatum, Magdalena Sinczak, Amun Sachdev, Victor Chong, Ophthalmology, Oxford University Hospitals NHS Trust, Oxford, United Kingdom.

**Purpose:** Heidelberg Spectralis Spectral Domain Optical Coherent Topography (SD-OCT) is often considered the current gold standard of SD-OCT. However, it does not have the ability to measure retinal function. In a previous study, microperimetry points from another machine were overlaid onto the SD-OCT scan. As the optics of the machines is different, it was not clear whether the point to point correlation was correct. The Optos OTI has the microperimetry in the same machine, allowing point to point co-localisation. In this study we compared the measurements of these two machines in patients with diabetic macular edema (DME).

**Methods:** Patients with early DME were recruited in this study. Best corrected visual acuity (BCVA) was measured by letter counting with the ETDRS chart. SD-OCT was measured by Spectralis and OTI in the same setting, one after the other. The central subfield and the parafoveal subfield (3mm) were analysed and compared between the two machines. The statistical analysis was calculated with SPSS.

**Results:** There were 62 eyes included in the study. The mean age was 58.1 years, the mean BCVA was 77.2 letters, and the mean retinal thicknesses were 310, 343, 344, 332, and 340 microns in the central, superior, temporal, inferior and nasal sub-field respectively, while the mean retinal thicknesses as measured by OTI were 237, 298, 297, 289, 290 microns in the central, superior, temporal, inferior and nasal sub-field specifically. The correlation of the two machines was highly significant in all five subfields (p<0.0001). The Pearson Correlations were 0.752, 0.85, 0.928, 0.839, and 0.823 in the central, superior, temporal, inferior and nasal sub-field respectively.

**Conclusions:** Although the absolute measurements of the two machines are significantly different, the correlation is over 75% in all sub-fields. This suggests that while it is not possible to transfer absolute measurements from one machine to the other, the OTI machine can be used for OCT measurements in patients with early DME requiring microperimetry assessment. Further studies are needed to identify the reason for these differences, which might allow us to have an even better correlation between the two machines.

**Commercial Relationships:** Samia Fatum, None; Magdalena Sinczak, None; Amun Sachdev, None; Victor Chong, Novartis (C), Bayer (C), Allergan (C), Pfizer (F), Novartis (F), Alimera Science (C), Quantel (R)
Ultra-wide field fluorescein angiography in patients with diabetic retinopathy
taneto tomiyasu, Shuichiro Hirahara, Manenori Yoshida, Miho Nozaki, Yuichiro Ogura. ophthalmology, Nagoya Univ Medical School, Nagoya, Japan.

**Purpose:** The ultra-wide field scanning laser ophthalmoscope (Optos®200Tx, Optos, Scotland, UK) provides retinal images of 200 degrees in a single capture which covers more than 80% of the retina. Fluorescein angiography (FA) with Optos®200Tx is useful to visualize the microcirculations of peripheral retina. It allows to evaluate peripheral pathology more precisely than the conventional fundus photography. The purpose of this study is to evaluate the FA findings of the eyes in diabetic retinopathy patients by using ultra-wide field FA (UWFA).

**Methods:** The UWFA was performed on 154 eyes of 77 patients with diabetic retinopathy (62 male, 15 female, average of age; 60.2±11.8 years). We divided the fundus into three zones, the posterior pole, the mid-periphery, and the far-periphery. Capillary non-perfusion areas in each zone were evaluated.

**Results:** One hundred thirty eyes (86%) exhibited capillary non-perfusion areas. The ischemic area was found in the posterior pole (60 eyes, 46%), the mid-peripheral zone (113 eyes, 87%), and the far-peripheral zone (84 eyes, 65%), respectively. Twenty-one eyes (16%) were found to have the capillary non-perfusion area only in the mid-periphery, while 10 eyes (8%) showed the non-perfusion area only in the far-periphery without any evidences of non-perfusion in the posterior pole and the mid-periphery. Fifty nine eyes (38%) exhibited neovascularization. They were found in the posterior pole (26 eyes, 44%), the mid-peripheral zone (53 eyes, 90%), and the far-peripheral zone (4 eyes, 7%), respectively.

**Conclusions:** The UWFA revealed the microcirculatory disturbance in the peripheral retina of diabetic patients which was not evident by the conventional fundus photography. The UWFA was useful for evaluating the status of diabetic retinopathy.

**Commercial Relationships:** taneto tomiyasu, None; Shuichiro Hirahara, None; Manenori Yoshida, None; Miho Nozaki, None; Yuichiro Ogura, None

**Program Number:** 5873 Poster Board Number: D0184
**Presentation Time:** 8:30 AM - 10:15 AM
**Repeatability and Reproducibility of Spectral-domain Optical Coherence Tomography in Measurement of Retinal Thickness in Rats**
TaeGi Kim, Ji Ho Yang, Jisang Han, Seung-Young Yu, Hyung-Woo Kwak. Ophthalmology, Kyung Hee University Hospital, Seoul, Republic of Korea.

**Purpose:** To evaluate the repeatability and reproducibility of spectral-domain optical coherence tomography (SD-OCT) .

**Methods:** 20 eyes of 10 LEO rats were anesthetized and RNFL circular scans were centered on optic nerve head with SD-OCT using built in Autorescan software. In each eyes, OCT scans were performed three times by two independent examiners. Rats were repositioned between scans. The interval between session 1 and session 2 was 1 day. The variability of total retinal thickness (TRT), thickness of retinal nerve fiber layer (RNFL) was measured. TRT and thickness of RNFL was assessed, standard deviation (SD), intraclass correlation coefficients (ICC) and coefficients of variation (CV) were calculated. Inter-examiner reproducibility was visualized by using Bland-Altman analysis.

**Results:** For TRT, intrasession and intersession ICCs with SD-OCT was 0.85 or higher. CV raged from 3.9 % to 4.8%. For RNFL thickness, intrasession and inter-session ICCs with SD-OCT was higher 0.65 or higher except session 1 of examiner 2. Inter-examiner ICCs was 0.74 for TRT and 0.70 for RNFL. The CV was 4.4 % for TRT and 6.0% for RNFL.

**Conclusions:** Measurement of TRT and thickness of RNFL show high intra-session, inter-session and inter-examiner repeatability and reproducibility in in vivo using SD-OCT. This method will help to allowing longitudinal study designs, following disease processes over time, and evaluation of therapeutic effects after experimental intervention.

**Commercial Relationships:** TaeGi Kim, None; Ji Ho Yang, None; Jisang Han, None; Seung-Young Yu, None; Hyung-Woo Kwak, None

**Program Number:** 5921
**Presentation Time:** 10:30 AM - 10:45 AM
**SD-OCT Progressive Alterations in a Family Affected with Müller Cell Sheen Dystrophy**
Valentina Franco-Cardenas, Jose Dalma-Weiszhausz, Rosa E. Martínez-Munoz, Alejandro Dalma. Retina, Asociacion para Evitar la Ceguera en Mexico, Mexico City, Mexico.

**Purpose:** Müller cell sheen dystrophy is a late onset autosomal dominant bilateral symmetric retinal disorder characterized by a wrinkled sheen-like appearance involving the posterior pole first reported by our group in 1991. The purpose of this study is to describe the spectral-domain optical coherence tomography (SD-OCT) findings in retinal architecture occurring during different stages of the disease in an affected family.

**Methods:** Case series. Forty-eight patients spanning three generations of a single family affected by Müller cell sheen dystrophy underwent full ophthalmological evaluation and SD-OCT on the same day. SD-OCT was evaluated for presence of posterior vitreous detachment (PVD), cysts location, foveal thickness and IS/OS disruption. Findings were cross-related to the patients visual acuity and age.

**Results:** Ten patients (19 eyes) affected with Müller cell sheen dystrophy presented with macular alterations on SD-OCT and were included in this case series. SD-OCT alterations presented as cystic spaces. The youngest patient with an altered SD-OCT was 48 years old. SD-OCT alterations increased with age and visual acuity declined over time. Alterations started in the internal layers of the retina and extended towards the external layers with time. None of the patients presented with a PVD. First, cystic spaces were noted between de internal limiting membrane (ILM) and retinal nerve fiber layer (RNFL); this change was noted in 19 eyes. The second change noted was optically empty spaces in the ganglion cell layer (GCL) in 16 eyes, followed by cysts in the inner nuclear layer (INL) in 14 eyes. When these cystic spaces reached the outer nuclear layer (ONL) the fovea became involved (10 eyes), macular edema appeared and visual acuity declined. End-stage changes included loss of the layered architecture of the retina (3 eyes) with significant retinal atrophy and IS/OS disruption (2 eyes)

**Conclusions:** SD-OCT changes in patients affected with Müller cell sheen dystrophy appear around the 5-6th decade of life. Small cystic spaces begin to appear around the arcades in the internal layers of the retina, they progress toward the external layers finally disrupting retinal architecture. Müller cells are present in all layers affected. This correlates with previous ERG findings, pointing towards Müller
cell dysfunction. It is possible that the cystic spaces seen on SD-OCT are a result of Müller cell degeneration.

![Diagram showing changes in steps and change noted](image)

Commercial Relationships: Valentina Franco-Cardenas. None; Jose Dalma-Weizhausz. None; Rosa E. Martinez-Munoz. None; Alejandro Dalma. None

Program Number: 5922
Presentation Time: 10:45 AM - 11:00 AM

**Outer Retina Analysis by Optical Coherence Tomography in Cone-Rod Dystrophy Patients**
Luiz H. Lima1, Juliana M. Sallum1, Richard F. Spaide2.
1Ophthalmology, Federal Unive of Sao Paulo-UNIFESP, Sao Paulo, Brazil; 2Vitreous, Retina, Macula Consultants of New York, New York, NY.

**Purpose:** To analyze the outer retinal layers with spectral-domain optical coherence tomography (SD-OCT) in patients with cone-rod dystrophy (CRD).

**Methods:** The diagnosis of CRD was determined by primary cone involvement or concomitant loss of both cones and rods. Electroretinography showed implicit time shift at 30-Hz flicker response and prevalent decrease of photopic over scotopic responses. Using SD-OCT, the outer retina was retrospectively evaluated in twenty-four eyes of twelve CRD patients. From the innermost to the outermost, the 4 studied hyperreflective outer retinal bands were labeled Band 1, the external limiting membrane (ELM), Band 2, the ellipsoid zone (EZ), Band 3, the interdigitation zone (IZ) between the cone outer segments and the apical processes of the retinal pigment epithelium (RPE) and Band 4, the retinal pigment epithelium (RPE) complex.

**Results:** The mean age of study patients was 30 years and the median visual acuity was 20/30. A ring maculopathy appearance involving the fovea area was observed in all study eyes. There was an absence of IZ in the entire length of SD-OCT scan, including the foveal area, in all 24 study eyes. Outside the foveal area, the ELM and EZ were intact in all study eyes. The intensity of the EZ was decreased in the entire length of SD-OCT scan in all study eyes. Within the foveal area, there was loss of the ELM and EZ in twenty (83%) and twenty-two eyes (92%), respectively. The RPE complex was identified in all study eyes. None of the study eyes revealed cystoid macular edema.

**Conclusions:** SD-OCT scans demonstrated complete absence of the IZ in CRD patients. Consistent with known histology of animal models of cone dystrophy, this finding may represent abnormal outer retinal morphology, including an absence of the outer segments themselves or a defective or absent interdigitation between the apical processes of the RPE with the cone outer segments.

Commercial Relationships: Luiz H. Lima. None; Juliana M. Sallum. None; Richard F. Spaide. Topcon (P), Thrombogenics (C), Bausch and Lomb (C)

Program Number: 5923
Presentation Time: 11:00 AM - 11:15 AM

**Atypical findings in Spectral Domain Optical Coherence Tomography of Ocular Toxoplasmosis with Active Lesions**
Florian M. Heusen, Yanling Ouyang, Qing Shao, Antonia M. Joussen, Uwe Pleyer. Ophthalmology, Charite - University Medicine Berlin, Berlin, Germany.

**Purpose:** To use the spectral domain optical coherence tomography (SD-OCT) to investigate the characteristic features in patients with active ocular toxoplasmosis (OT).

**Methods:** Patients with OT in at least one eye who underwent SD-OCT exam using a Spectralis OCT (Heidelberg Engineering, Germany) between June 28, 2010 and November 8, 2012 were retrospectively collected. Eyes with an active lesion that OCT scans covered were included. Detailed morphological features observed by SD-OCT were evaluated at baseline.

**Results:** One hundred forty four patients diagnosed with OT were reviewed. Among them, 14 eyes from 14 patients with active lesions were included (7 females). Their mean age was 35 (range, 18-35) year-old. Twelve lesions located in the macula and 11 in the fovea. Commonly reported abnormalities, including presence of vitreous cells (10 eyes), thickened hyaloid (7 eyes), epiretinal membrane (8 eyes), inner retinal layer irregularity (InRI, 7 eyes), outer retinal layer irregularity (OutRI, 10 eyes), intraretinal hyperreflective foci (7 eyes), intraretinal cystoid degeneration/cystoid macular edema (7 eyes), photoreceptor layer irregularity (10 eyes), retinal pigment epithelium (RPE) irregularity (4 eyes), RPE detachment (2 eyes), subretinal detachment (4 eyes) were observed. In addition, rare or unreported features, including spherical deposition on vitreoretinal interface (4 eyes), huge cystoid space (HCS, 4 eyes), splits in the outer photoreceptor layer (SOPRL, 3 eyes), splits in RPE/Bruch (SRPEB, 1 eye) and increased choroid intensity (ICI, 1 eye) were also found in these eyes. Regarding the involved retinal/choroidal layers, one eye with only InRI and 6 eyes with only OutRI, as well as 1 eye with only ICI without other abnormalities evaluated were observed in the study.

**Conclusions:** It is widely held that ocular toxoplasmosis involves inner retinal layers in the early course of the disease. Our findings including eyes with only OutRI or ICI were contrary to this understanding. In addition, HCS and SOPRL were not reported in OT, but other types of uveitis. Atypical features and atypical location of the lesion regarding the retinal choroidal structures found in our study may facilitate better understanding of the clinical manifestations and pathogenesis of the disease.

Commercial Relationships: Florian M. Heusen. Novartis (C); Yanling Ouyang. Bayer healthcare Pharmaceuticals Inc (R); Qing Shao. None; Antonia M. Joussen. None; Uwe Pleyer. None

Support: DLR ToxoNet02

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Changes after Phacoemulsification in Eyes with No Pre-operative Macular Pathology
Yulia Wolfson, Walter Stark, Susan B. Bressler, Neil M. Bressler.
Ophthalmology, Wilmer Eye Institute, Johns Hopkins University, Baltimore, MD.

Purpose: To evaluate short-term changes in macular retinal thickness following cataract surgery in eyes with no pre-operative macular pathology clinically across 3 different spectral domain optical coherence tomography (SD-OCT) devices.

Methods: With IRB approval, a consecutive, convenient cohort of patients scheduled for cataract surgery (89 patients, 101 eyes) with no clinical macular pathology were enrolled prospectively. Predispensing conditions for the post-surgical macular edema, such as diabetes or uveitis, were not exclusion criteria if the pre-op clinical exam of the macula was normal. SD-OCT macular scans on Optovue and either Cirrus or Spectralis SD-OCT devices were performed approximately 15 days pre- and 1-2 months post-op.

Results: Among 92 eyes completing the study, mean central subfield thickness (CST) increased 11, 13 and 9 microns, respectively, from the pre- to post-op visit for Optovue, Cirrus, and Spectralis OCTs, respectively. 6 eyes (7.7%), 4 eyes (10.2%), and 2 eyes (4.5%) experienced at least a 10% increase in the CST using Optovue, Cirrus, and Spectralis scans, respectively. A 3% or greater increase in macular volume was observed in 36%, 51%, and 47% of eyes evaluated by Optovue, Cirrus, and Spectralis OCTs, respectively. One case of post-surgical clinical CME, as diagnosed by the cataract surgeon, was identified among the 92 eyes at day 40.

Conclusions: In the short-term following cataract surgery in eyes with no pre-operative macular pathology, mild macular retinal thickening can be expected, as demonstrated in this study by 3 different SD-OCT devices. Although central retinal thickening is not likely to be clinically relevant in most cases, the integrated change in thickness across all 9 ETDRS subfields, expressed as an increase in the macular volume, can be expected in about half of the eyes. These findings extend previous results using time-domain OCT and provide data which can be considered when evaluating short-term changes in eyes with pre-operative pathology, such as diabetic macular edema, as the findings in this study likely represent the expected distribution of short-term change in retinal thickness and volume following cataract surgery in a population of eyes without pre-operative macular pathology.

Commercial Relationships: Yulia Wolfson, None; Walter Stark, VueCare (C); Susan B. Bressler, Novartis (F), Bausch and Lomb (F), Genentech (F), Thrombogenics (F), Lumenis (F), Notal vision (F), GlaxoSmithKline (C), allergan (F); Neil M. Bressler, Abbott Medical Optics, inc (F), Alimera Sciences (F), Allergan (F), Bausch &Lomb, Inc (F), Bayer (F), Carl Zeiss Meditec, Inc (F), ForSight Labs, LLC (F), Genentech, Inc (F), Genzyme Corporation (F), Lumenis, Inc (F), Notal Vision (F), Novartis Pharma AG (F), Pfizer, Inc (F), Regeneron Pharmaceuticals, Inc (F), Roche (F), Thrombogenics (F)

Support: 2011-12 Wilmer Research Grant Award (Johns Hopkins University School of Medicine)

Program Number: 5925
Presentation Time: 11:30 AM - 11:45 AM

Macular vascular development assessed by fluorescein angiography in premature newborn patients with retinopathy of prematurity
Maria A. Martinez-Castellanos, None; Rafael Romero Vera, Samantha Salinas Longoria, Fernando Schoenewolff, Virgilio Morales-Canton, Jans J. Fromow-Guerra, Maria A. Martinez-Castellanos. Assoc Para Evitar la Ceguera en Mexico, IAP, Mexico.

Purpose: To describe the macular characteristics with fluorescein angiography (FA) in retinopathy of prematurity (ROP), through the development of retinal vascularization.

Methods: Retrospective case series of infants who underwent retinal imaging and FA using a wide-angle device (RetCam-II; Clarity Medical System, Pleasanton, CA), under topical anesthesia. An intravenous injection of 10% solution of fluorescein, with total dosage 0.1ml/kg, was used.

Results: We included 23 eyes (12 patients) that were diagnosed with ROP stage 1, 2 or 3 with clinical normal macula. All the patients included presented an abnormal diffuse capillary leakage pattern upon FA. Mean gestational age at birth was 30 weeks (range 26-33). Mean postmenstrual age (PMA) at the first study was 41.42 weeks (range 33-45 weeks). Mean PMA at the last examination when the capillary leakage pattern disappears was 50.09 weeks (range 39-57 weeks). In the 23 eyes (100%) the capillary leakage pattern in the macula disappears once the retinal vasculature has reached the ora serrata.

Conclusions: Macular abnormalities in ROP eyes seen on angiographic evaluation could be explain due to parietal leakage because of vascular immaturity, related to the formation of the vessels walls. This study helps to understand the macular development. Largr studies should be performed to confirm these findings.

Commercial Relationships: Alberto Hernandez-Vargas, None; Guillermo Salcedo-Villanueva, None; Rafael Romero Vera, None; Samantha Salinas Longoria, None; Fernando Schoenewolff, None; Virgilio Morales-Canton, Clearside Biomedical (F); Jans J. Fromow-Guerra, None; Maria A. Martinez-Castellanos, None

Program Number: 5926
Presentation Time: 11:45 AM - 12:00 PM
Three-year multimodal imaging and predictive value of retinal nerve fiber layer axoplasmic debris in branch retinal vein occlusion
Marion R. Munk1, Stefan Sacu2, Roman Dunavoxelgyi3, Magdalena Baratisti1, Alessio Montuoro1, Gerlinde Matt1, Christopher G. Kiss1, Wolf Buehl1, Ursula Schmidt-Erfurth1. 1Dept of Ophthalmology, Medical University Vienna, Vienna, Austria; 2Vienna Reading Center, Medical University Vienna, Vienna, Austria.

Purpose: To assess the development and resolution of axoplasmic debris, presenting as cotton-wool spots (CWS) in branch retinal vein occlusion (BRVO) as well as their predictive-value for the need of treatment over three years.

Methods: Presence, size and fluorescent characteristics of CWS of 24 patients with BRVO≤8 weeks were retrospectively analyzed in color-fundus (CF), Spectralis SD-OCT, infrared and fluorescein angiography (FA) every 3 months for 3yrs. Using dedicated software, images from all devices were superimposed and presentation of axoplasmic-debris was compared in a point-to-point analysis. CWS were further evaluated as predictor for the number of ranibizumab-injections and for the need of argon-laser-coagulation (ALC) for 3yrs.

Results: 29 central lesions were analyzed. At baseline, 100% of the CWS were visible in SD-OCT, only 65.5% in CF-images. 86.2% CWS presented with corresponding changes in the IR-image and 100% in the FA. 31% of the CWS were hypofluorescent, 13.8% hyperfluorescent and 55.2% were initially hypofluorescent becoming...
en face map of segmented IS-OS layer- black area indicates absence of layer

Commercial Relationships: Barbara A. Blodi, None; Susie Chen, None; Yijun Huang, EyeKor, LLC. (I), Haag Streit USA (C); Jeong W. Pak, None; Amitha Domalpally, None

543 Proliferative Vitreoretinopathy
Thursday, May 09, 2013 10:30 AM-12:15 PM
Exhibit Hall Poster Session
Program #/Board # Range: 6250-6262/D0058-D0070
Organizing Section: Retina

Program Number: 6250 Poster Board Number: D0058
Presentation Time: 10:30 AM - 12:15 PM
Comparison of Gene Expression Profile of Epiretinal Membranes obtained from Eyes with Proliferative Vitreoretinopathy to that of Secondary Epiretinal Membranes
Shigeyo Yoshida, Ryo Asato, Takahito Nakama, Keijiro Ishikawa, Shintaro Nakao, Yukio Sassa, Hiroshi Enaida, Yuji Oshima, Tatsuro Ishibashi, Ophthalmology, Kyushu University, Fukuoka, Japan.

Purpose: Proliferative vitreoretinopathy (PVR) is a destructive complication of retinal detachment and vitreoretinal surgery which can lead to severe vision reduction by tractional retinal detachments. The purpose of this study was to determine the gene expression profile of epiretinal membranes (ERMs) associated with a PVR (PVR-ERM) and to compare it to the expression profile of less-aggressive secondary ERMs.

Methods: A PCR-amplified complementary DNA (cDNA) library was constructed using the RNAs isolated from ERMs obtained during vitrectomy. The sequence from the 5’ end was obtained for randomly selected clones and used to generate expressed sequence tags (ESTs).

Results: We obtained 1116 nonredundant clusters representing individual genes expressed in PVR-ERMs, and 799 clusters representing the genes expressed in secondary ERMs. The transcriptome of the PVR-ERMs was subdivided by functional subsets of genes related to metabolism, cell adhesion, cytoskeleton, signaling, and other functions, by FatiGo analysis. The genes highly expressed in PVR-ERMs were compared to those expressed in the secondary ERMs, and these were subdivided by cell adhesion, proliferation, and other functions. Querying 10 cell adhesion-related genes against the STRING database yielded 70 possible physical relationships to other genes/proteins, which included an additional 60 genes that were not detected in the PVR-ERM library. Of these, soluble CD44 and soluble vascular cellular adhesion molecule-1 were significantly increased in the vitreous of patients with PVR.

Conclusions: Our results support an earlier hypothesis that a PVR-ERM, even from genomic points of view, is an aberrant form of wound healing response. Genes preferentially expressed in PVR-
ERMes may play an important role in the progression of PVR and could be served as therapeutic targets.

**Commercial Relationships:** Shigeo Yoshida, None; Ryo Asato, None; Takahito Nakama, None; Keijiro Ishikawa, None; Shintaro Nakao, None; Yukio Sassa, None; Hiroshi Enaide, None; Yuji Oshima, None; Tatsuro Ishibashi, None

**Support:** Grants-in-Aid for Scientific Research from JSPS (23592574)

**Program Number:** 6251 Poster Board Number: D0059

**Presentation Time:** 10:30 AM - 12:15 PM

**miR-135b Regulates TGF-β1-Mediates Retinal Pigment Epithelial-Mesenchymal Transition**

*Fang Wang, Hui Li, Min Li.* Tenth People’s Hospital of Tongji University, Shanghai, China.

**Purpose:** To investigate the role of microRNAs (miRNAs) in TGF-β1-induced retinal pigment epithelial-mesenchymal transition (EMT) during proliferative vitreoretinopathy (PVR).

**Methods:** Microarray assay was performed for the identification of differentially expressed miRNAs in human retinal pigment epithelium (RPE) cell line ARPE-19 under normal and TGF-β1. The results were verified by quantitative real time RT-PCR (qRT-PCR). The function of miRNAs in TGF-β1-induced retinal pigment epithelial-mesenchymal transition was assessed by the transfection of specific miRNA inhibitors and mimics. Luciferase reporter gene assays and western blot analysis were performed to validate the target genes of miRNA.

**Results:** Microarray analysis identified six specific miRNAs which expressed differentially in normal ARPE-19 cells as compared to TGF-β1 treated ARPE-19 cells. Among them, miR-135b, miR-550a and miR-29b were downregulated and miR-455-3p, miR-22* and miR-3138 were upregulated. qRT-PCR was carried out to warrant the accuracy of the microarray assay. The results showed that miR-3138 was downregulated. We further investigate the role of miR-135b in TGF-β1 induced RPE cells EMT. Enforced expression of the miR-135b was sufficient to prevent TGF-β1-induced EMT. Conversely, inhibition of the miR-135b was sufficient to induce EMT.

**Conclusions:** These data suggest that downregulation of the miR-135b may be an important step in TGF-β1 induced retinal pigment epithelium EMT during PVR.

**Commercial Relationships:** Fang Wang, None; Hui Li, None; Min Li, None

**Support:** National Nature Science Funding of China (81271029)

**Program Number:** 6252 Poster Board Number: D0060

**Presentation Time:** 10:30 AM - 12:15 PM

**β-catenin signaling in RPE in experimental PVR**

*Kazuhiko Umazume¹, ², Lanhsin Liu¹, Kevin McDonald¹, Hiroshi Goto², Henry J. Kaplan¹, Shigeo Tamiya¹.* ¹Ophthalmology & Visual Sciences, University of Louisville, Louisville, KY; ²Ophthalmology, Tokyo Medical University, Tokyo, Japan.

**Purpose:** β-catenin signaling is an essential pathway that regulates numerous cellular processes. In this study, we investigated the role of β-catenin signaling in RPE cells in the development of proliferative vitreoretinopathy (PVR) using a swine model.

**Methods:** Western blot analysis and immunostaining were used to detect total β-catenin and active β-catenin (ABC) expression on RPE sheets. The role of β-catenin in RPE during epithelial-mesenchymal transition (EMT), cell migration, cell proliferation and cell contraction were assessed by marker protein staining using a scratch assay and type 1 collagen contraction assay. The effect of FH535, a β-catenin/TCF signaling inhibitor, on these features of cell de-differentiation was also investigated. The swine model of experimental PVR, in which RPE cells were injected into vitrectomized eyes, was used to assess the efficacy of FH535 in preventing a traction retinal detachment (TRD).

**Results:** Staining for ABC was detected in the nucleus of de-differentiated RPE cells but not in the nucleus of differentiated cells. Nuclear ABC expression in de-differentiated RPE cells was accompanied by reduced total β-catenin expression, suggesting that signaling and the subsequent degradation of β-catenin is occurring during or after EMT. FH535 prevented RPE cell EMT, migration, proliferation, and ECM contraction in a dose-dependent manner. Furthermore, FH535 significantly prevented TRD in vivo in the experimental swine PVR model. While TRD was observed in 7 out of 8 animals under control conditions, no animals treated with FH535 developed TRD (0/9).

**Conclusions:** β-catenin signaling is involved in EMT, migration, proliferation, and contraction of RPE cells and could be acting as one of the key regulators of PVR progression. The β-catenin/TCF signaling inhibitor FH535 significantly inhibited PVR-related RPE changes in vitro and prevented TRD in an experimental PVR model in the swine in vivo.

**Commercial Relationships:** Kazuhiko Umazume, None; Lanhsin Liu, None; Kevin McDonald, None; Hiroshi Goto, None; Henry J. Kaplan, None; Shigeo Tamiya, None

**Support:** Grant DM090475 from the DOD

**Program Number:** 6253 Poster Board Number: D0061

**Presentation Time:** 10:30 AM - 12:15 PM

**Periostin Promotes the Generation of Fibrous Membranes in Proliferative Vitreoretinopathy**

*Keijiro Ishikawa¹, Shigeo Yoshida¹, Shintaro Nakao¹, Takahito Nakama¹, Takeshi Kita¹, Yukio Sassa¹, Hiroshi Enaide¹, Yuji Oshima¹, Yoshihiro Kono², Tatsuro Ishibashi².* ¹Ophthalmology, Kyushu University, Fukuoka, Japan; ²Ophthalmology, Fukuoka University Chikushi Hospital, Fukuoka, Japan.

**Purpose:** We previously reported the increased expression of periostin in patients with proliferative vitreoretinopathy (PVR) and that periostin enhanced the proliferation, adhesion, migration and collagen synthesis through integrin αV-mediated FAK and AKT phosphorylation of retinal pigment epithelial (RPE) cells. The purpose of this study was to investigate, in vivo, the suppressive effect of periostin on the pathogenesis of fibrous membrane with PVR.

**Methods:** We generated mouse PVR model using C57BL/6 WT and periostin knockout mice according to the previous report. Masson’s trichrome staining and immunofluorescence staining with collagen type I antibody were performed to evaluate the formation of the fibrous membranes. We observed the effect of periostin neutralizing Ab (NAb) on rabbit PVR model that involves injecting RPE cells in the vitreous. Electrotetroinography and histological examination were performed to evaluate the retinal function after intravitreal injections of periostin NAb.

**Results:** The findings of Masson’s trichrome staining showed scarce collagen deposition in the lesions of periostin knockout mice compared to WT mice. The areas of fibrous membrane were significantly decreased in the RPE/choroidal flat mount preparations in periostin knockout mice compared to WT mice (p <0.05). Administration of periostin NAb significantly suppressed the progression of PVR from day 5 to day 21. The mean amplitude of the photopic b wave in the rabbit eye treated with periostin NAb was not significantly different from that of the control eye. The histological structure of the rabbit retina in the eyes injected with periostin NAb appeared normal.

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Methods: Human retinal pigment epithelial ARPE-19 cells were treated with proteasome inhibitor MG132 (2.5, 5, 10, 20, or 50μM) for 24h, 48h or 72h. Cell proliferation was determined using the CCK-8 reagent. Cell cycle and cell apoptosis were analyzed through propidium iodide (PI) and Annexin V staining using flow cytometry. Cell migration was tested by cell scratch assay. Also, ARPE-19 cells were treated with transforming growth factor-β (TGF-β) alone or plus MG132 for 24h, 48h or 72h. Cell morphology was observed with phase-contrast microscope. The expression of EMT markers was determined by RT-PCR, western blot and immunofluorescence.

Results: Compared with control group, cell proliferation was greatly suppressed by MG132 at 24h, 48h and 72h. Cell cycle was delayed and apoptosis rate was increased after MG132 treatment. Cell scratch assay indicated that the number of APRE cells migrated into the wounded area was lower in MG132 treated group. TGF-β treatment caused cells converted to a fibroblast-like shape, and upregulated the expression of EMT markers (α-SMA, fibronectin, N-cadherin, vimentin and Collagen IV). Inhibition of proteasome reversed TGF-β-induced cell change to a mesenchymal phenotype, and downregulated the expression of EMT markers.

Conclusions: These data suggest that proteasome inhibition decreases the proliferation, migration and EMT of ARPE-19 cells. These findings indicate that proteasome inhibitor MG132 may be an attractive candidate for blocking development of PVR.
Factor Xa and thrombin induce the expression of mesenchymal markers like α-SMA and collagen in a PDGF dependent manner. These data demonstrate that factor Xa and thrombin may contribute to PVR-associated changes in RPE cell behaviour.

**Commercial Relationships:** Jeroen Bastiaans, None; Jan C. van Meurs, None; Conny van Holten - Neelen, None; Petrus M. Van Hagen, None; Nicole Nagtzaam, None; Herbert Hooijkaas, None; Willem A. Dik, None

**Support:** COBR project code: 3.1.0

**Program Number:** 6256 Poster Board Number: D0064

**Presentation Time:** 10:30 AM - 12:15 PM

**AQUAPORIN-1 EXPRESSION IN MEMBRANES FROM PROLIFERATIVE VITREORETINOPATHY AND IN EPIRETINAL MEMBRANES**

Laure E. Caspers, Elie Motulsy, Dany Salik, Xavier Janssens, Bart Pion, Nargis Bolaky, Francoise Gregoire, Jason Perret, Francois Willermain, Christine Delporte.

**Ophthalmology, CHU Saint-Pierre Hospital - ULB, Brussels, Belgium; Laboratory of Pathophysiological and Nutritional Biochemistry, Université Libre de Bruxelles (ULB), Brussels, Belgium; Ophthalmology, Saint-Anne Saint-Rémi Hospital, Brussels, Belgium; R.I.B.H.M, Université Libre de Bruxelles (ULB), Brussels, Belgium.

**Purpose:** As Aquaporin-1 (AQP1) is involved in cell migration and proliferation, the purpose of the study was to investigate its expression in membranes from proliferative vitreoretinopathy (PVR) and epiretinal membranes (ERM).

**Methods:** 19 Membranes from PVR and ERM were collected following eye surgery. AQP1 mRNA and protein expression were determined by RT-qPCR and immunofluorescence in both PVR and ERM.

**Results:** AQP1 mRNA and protein were expressed in both PVR and ERM as shown by RT-qPCR and immunofluorescence. However, AQP1 protein expression was heterogeneous among and between PVR and ERM. AQP1 was colocalized with alpha-smooth muscle actin (α-SMA or Act) and colocalized with glial fibrillary acidic protein (GFAP). All the markers used including AQP1, GFAP and α-SMA were all statistically positively correlated. All the correlation coefficients calculated were all statistically significant except the correlation coefficient calculated between GFAP and GFAP+AQP1.

**Conclusions:** AQP1 mRNA and protein were expressed in both PVR and ERM. Due to the absence of α-SMA and GFAP colocalization, it is likely that AQP1 is expressed by at least two distinct cell types. AQP1 might play a role in cell migration and proliferation occurring during the formation of PVR and ERM. Therefore, AQP1 could represent a new therapeutic target.

**Commercial Relationships:** Laure E. Caspers, None; Elie Motulsy, None; Dany Salik, None; Xavier Janssens, None; Bart Pion, None; Nargis Bolaky, None; Francoise Gregoire, None; Jason Perret, None; Francois Willermain, None; Christine Delporte, None

**Program Number:** 6257 Poster Board Number: D0065

**Presentation Time:** 10:30 AM - 12:15 PM

**Distribution of MDM2 T309G polymorphism in European patients with Proliferative Vitreoretinopathy. Retina 4 project**

Salvador Pastor1,2, Irene Rodriguez-Hernandez2, Jimena Rojas Spano1, Rogelio Gonzalez-Sarmiento2, Jose-Carlos Pastor1.

1Ophthalmology, IOBA-University of Valladolid, Valladolid, Spain; 2Medicine, Molecular Medicine Unit, IBMMC and IBSAL, Salamanca, Spain.

**Purpose:** Our group has recently reported a significant association between p53 and Proliferative Vitreoretinopathy (PVR) after rhegmatogenous retinal detachment (RD). Murine double minute 2 (MDM2) gene codes for a protein that plays an important role as negative regulator of p53. The aim of this study has been to assess the distribution of MDM2 T309G genotypes among a series of patients suffering primary RD and secondary PVR.

**Methods:** As a component of the Retina 4 project (European multicentric study for analysing the genetic component of PVR) 555 DNA samples from patients with PVR (n:134) secondary to a primary RD (cases) and Non PVR (n:421) (controls) were analyzed for the MDM2 T309G polymorphism (rs2279744) using allele specific primer PCR. Genotypic and allelic frequencies were compared between cases and controls. The proportions of genotypes between sub-samples from different countries were analyzed.

**Results:** Significant differences (p<0.05, Fisher test) were observed regarding the MDM2 genotype frequencies at position 309 of intron 1 between the PVR cases (GG: 21.6%, TG: 54.5%, TT: 23.9 %) and controls (GG: 7.4%, TG: 43.9%, TT: 48.7%) and in G homozygote carriers between controls (95% CI G homozygote: 26.3 to 32.4) and cases (95% CI G homozygote: 42.9 to 54.9). The odd ratio of G carriers was 5.9 (95% CI: 3.2 to 11.2). The comparison of proportions of genotypes between sub-samples from different countries showed also significant differences between cases and controls. Distribution of G homozygote carriers between cases and controls revealed differences in Spain [35.1-53.0]/[22.6-32.9], Portugal [38.9-74.4]/[21.4-38.9], Holland [40.6-66.3]/[25.3-38.8] and also in UK [37.5-62.4]/[23.3-34.2]. The odds ratio of G carriers from Spain and Portugal was 5.4 (95% Confidence Interval (CI):2.3-12.7; p<0.05), whereas the odds ratio of G carriers from UK and Holland was 7.3 (95% CI: 2.8-19.1; p<0.05 ). All control samples were in Hardy-Weinberg equilibrium.

**Conclusions:** Our results suggest that the G allele of MDM2 SNP309 polymorphism is associated with a higher risk of developing PVR after a primary RD. Further studies are necessary to know if a down-regulation in the p53 tumor suppressor pathway could be an important key in developing of PVR. These findings could open new therapeutic targets in the prophylaxis of PVR.

**Commercial Relationships:** Salvador Pastor, None; Irene Rodriguez-Hernandez, None; Jimena Rojas Spano, None; Rogelio Gonzalez-Sarmiento, None; Jose-Carlos Pastor, None

**Program Number:** 6258 Poster Board Number: D0066

**Presentation Time:** 10:30 AM - 12:15 PM

**Epithelial cells promote fibroblast-mediated contraction of collagen gels by secreting bFGF**

Maryada Sharma, Hetian Lei, Steven Pennock, Andrius Kazlauskas, The Schepens Eye Research Institute, Massachusetts Eye and Ear Infirmary, Department of Ophthalmology, Harvard Medical School, Boston, MA.

**Purpose:** Fibrotic diseases compromise the function of many organs (e.g. skin, liver, heart, lung, kidneys) and arise at least in part from a breakdown in the relationship between epithelial and mesenchymal cells. One such disease is proliferative vitreoretinopathy (PVR), a blinding condition that has the quintessential feature of fibrotic diseases of being difficult to manage. In many cases, the pathogenesis of PVR involves formation of a tractional, fibrotic membrane populated by retinal pigment epithelial (RPE) cells and fibroblasts. The overall goal of this study was to investigate the nature of the relationship between these two cell types, with a particular focus on contraction.

**Methods:** Collagen gel contraction assay, which is an in vitro model for PVR, was used to assess the contraction abilities of RPE cells and fibroblasts in absence or presence of desired treatments. Condition medium (CM) was generated from RPE cells grown at high cell
density in DMEM without serum for 24-48 hr. A panel of 16 growth factors and cytokines that are implicated in PVR were quantified in CM by multiplex assay, and the best candidates were tested for their relative contribution to contraction by using neutralizing antibodies against them. The CM and potential candidate were tested for their ability to promote signalling events that are intrinsic to PVR.

**Results:** We discovered that while the intrinsic ability of RPE cells to contract collagen type I gels was dramatically lower than fibroblasts, RPEs greatly enhanced contraction of fibroblast-loaded collagen gels by secreting soluble factors. bFGF (basic fibroblast growth factor) was an essential component of the contraction promoting activity that RPEs secreted. Conditioned medium from human mammary epithelial cells also induced maximal contraction of fibroblast-containing collagen gels, and this activity was dependent on bFGF. In contrast to the nearly complete contraction of collagen gels observed under these conditions, TGFβs (transforming growth factor βs) or PDGF (platelet-derived growth factor) induced only a submaximal response.

**Conclusions:** We conclude that epithelial cells promote maximal contraction of fibroblasts by secreting growth factors such as bFGF. These insights provide a conceptual foundation for the design of approaches to prevent and manage fibrotic diseases that are driven by a dysfunctional relationship between epithelial cells and fibroblasts.

**Commercial Relationships:** Maryada Sharma, None; Hetian Lei, None; Steven Pennock, None; Andrius Kazlauskas, None

Support: EY012509

**Program Number:** 6259 **Poster Board Number:** D0067

**Presentation Time:** 10:30 AM - 12:15 PM

**Analysis of vitreous hyaluronan status in vitreoretinal diseases Koichi Nishitsu, 1 Mari Narumi, 1 Yoshiko Kashihigaki, 2 Takuma Shibata, 3 Jin Gong, 3 Hidemitsu Furukawa, 3 Hidetoshi Yamashita. 1Ophthalmology/Vis Sci, Yamagata University Sch of Med, Yamagata-shi, Japan; 2Yonezawa Women's Junior College, Yonezawa, Japan; 3Mechanical Systems Engineering, Graduate School of Science and Engineering, Yamagata University, Yonezawa, Japan.

**Purpose:** Vitreous plays important roles in the pathogenesis of vitreo-retinal diseases. It is mandatory to clarify the status of HA in vitreous. As the first step to investigate the roles of vitreous, we measured HA concentration in vitreous cavity and investigated microstructure of vitreous specimens obtained from the patients.

**Methods:** The study was based on the recommendation of the Declaration of Helsinki and approved by the Ethics Committee of the Yamagata University Faculty of Medicine, Japan. The vitreous specimens were obtained during vitrectomy for 24 subjects after securing written permission. The vitrectomy was performed using 23-gauge system by one surgeon (K.N). We devided the subjects 2 groups: “Quiescent group” (with little inflammatory reaction:3 with epiretinal membrane, 1 with macular hole) and “Active group” (with active inflammatory reactions:5 with proliferative diabetic retinopathy, 12 with retinal detachment, 2 with intraocular foreign body, 1 with branch retinal vein occlusion). To collect the undiluted vitreous samples, the core para plana vitrectomy without infusion was performed. Observed was the status whether the posterior vitreous detachment (PVD) occurred or not (PVD(+), PVD(-), respectively). We measured the HA concentration in the vitreous specimens by ELISA. The microstructure of gel-like network structure (mesh size) of HA of the vitreous specimens was investigated with scanning microscopic light scattering (SMILS) using newly developed analyzer to observe the microstructure containing heterogeneous gel materials.

**Results:** The mean HA concentration of the Quiescent group was higher than Active group (657.9 vs 134.7 ng/ml, respectively, p=0.036). The mean HA concentration of the PVD(-) group was higher than that of PVD(+) group (445.8 vs 61.97 ng/ml, respectively, p=0.0012). In the Active group, the mean HA concentration of the PVD(-) group was higher than that of PVD(+) group (304.5 vs 61.97 ng/ml, respectively, p=0.011). The mesh sizes of the specimens were different between PVD(+) group and PVD(-) group. (5.38 vs 1.03 nm, respectively)

**Conclusions:** The vitreous HA concentration was higher in the vitreous with inflammatory reaction than in that with less inflammatory reactions. HA concentration was higher in the vitreous without PVD than in that with PVD. The microstructure by measuring mesh sizes of HA of the vitreous specimens was different depending on the status of PVD.

**Commercial Relationships:** Koichi Nishitsu, None; Mari Narumi, None; Yoshiko Kashiwagi, None; Takuma Shibata, None; Jin Gong, None; Hidemitsu Furukawa, None; Hidetoshi Yamashita, Senju (C), Senju (P)

**Program Number:** 6260 **Poster Board Number:** D0068

**Presentation Time:** 10:30 AM - 12:15 PM

**Effect of SAHA on Fibrotic Change in Primate Retinal Pigment Epithelium Cells and Vitreous Cells Hiroki Hatanaka, 1 Naoki Okumura, 2 Noriko Koizumi, 2 Eri Mizuura, 1 Hiroatsu Hirano, 1 Junji Hamuro, 1 Shigeru Kinoshita. 1Ophthalmology, Kyoto Prefectural Univ of Med, Kyoto, Japan; 2Biomedical Engineering, Faculty of Life and Medical Sciences, Doshisha University, Kyotanabe, Japan.

**Purpose:** Proliferative eye diseases such as proliferative vitreoretinopathy and proliferative diabetic retinopathy are a major cause of blindness. The fibroblastic change of retinal pigment epithelial (RPE) cells and vitreous cells induce fibroblastic membrane, and ultimately carry out tractional retinal detachment via contraction. The purpose of this present study was to examine the feasibility of using suberoylanilide hydroxamic acid (SAHA) as a therapeutic tool for proliferative diseases using primary cultured primate RPE cells and rabbit vitreous cells.

**Methods:** As in the method described in our previous reported (Invest Ophthalmol Vis Sci 53: 6995-6963, 2012.), monkey RPE (MRPE) cells were isolated from the eyes of a cynomolgus monkey and then subcultured with culture medium containing 2% fetal bovine serum. MRPE cells and rabbit vitreous cells were then cultured. The culture medium was then replaced with fresh TGF-β2 (3ng/ml) medium with SAHA (300, 1000, and 3000 nM). Culture medium containing TGF-β2 without SAHA was used for the control. Cell morphology was examined by phase contrast microscopy after 48 hours of incubation. As an in vitro contraction model, rabbit vitreous cells were cultured in collagen gels at the density of 5x105 cells/mm2. The culture medium was then replaced with fresh medium containing TGF-β2 with or without SAHA (3, 10, and 30 µM). The collagen gel contraction was then evaluated by Image J software after 5 days of incubation.

**Results:** The fibroblastic change of MRPE cells were suppressed by 1000 nM of SAHA, while fibroblastic change was observed in the control cells. The incidence of fibrotic MRPE cells was significantly reduced from 38.6±1.3% in the TGF-β2 group to 9.3±1.3% in the TGF-β2 with SAHA group. In the in vitro contraction model, contraction induced by TGF-β2 was not observed in ARPE-19, but was observed in vitreous cells. The mean area of the collagen gels in the TGF-β2 with SAHA group (30µM) was 77.6%, while that in the TGF-β2 group was 66.0% as a ratio of the initial area, respectively (p<0.05).

**Conclusions:** The results of this study demonstrate that SAHA
inhibits the fibrotic change of RPE cells and the contraction of vitreous cells. We speculate that SAHA will become an applicable pharmaceutical treatment for proliferative vitreous eye diseases. **Commercial Relationships:** Hiroki Hatanaka, None; Naoki Okumura, None; Noriko Koizumi, None; Eri Mizuhara, None; Hiroatsu Hirano, None; Junji Hamuro, None; Shigeru Kinoshita, Senju Pharmaceutical Co (P), Santen Pharmaceutical Co (P), Otsuka Pharmaceutical Co (C), Alcon (R), AMO (R), HOYA (R)

**Program Number:** 6261 Poster Board Number: D0069

**Presentation Time:** 10:30 AM - 12:15 PM

**Immunospecific targeting of fibronectin towards an anti-fibrotic therapy, with special emphasis on proliferative vitreoretinopathy (PVR)**  
**Manni Luthra-Guptasarma**, Maryada Sharma1, Shweta Sharma1, Anil Tiwari1, Vishali Gupta2, Anam Gupta2, Immunopathology, PGIMER Chandigarh, Chandigarh, India; 2Ophthalmology, PGIMER Chandigarh, Chandigarh, India; 3The Schepens Eye Research Institute; Department of Ophthalmology and Visual Sciences, Harvard Medical School, Boston, MA

**Purpose:** Proliferative vitreoretinopathy (PVR) involves fibrotic pathology. Fibrosis is characterized by excessive accumulation of scar tissue due to exaggerated deposition of extracellular matrix components (ECM). Contractile membranes formed during PVR contain various cell types, including retinal pig epithelial cells (RPE). The ECM surrounding RPE cells mainly consists of the protein, fibronectin. Together with the vitreous, fibronectin creates microenvironments in which RPE cells proliferate. Our purpose was to target fibronectin, using phage display-selected and re-engineered single chain variable fragment (scFv) antibodies, to prevent ECM deposition.

**Methods:** Phage display-based human scFv antibody library screening was done against the N-terminal 30 kDa region of fibronectin to identify scFv antibodies capable of binding to this region. One chosen antibody (Fn52) was engineered to introduce an N-terminal RGDS tag, to create the Fn52RGDS antibody. Both antibodies were used in cultures of D407 RPE cells grown in the presence of patient-derived vitreous and sub-retinal fluid. A variety of cell-based assays were used to examine the effect of the antibodies on cell viability, proliferation, adhesion, migration, collagen gel contraction, and fibronectin deposition levels.

**Results:** We have successfully developed fully human, fibronectin-specific single chain variable fragment antibodies that act in one, or both, of the following ways: i) they bind to cryptic sites in fibronectin, preventing its self polymerization/fibrillogenesis, and ii) they interact with cell surface receptors (integrins) through an ‘RGD’ sequence tag, blocking downstream signaling. Fn52RGDS effectively inhibits hallmark features of fibrosis, such as proliferation, migration, adhesion, fibronectin polymerization, matrix metalloprotease (MMP) expression, as well as reduced collagen gel contraction (a model of fibrotic tissue remodeling).

**Conclusions:** Fn52RGDS is a novel anti-fibrotic candidate therapeutic agent that may be used to reduce fibrosis in PVR and also in pathological situations involving tumors and thrombosis.

**Commercial Relationships:** Manni Luthra-Guptasarma, None; Maryada Sharma, None; Shweta Sharma, None; Anil Tiwari, None; Vishali Gupta, Allergan (R); Amad Gupta, None

**Support:** Department of Science and Technology (DST), Government of India

**Program Number:** 6262 Poster Board Number: D0070

**Presentation Time:** 10:30 AM - 12:15 PM

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John G. Edwards¹, Gregory R. Jackson². ¹MacuLogix, Inc, Atlanta, GA; ²Penn State College of Medicine, Hershey, PA.

Purpose: For acceptance of dark adaptation as a clinical trial endpoint in studies of age-related macular degeneration (AMD), it is necessary to identify a single parameter that describes the speed of rod-mediated recovery. In addition, the parameter must be calculated using the same algorithm for every study participant. To fulfill these requirements, we developed the rod intercept. This poster describes the rod intercept algorithm and compares it to conventional nonlinear regression modeling.

Methods: Representative dark adaptation curves were selected for the four dark adaptation phenotypes encountered in AMD studies. Dark adaptation speed was estimated using the rod intercept algorithm and multiple nonlinear regression models. The resulting parameters were compared and assessed against the requirements for a single summary parameter and a uniform methodology.

Results: A case series of eight dark adaptation curves was analyzed, two each for the four dark adaptation phenotypes. The rod intercept algorithm successfully estimated dark adaptation speed in all cases (8/8). None of the nonlinear regression models was able to estimate dark adaptation speed for more than two cases (2/8). To estimate dark adaptation speed for all eight cases using nonlinear regression, four different models were required. The common practice in general research of selectively deleting data segments to make a single model work for all dark adaptation phenotypes is considered data adulteration in clinical trials and is not acceptable.

Conclusions: The rod intercept algorithm provides a single, uniform methodology for estimation of dark adaptation speed. This satisfies the need in clinical studies of AMD to use the same methodology to analyze the full range of dark adaptation phenotypes encountered. Furthermore, the rod intercept is robust to changes in the dark adaptation phenotype of an individual over time.

Commercial Relationships: John G. Edwards, MacuLogix, Inc (I), MacuLogix, Inc (E), MacuLogix, Inc (P), MacuLogix, Inc (S); Gregory R. Jackson, MacuLogix (F), MacuLogix (I), MacuLogix (E), Genentech (R)

Program Number: 6264 Poster Board Number: D0080
Presentation Time: 10:30 AM - 12:15 PM

Specular Photomicrographic Assessment of the Effect of Anti-VEGF Intravitreal Injections on Corneal Thickness and Endothelial Cell Density (CD) and Morphology
Faysal El-Jabali, Georgios Papastergiou, Michael D. Bennett, Karl E. Waite. Ophthalmology - Retina, Retina Institute of Hawaii, Honolulu, HI.

Purpose: Patients with active Wet Age-related Macular Degeneration (Wet AMD) often receive multiple intravitreal injections of Anti-VEGF medications. The objective of this study was to assess changes in corneal endothelial cell density (CECD) and morphology, as well as on corneal thickness in patients receiving anti-VEGF treatments over a period of six to twelve months of therapy.

Methods: Fifty five patients with active Wet AMD, who were actively receiving anti-VEGF intravitreal medications were enrolled in a prospective study to measure the changes in corneal endothelial cell density, morphology and associated corneal thickness measurements. Six and twelve month non-contact spectral photomicrographic assessments (Tomey EM-3000) were obtained. Study parameters including number and type of anti-VEGF medication received, corneal endothelial cell density (CECD), central corneal pachymetry, and morphology changes (coefficient of variation C, standard deviation of cell area SD, mean cell area MCA). The fellow untreated eyes of each patient served as age matched control eyes.

Results: During the first six months, study eyes received an average of 4 ± 1 treatments, and averaged 8 ± 1 treatments by twelve months. The baseline CD of treated eyes was 2152 ± 286 /mm2 and decreased to 2089 ± 290 (P > 0.05) at the midpoint datapoint. Similarly, the average baseline CD of control eyes was 2351 ± 270 with a decrease to 2274 ± 272 (p<0.05) at the final data point. Average central corneal pachymetry was 540 ± 25 μm at baseline. There was no statistically significant change in central corneal pachymetry, mean C, SD or MCA at the end of the observation period.

Conclusions: The study suggests that frequent administration of anti-VEGF agents over a period of six and twelve months, does not seem to significantly affect corneal endothelial cells or corneal thickness. A longer follow-up is required to determine long-term effects of anti-VEGF on corneal endothelial density and morphology.

Commercial Relationships: Faysal El-Jabali, None; Georgios Papastergiou, None; Michael D. Bennett, None; Karl E. Waite, None

Program Number: 6265 Poster Board Number: D0081
Presentation Time: 10:30 AM - 12:15 PM

Retinal and Choroidal Thickness Changes Over Time in Patients with Neovascular Age-related Macular Degeneration Treated with Anti-VEGF

Purpose: To assess changes over time in central macular thickness, central foveal thickness, volume and choroidal thickness in patients with exudative age-related macular degeneration (AMD) treated with intravitreal anti-VEGF using spectral-domain optical coherence tomography (SD-OCT).

Methods: Consecutive subjects with exudative AMD were studied. Data from January 2008 to October 2012 was reviewed. Inclusion criteria: minimum of 3 anti-VEGF injections and at least 6-month follow up. SD-OCTs at time-points without signs of CNV activity were analyzed (i.e. no subretinal and/or intraretinal fluid). Patients with evidence of subfoveal fibrosis, epiretinal membrane, macular hole, high myopia and CNV other than AMD were excluded. Measurements were obtained by Spectralis (Heidelberg, Germany) and Image J® software, including Central Foveal Thickness (CFT), Central macular thickness (CMT), macular volume and choroidal thickness. Manual correction was performed on retinal thickness b-scans. Baseline OCT image was compared with last follow-up visit. Changes between baseline and follow-up CFT, CMT, macular volume and choroidal thickness were calculated.

Results: 20 eyes of 20 patients with exudative AMD were analyzed. 55% of patients were female with mean age of 86.9 years ± 6.53. The mean study interval was 25.9 months (±11.78, range 7.5-4.5). The mean baseline best-corrected visual acuity was 20/95 (0.68 logMAR, ± 0.39) and after injections was 20/67 (0.53 logMAR ± 0.38). Mean number of injections was 11. Mean baseline CFT, CMT, macular volume at 6mm, macular volume at 3mm and choroidal thickness were 224.05 μm ± 37.31, 259.1 μm ± 29.16, 7.51 mm3 ± 0.85, 2.08 mm3 ± 0.14 and 172.3 μm ± 80.59, respectively. From baseline to final exam, CFT showed 24.25 μm decrease to a mean of 199.8 μm ± 32.05 (p<0.001). The CMT showed 4.45 μm ± 21.22 decrease to a mean of 254.65 μm ± 35.54 (p=0.180). Macular volume at 6 mm showed 0.15 ± 0.22 decrease to a mean of 7.36 mm3 ± 0.87 (p=0.0041) and at 3 mm showed 0.05 mm3 ± 0.11 decrease to a mean of 2.01 mm3 ± 0.16 (p=0.0159). The choroidal thickness showed 11.65 μm ± 11.38 decrease to a mean of 160.65 μm ± 76.43 (p<0.0001). CFT thinning was observed in 90% of patients (p=0.0001).
Conclusions: After a time interval, treated patients with exudative AMD underwent a reduction in central foveal thickness, central macular thickness, macular volume and choroidal thickness.

Commercial Relationships: Thais S. Mendes, None; Moreno Menghini, None; Ashleigh L. Levison, None; Soraya Rofagha, None; Robert B. Bhisitkul, Genentech (C)

Program Number: 6266 Poster Board Number: D0082
Presentation Time: 10:30 AM - 12:15 PM
Is foveal RPE autofluorescence a predictor of visual outcome in wet Age Related Macular Degeneration patients treated with Ranibizumab?
Maria Dimitry, Nitin Jain, Lorraine North, Manju N. Chandran, Geeta Menon. Frimley Park Hospital, Frimley, United Kingdom.

Purpose: Autofluorescence (AF) images are thought to represent the metabolic turnover of retinal pigment epithelial cells where increased AF may be due to poor outer segment photoreceptor function.

Increased foveal AF has been proposed as a poor prognostic factor for visual acuity outcome in wet AMD patients on anti-VEGF therapy. The aim of this study is to evaluate the correlation between AF imaging and visual outcome.

Methods: This is a retrospective study of 58 patients and 60 eyes with treatment-naive exudative macular degeneration identified during the 6 months period (Oct 2010 to March 2011). Patients were treated with three standard loading doses of Ranibizumab and followed up monthly with further injections if required. Foveal AF images (Heidelberg Retina Angiograph) were analysed for normal, increased, decreased or increased + decreased AF within a 500 to 1000 microns radius from the fovea at presentation. Best corrected visual acuity (BCVA) was measured at presentation and 12 months follow-up. The non parametric Mann-Whitney U test was used to analyse the data.

Results: At presentation, analysis of AF showed a significant difference in BCVA in eyes with changes on autofluorescence within 500 microns (p=0.039) and 1000 microns (p=0.020). At 12 months, analysis of AF showed no significant difference in BCVA in eyes with changes on autofluorescence within 500 microns (p=0.08) and 1000 microns (p=0.079).

At presentation and 12 months, comparison of eyes with normal AF and increased AF show no significant difference in visual acuity in 500 microns (0 months p=0.434; 12 months p=0.497) and 1000 microns (0 months p=0.231; 12 months p=0.435).

Conclusions: Visual outcomes following treatment of wet age related macular degeneration is multifactorial. A previous suggestion that a change or increase in foveal AF at presentation may affect visual outcome was based on a follow-up period of less than 6 months. At 12 months follow-up, this study shows no significant correlation between changes or increase in AF at presentation and visual outcome.

Commercial Relationships: Maria Dimitry, None; Nitin Jain, None; Lorraine North, None; Manju N. Chandran, None; Geeta Menon, NOVARTIS (R), ALLERGAN (R), BAYER (R)

Program Number: 6267 Poster Board Number: D0083
Presentation Time: 10:30 AM - 12:15 PM
Intravitreal anti-VEGF therapy for vascularized serous pigment epithelial detachment in age-related macular degeneration
Lucia Finocchio, Daniela Bacherini, Fabrizio Gianciotti, Giovanni Giacomelli, Cinzia Mazzini, Lorenzo Vannozzi, Ilaria Biagini, Gianni Virgili, Ugo Menchini. Department of Specialistic Surgical Sciences, Eye Clinic, University of Florence, Florence, Italy.

Purpose: To assess the efficacy of intravitreal bevacizumab and/or ranibizumab in the treatment of choroidal neovascularization (CNV) associated with serous pigment epithelial detachment (s-PED) due to age-related macular degeneration (AMD).

Methods: Retrospective, non comparative case series. We studied 26 consecutive eyes with occult CNV and serous PED secondary to AMD. Patients with a mean age of 75.3 years (SD:5.8) were treated with intravitreal anti-VEGF according to a pro re nata regimen (first loading phase of three monthly injections and then maintenance with injections as needed). 11 patients received ranibizumab, 6 bevacizumab and 9 eyes received both drugs. Best corrected ETDRS visual acuity (BCVA), optical coherence tomography (OCT) and fluorescein angiography (FA) were evaluated at baseline and quarterly. Mean follow-up ranged from 9 to 26 months (mean:13.5) after the first injection.

Results: Mean baseline BCVA worsened from 0.46 LogMAR to 0.70 LogMAR at 9 months, up to 0.79 LogMAR at 1-year follow-up, which was a loss of 0.33 LogMAR. Mean greatest linear diameter (GLD) of PED increased from 4486 μm (SD:1324μm) at baseline to 4860 μm (SD:1924μm) at 1-year follow-up. The mean maximum height of PED was 578 μm (SD:304μm) at baseline and 344 μm (SD:223μm) after 12 months. The mean central retinal thickness (CRT) decreased from 271 μm (SD:90μm) at baseline to 260 μm (SD:126μm) at 1-year follow-up. There was no influence of either baseline BCVA or of number of anti-VEGF injections on visual outcomes (p>0.10). There was a borderline trend (p=0.064) of GLD on affecting response to treatment. Maximum height of PED and CRT did not influence functional outcomes (p>0.10). The mean number of injections was 5.5. An RPE tear occurred in 27% of the patients (n=7) on average after 3.5 injections.

There was no difference in baseline GLD size and maximum height of PED between patients that developed RPE tear and patients without it.

Conclusions: In our study intravitreal anti-VEGF therapy did not prevent visual acuity loss and RPE tear rate was high. Therefore we believe that closer follow-up should be performed or a different treatment regimen should be adopted in this special subgroup of lesions. Patients should be alerted about the severe prognosis and the risk of vision loss due to RPE tear after anti-VEGF therapy.

Commercial Relationships: Lucia Finocchio, None; Daniela Bacherini, None; Fabrizio Gianciotti, None; Giovanni Giacomelli, None; Cinzia Mazzini, None; Lorenzo Vannozzi, None; Ilaria Biagini, None; Gianni Virgili, None; Ugo Menchini, None

Program Number: 6268 Poster Board Number: D0084
Presentation Time: 10:30 AM - 12:15 PM
Outer Retinal Tubulations in the Comparison of AMD Treatments Trials (CATT)
Joo Yong Lee1,2, Francisco A. Folgar1, Cynthia A. Toth1, Glenn J. Jaffe1, 2Duke Eye Center, Durham, NC; 3Ophthalmology, Asan Medical Center, University of Ulsan, Seoul, Republic of Korea.

Purpose: To determine the prevalence of outer retinal tubulation (ORT) seen on spectral domain optical coherence tomography (SD-OCT) in eyes with neovascular age-related macular degeneration (ARM) following anti-VEGF therapy, and to correlate ORTs with intra-retinal fluid (IRF), subretinal fluid (SRF), and retinal, subretinal fluid, and subretinal tissue complex (SRTC) thickness.

Methods: Participants in CATT were randomly assigned to ranibizumab (0.5mg) or bevacizumab (1.25mg) treatment and to a monthly or PRN injection dosing regimen. A subset, 81 eyes had SD-OCT scans beginning at Week 56. The original CATT grading protocol did not distinguish ORTs from cysts in eyes with IRF, or ORTs from small SRF pockets in eyes with SRF. Accordingly the subset of 58 eyes at Week 56 with IRF and SRF was selected for ORT analysis. Horizontal SD-OCT B-scan images as determined by ©2013, 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 arvo@arvo.org.
the CATT OCT Reading Center, were evaluated. Cirrus 512x128 or Spectralis 20°x20° volume cube scan protocols were used to acquire SD-OCT images. 2 independent readers graded scans, and a senior reader arbitrated discrepant grades. The prevalence of ORTs, identified as a tubular structure seen on at least 3 consecutive Cirrus B scans or 2 consecutive Spectralis B scans was determined. Retinal, SRF, and SRTC focal center thicknesses were compared in eyes with and without ORTs.

**Results:** Of the 81 eyes, 7 (8.4%) had ORTs. Among the 38 eyes with IRF, 7 (18.4%) also had ORTs and among 20 eyes with only SRF none had ORTs. Among eyes with IRF and ORT, the mean foveal center retinal, SRF, and SRTC thicknesses were 116.1±40.6, 4.7±12.5 µm, and 96.4±68.3, respectively. The corresponding mean thicknesses in eyes without ORTs were 180.6±92.5µm, 4.8±18.6µm, and 146.9±126.8µm respectively. The difference in mean retinal thickness (64.5 µm) in eyes with and without ORTs was statistically significantly (p=0.009).

**Conclusions:** ORTs were seen relatively commonly in eyes with neovascular AMD and residual IRF following anti-VEGF therapy. Eyes with ORTs had thinner retinas than those without ORTs. These findings suggest that ORTs are related to degenerative changes in neural tissue in eyes with residual IRF.

**Commercial Relationships:** Joo Yong Lee. None; Francisco A. Folgar. None; Cynthia A. Toth, Genentech (F), Biogen (F), Physical Sciences Inc. (F), Unlicensed (P); Glenn J. Jaffe, Heidelberg Engineering (C), Regeneron Pharmaceuticals (F), Neurotech USA (C), Abbott (C), Psivida (F), Pfizer (C), Bayer (C)

**Clinical Trial:** NCT00593450

**Program Number:** 6269 **Poster Board Number:** D0085

**Presentation Time:** 10:30 AM - 12:15 PM

**Retinal Pigment Epithelium Atrophy in Patients Receiving Intravitreal Anti-Vascular Endothelial Growth Factor Therapy for Neovascular Age-Related Macular Degeneration**

Luna Xu1 2, Sarah Mrejen1 4, Roberto Gallego-Pinazo4, Jesse J. Jung1 3, Marcela Marsiglia1 4, Sucharita Boddu1, K Bailey Freund4, 5, Vitreous Retina Macula Consultants of New York, New York, NY; 1Department of Medicine, St. Vincent's Medical Center, Bridgeport, CT; 2Department of Ophthalmology, New York University School of Medicine, New York, NY; 3LuEsther T. Mertz Retinal Research Center, Manhattan Eye, Ear, and Throat Hospital, New York, NY; 4Department of Ophthalmology, University and Polytechnic Hospital La Fe, Valencia, Spain.

**Purpose:** To examine factors associated with the progression of retinal pigment epithelium (RPE) atrophy in treatment naïve eyes with neovascular age-related macular degeneration (AMD) using combined confocal scanning laser ophthalmoscope (cSL0) near-infrared reflectance (IR) and Spectralis eye-tracked spectral-domain optical coherence tomography (SD-OCT).

**Methods:** We retrospectively analyzed a consecutive series of patients with newly diagnosed neovascular AMD who initiated intravitreal anti-vascular endothelial growth factor therapy from January 2006 to November 2011. Inclusion criteria were age over 50 years, best corrected visual acuity of 20/40 to 20/800, new onset of treatment-naïve CNV, absence of permanent structural damage to the central fovea, baseline IR and SD-OCT imaging at diagnosis and a minimum of 12-months of follow-up. Two independent graders measured areas of RPE atrophy identified using combined IR and eye-tracked SD-OCT at baseline and last follow up. The RPE atrophy progression rate was calculated. The neovascular lesion subtypes were classified based on both fluorescein angiography and SD-OCT as type 1 (subRPE), 2 (subretinal), 3 (intraretinal) or 4 (mixed). The RPE atrophy progression rate was correlated to the lesion subtype.

The RPE atrophy progression rate was also evaluated in fellow dry eyes for the purpose of comparison.

**Results:** Among the 748 cases reviewed, 153 patients (103 eyes) fit the inclusion criteria. The mean patient age was 81 years with a mean follow up duration of 31 months. The mean progression rate of RPE atrophy was 0.8 mm2/year (range 0 - 6.3 mm2/year). There were 43 patients who had a fellow dry AMD eye. The mean RPE atrophy progression rate in the fellow dry eyes was 0.3 mm2/year (range 0 - 1.99 mm2/year), significantly less than in the treated CNV eyes (p<0.05). In the eyes with neovascular AMD, the RPE atrophy progression rate varied by lesion subtype, and eyes with type 3 (RAP) lesions had the highest rate of progression of RPE atrophy (p<0.05).

**Conclusions:** The RPE atrophy progression rate in treatment naïve CNV eyes was similar to what has been previously reported in geographic atrophy in dry AMD, but this rate was higher than in the fellow dry eyes. Eyes with type 3 (RAP) lesions had the highest rate of progression of RPE atrophy compared to other neovascular lesion subtypes.

**Commercial Relationships:** Luna Xu, None; Sarah Mrejen, None; Roberto Gallego-Pinazo, Bayer (R), Novartis (R), Novartis (C), Carl Zeiss Meditec (R); Jesse J. Jung, None; Marcela Marsiglia, None; Sucharita Boddu, None; K Bailey Freund, Genentech (C), Regeneron (C), ThromboGenics (C), Bayer (C), DigiSight (C)

**Program Number:** 6270 **Poster Board Number:** D0086

**Presentation Time:** 10:30 AM - 12:15 PM

**Aflibercept (Eylea) Effect on Macula Thickness and Visual Acuity in Exudative AMD Patients Recalcitrant to Ranibizumab and Bevacizumab**

Vincent Hau, Mike Samuel, Michael Davis, Kristie Lin, Tom Chang, Retina Institute of California, Riverside, CA.

**Purpose:** To investigate the effect on visual acuity and macular thickness of intravitreal injections of 2.0 mg of aflibercept (Eylea) in eyes refractive to multiple treatments of bevacizumab and/or ranibizumab in exudative age-related macular degeneration (AMD).

**Methods:** This study investigated 35 patients (41 eyes) with recalcitrant exudative AMD (defined as having leakage on SD OCT despite monthly 0.5 mg ranibizumab injections and/or 1.25 mg bevacizumab) after being treated with 2.0 mg aflibercept intravitreal injections. Treatment was given if any evidence of CNVM activity on FA, OCT, or clinical exam. At all visits, patients were followed with clinical examinations, Snellen visual acuities, and Spectralis OCTs. Periodic FAs and ICGs were also done prior to treatment and during follow-up.

**Results:** Prior to aflibercept treatment, fluid was seen on OCT (intraretinal, subretinal, or sub-RPE) in all patients. At baseline, the median Snellen Va was 20/45 (range 20/25-20/300), mean central foveal thickness was 351.37 µm, and mean total volume was 8.52 mm3. Mean log MAR Va improved from 0.46 at pre-treatment to 0.37 at 6 months. Anatomically, mean central thickness and mean total volume improvement from baseline was 11.21 µm and 0.44 mm3 respectively at 1 month and 74.15 µm and 0.24 mm3 at 6 months. Foveal thickness at 6 months was statistically significant, whereas other end-points were not but showed a trend. No unexpected adverse effects were seen during follow-up.

**Conclusions:** Anatomic and visual acuity improvement was seen in patients given 2.0 mg aflibercept even in patients with persistent macular fluid after multiple monthly injections of ranibizumab and/or bevacizumab. This study supports the use of aflibercept as an effective treatment option for recalcitrant wet AMD patients to current standard anti-VEGF intravitreal injections.

**Commercial Relationships:** Vincent Hau, None; Mike Samuel, None; Michael Davis, Sequenom (C), Johnson and Johnson Research

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Comparison of Treatment Schedules in an Integrated Analysis of the VIEW Studies

Papp András¹, Bernd Sommerauer², Olaf Sowade³. ¹Department of Ophthalmology, Semmelweis University Budapest, Budapest, Hungary; ²Bayer Healthcare, Berlin, Germany.

**Purpose:** To compare intravitreal aflibercept injection (IAI) treatment schedules by functional outcomes in an integrated analysis of the 2 phase 3 VIEW studies.

**Methods:** Patients with neovascular age-related macular degeneration (n=2412) were randomized to monthly ranibizumab, every month dosing with IAI across subgroups, which included the 3-month subgroup, every other-month subgroup, and every other-month following 3 monthly dosesSubgroup analyses were performed post hoc.

**Results:** At both 52 and 96 weeks, treatment outcomes were similar for groups who received monthly or every-other-month treatment through Week 52 (Table). At 52 weeks, quartile analysis of visual acuity changes (<1, 1 to <6, 6 to <13, and ≥13 letters) showed comparable results for all dosing groups. At week 96, for all groups a slight, overall trend of vision loss was observed with reactive dosing (mean injections 4.1-4.7) compared to the results after 52-weeks of proactive dosing. During Weeks 52-96, visual acuity outcomes were maintained for the subgroup of patients who only received the 3 mandatory doses (~40-50% of patients in each dosing group). The incidence of ocular and systemic adverse events (AEs) was balanced across treatment groups in the overall population. The most frequent ocular AEs (>10% of patients) were conjunctival hemorrhage, eye pain, retinal hemorrhage, and reduced visual acuity.

**Conclusions:** These results show similar efficacy for monthly and every-other-month dosing with IAI across subgroups. Generally, a proactive treatment approach leads to more stable visual acuity results than reactive treatment.

<table>
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<th>Week</th>
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<td>7.9</td>
<td>7.6</td>
<td>6.6</td>
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</tr>
</tbody>
</table>

*Per protocol set; †Full analysis set; BCVA, best-corrected visual acuity

**Commercial Relationships:** Papp András, Bayer (C), Novartis (C), Bayer (F); Bernd Sommerauer, Bayer Pharma AG (E); Olaf Sowade, Bayer HealthCare AG (E)

Support: Study sponsored by Regeneron and Bayer

Clinical Trial: NCT00509795 and NCT00637377

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Methods: Patients at moderate to high risk of progression to choroidal neovascularization (CNV) associated with AMD were enrolled at retina clinics into a randomized trial to determine if home monitoring using the comprehensive visual field and tele-monitoring solution based on the ForeseeHome (FH) device improves detection of progression to CNV when compared with standard care. The primary objective is to determine whether home monitoring will lead to improved best corrected visual acuity (BCVA) at CNV diagnosis compared with standard of care. Secondary outcomes include time to CNV, CNV lesion characteristics, sensitivity/specificity of the device and BCVA 3 and 12 months after initiation of anti-VEGF treatment. The in-clinic screening exam required meeting ocular eligibility and successfully completing a test with the FH device. Subjects who passed the screening were randomized to standard care monitoring or standard care plus FH monitoring. Following shipment of the device, remote assistance with self-installation and training on the device followed. An initial series of tests were used to establish a baseline measurement for subsequent monitoring. Eyes that established a baseline entered the monitoring phase during which daily testing is recommended.

Results: 1520 of 1970 (77%) participants screened were enrolled in 44 clinical centers. Mean age of enrolled subjects was 72.5±7.5; mean baseline BCVA of study eyes was Snellen equivalent 20/25. The most common reason subjects failed screening was an inability to pass the device qualification test (76%) at the clinic. 1313 eyes of 763 subjects were randomized to the FH monitoring arm, among which 107 eyes (8.1%) failed to establish baseline values. 10 eyes of 6 pts (<1%) of device assigned participants stopped device monitoring within the 1st 90 days of monitoring, whereas the mean weekly device usage was 4.75 (±1.77) throughout this period.

Conclusions: The successful enrollment, randomization and stable rates of initial FH compliance are encouraging. The study will help clarify the optimal strategies for monitoring patients with intermediate AMD for early detection of CNV.

Commercial Relationships: Michael J. Elman, Genentech (C), Ohr Pharmaceuticals (I), Novartis (F), DRCR.net (F); Susan B. Bressler, Novartis (F), Bausch and Lomb (F), Genentech (F), Thrombogenics (F), Lumenis (F), Notal vision (F), GlaxoSmithKline (C), allergan (F); Traci E. Clemons, None; Emily Y. Chew, None

Program Number: 6274 Poster Board Number: D0091
Presentation Time: 10:30 AM - 12:15 PM
Predictive Factors for Visual Acuity “Gain and Maintain” after Ranibizumab Treatment for Age-Related Macular Degeneration and Polypoidal Choroidal Vasculopathy


Purpose: To investigate the predictive factors for each visual acuity responder type at one year after intravitreal injections of ranibizumab (IVR) for age-related macular degeneration (AMD), polypoidal choroidal vasculopathy (PCV) and retinal angiomatous proliferation (RAP) in Japanese patients.

Methods: Three hundred and thirty-seven eyes undergoing IVR treatment (AMD 183 eyes; PCV 141 eyes; RAP 13 eyes) were retrospectively studied. “Gain” was defined as best-corrected visual acuity (BCVA) increase in the study eye from baseline to month 3 and “maintain” was defined as a loss of no more than 0.1 log MAR in mean BCVA of the study eye at month 12 compared to month 3. “No initial gain” was defined as no initial gain and no gain during the PRN phase. Each responder type outcomes at one year after treatment were analyzed based on the following: age, sex, VA, type of disease, greatest linear dimension (GLD), central retinal thickness, injection numbers, hypertension, diabetes, and smoking habits.

Results: The “gain and maintain” group consisted of 140 eyes (42%). The BCVA increased steadily with the 3 initial doses and was maintained throughout the PRN phase with an average of 1.86 retreatments. The “gain but not maintained” group consisted of 80 eyes (24%) with 1.85 additional retreatments. In the “no initial gain” group, 117 eyes (34%) showed no initial gain and no gain during the PRN phase. Multivariate logistic regression analysis found the independent predictor for “gain and maintain” to be GLD (P=0.0006).

Conclusions: IVR is well tolerated in eyes of Japanese patients with AMD and PCV. Smaller GLD at baseline may be a good prognostic factor for VA “gain and maintain” after IVR.

Commercial Relationships: Yuji Oshima, None; Satomi Shiose, None; Miho Yasuda, None; Kumiko Kano, None; Ayako Yoshida, None; Keijiro Ishikawa, None; Shoji Notomi, Kyushu University (P); Shigeo Yoshida, None; Tatsuro Ishibashi, None
Support: JSPS KAKENHI Grant #23592573

Program Number: 6275 Poster Board Number: D0091
Presentation Time: 10:30 AM - 12:15 PM
Morphologic effects of anti-VEGF therapy on retinal pigment epithelium (RPE) and choroidal vasculature (CV) in neovascular age-related macular degeneration (AMD)

Ursula Schmidt-Erfurth,1 Christoph Schuechter,2 Sebastian M. Waldstein,3 Bianca S. Gerendas,1 Christian Simonader,1 Li Zhang2, Michael D. Abramoff1,4 Milon Sonka1, Bernhard Baumann2, Christoph K. Hitzenberger1. 1Department of Ophthalmology, Medical University of Vienna, Vienna, Austria; 2Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Vienna, Austria; 3Iowa Institute for Biomedical Imaging, University of Iowa, Iowa City, IA.

Purpose: Intravitreal VEGF inhibition is the recommended first-line therapy in neovascular age-related macular degeneration (AMD). Currently, clinical evidence was noted of therapy-related adverse effects on retinal pigment epithelium (RPE) and choroidal vasculature (CV). In this prospective study, advanced imaging modalities were used to monitor RPE- and CV-related changes under continued anti-angiogenic therapy.

Methods: 25 eyes with subfoveal neovascularization in AMD underwent standard ranibizumab treatment with a monthly regimen for 12 months, followed by PRN until month 24. RPE and CV layers were imaged at quarterly intervals during two years of follow-up. RPE alteration was determined by 3D polarization-sensitive optical coherence tomography (PS-OCT) with a resolution of 5 µm, a raster of 128x512 scans and an area of 6x6 mm. CV anatomy was reconstructed using a validated algorithm with Hessian analysis-based object detection followed by classic region-growing segmentation from spectral domain (SD)-OCT data (Zeiss Cirrus) and CV thickness was quantified by fitting a thin-plate spline of both sides.

Results: Best-corrected visual acuity (BCVA) improved from 58 letters at baseline to 68 letters at 12 months and reached 57 letters at 24 months, while central retinal thickness (CRT) decreased from 453 µm to 275 µm and 325 µm, respectively. PS-OCT demonstrated persistent RPE integrity in 10 eyes, novel development of geographic atrophy (GA) in 14 eyes with 7 extrafoveal lesions. Progressive growth of GA with 0.25mm/0.51mm at 12/24 months was significant (p<0.01). Mean CV thickness in the central 6x6 mm area decreased from 143 µm at baseline to 138, 140 and 120 µm at month 3, 12 and 24, representing a progressive, but non-significant trend.

Conclusions: Continued anti-VEGF therapy of neovascular AMD

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appears to induce morphological changes at the level of RPE and choroid. RPE atrophy was progressive and significant, choroidal thinning was discrete, but detectable. Advanced imaging modalities are useful to identify and quantify disease- and treatment-related changes in a precise and reproducible manner, particularly since changes may be minor initially and progress slowly over time.

Commercial Relationships: Ursula Schmidt-Erfurth, Alcon (C), Bayer Healthcare (C), Novartis (C); Christopher Schuetze, None; Sebastian M. Waldstein, None; Bianca S. Gerendas, None; Christian Simader, None; Li Zhang, None; Michael D. Abramoff, IDx LLC (E), IDx LLC (I); University of Iowa (P); Milan Sonka, US 7,995,810 (P); Bernhard Baumann, Canon Inc. (F); Christoph K. Hitzenberger, Canon Inc. (F), Canon Inc. (C)

Program Number: 6276 Poster Board Number: D0092
Presentation Time: 10:30 AM - 12:15 PM

Association Between Required Length of Intravitreal Anti-VEGF Therapy in Exudative Age-Related Macular Degeneration and Initial Central Macular Thickness as Measured by Optical Coherence Tomography

Blake Isernhagen, Stephen R. Fransen. Dean McGee Eye Institute, Oklahoma City, OK.

Purpose: Anti-VEGF therapy has revolutionized the treatment of exudative age-related macular degeneration (AMD). Optical coherence tomography (OCT) is commonly used to help diagnose this disease and guide therapy. To date, no study has examined whether an association exists between OCT measured initial central macular thickness (CMTi) and required length of treatment in these patients.

Methods: Medical records were reviewed from patients at the Dean McGee Eye Institute with newly diagnosed exudative AMD from 2009 to 2010 who received intravitreal bevacizumab or ranibizumab therapy. Patients were divided into two groups: those who were able to stop therapy within 6 months of initiating treatment (Group 1) and those who had to continue therapy beyond 6 months or had to restart therapy after 6 months without treatment (Group 2). CMTi was recorded for all patients. We hypothesized that CMTi is significantly different between Group 1 and Group 2 patients.

Results: Group 1 consisted of 88 eyes from 88 patients with an average age of 78.3 years, 43% were male. Mean CMTi was 318.1±µm with maximal macular thickness of 384.5 µm. The range was 137 to 791 and 246 to 1156 respectively. Mean treatment duration was 4.2 months with a mean follow-up period of 16 months. Group two consisted of 96 eyes from 96 patients with an average age of 78.9 years, 40.6% were male. Mean CMTi was 375.9 µm with maximal macular thickness of 434.9 µm. The range was 207 to 818 and 263 to 818 respectively. The mean follow-up period was 18 months. CMTi and maximum macular thickness differences between Group 1 and 2 were statistically significant (Student's t-test, p < 0.05).

Conclusions: This is the first study demonstrating an association between initial macular thickness and how long a patient will require treatment for exudative AMD. We found a statistically significant difference between two groups requiring different durations of treatment. The mean CMTi difference was 67.8 µm and mean maximum macular thickness difference 50.4 µm. Initial OCT measurements may help predict how a patient will respond to anti-VEGF therapy.

Commercial Relationships: Blake Isernhagen, None; Stephen R. Fransen, None

Program Number: 6277 Poster Board Number: D0093
Presentation Time: 10:30 AM - 12:15 PM

Quantification of the area of retinal pigment epithelium tears in age-related macular degeneration

Christoph R. Clemens, Florian Alten, Christine Baumgart, Peter Heiduschka, Nicole Eter. Ophthalmology, University Eye Hospital, Muenster, Germany.

Purpose: To compare different quantification tools based on confocal scanning laser ophthalmoscopy (cSLO) for assessment of retinal pigment epithelium (RPE) tear size.

Methods: cSLO fundus autofluorescence (FAF) and near-infrared reflectance (IR) imaging were performed in 23 patients with RPE tear after intravitreal injection for pigment epithelium detachment due to exudative age-related macular degeneration (AMD) at baseline and additionally in 11 patients after 5.1 ± 1.8 months follow-up. RPE tear area was measured by three independent readers using three methods: manually on cSLO FAF images, manually on cSLO IR images, and using a FAF-based semi-automated software. Tears were also subdivided into unilobar and multilobar tear patterns.

Results: Confidence intervals were 0.08 and 0.12 for FAF, 0.11 and 0.09 for FAF-based semi-automated software and 0.25 and 0.27 for IR for intraobserver (reader 1) and interobserver agreements (readers 1 and 2), respectively. The average values of the square errors of the quantification methods were 0.040 ± 0.033 mm2 (FAF), 0.035 ± 0.060 mm2 (software) and 0.187 ± 0.219 mm2 (IR). Mean area of RPE tears at baseline given as the average measurement of all three readers using FAF-based semi-automated software was 5.77±4.62 mm2 (range 0.13-14.74 mm2). Follow-up measurements of unilobar RPE tears (8 patients) showed no change in lesion area size (0.14 ± 0.33 mm2), in contrast, multilobar RPE tears (3 patients) showed a progression in lesion area size of 1.80 ± 0.74 mm2.

Conclusions: Manual FAF-based and semi-automated FAF-based quantifications of RPE tears are accurate and reproducible and superior to manual IR-based measurement. RPE tear area quantification is clinically relevant regarding progression following further intravitreal treatment, particularly in multilobar RPE tears.

Commercial Relationships: Christoph R. Clemens, Heidelberg Engineering (F), Novartis (F); Florian Alten, Novartis Pharma (F), Heidelberg Engineering (F); Christine Baumgart, None; Peter Heiduschka, None; Nicole Eter, Novartis (F), Bayer (R), Heidelberg Engineering (R), Sanofi Aventis (C), Allergan (C), Bausch and Lomb (C)

Program Number: 6278 Poster Board Number: D0094
Presentation Time: 10:30 AM - 12:15 PM

Correlation Between Fluid Status at Week 12 and Week 52 Following Intravitreal Aflibercept Injections in the VIEW Study of wAMD Patients

Jeffrey L. Marx1, Darius M. Moshefghii2, Seenu M. Hariprasad3, Jeffrey S. Heier3. 1Department of Ophthalmology, Lahey Clinic, Peabody, MA; 2Department of Ophthalmology, Stanford University, Palo Alto, CA; 3Department of Ophthalmology, University of Chicago, Chicago, IL; 4Ophthalmic Consultants of Boston and Tufts University School of Medicine, Boston, MA.

Purpose: To determine the proportion of patients with and without fluid at week 12, one month after three initial doses of intravitreal aflibercept injections (IAI). To determine if fluid status at week 12 was associated with fluid status at week 52 and whether BCVA at week 52 was influenced by fluid status at week 12.

Methods: A total of 2457 patients with age-related macular degeneration were randomized to four treatment groups: IAI 2 mg every 4 weeks (2q4), 0.5 mg every 4 weeks (0.5q4), 2 mg every 8 weeks (2q8, after three initial monthly doses), or ranibizumab 0.5 mg every 4 weeks (Rq4). “No fluid” was defined as the absence of both cystic retinal edema and subretinal fluid. Relative risks of various
events were computed using Rq4 as the control group.

**Results:** Compared with Rq4, the relative risks (95% CI) of having retinal/subretinal fluid at week 12 were 0.74 (0.63-0.88), 1.18 (1.03-1.36), and 0.80 (0.68-0.94) for 2q4, 0.5q4, and 2q8, respectively. In patients with fluid at week 12, the unadjusted relative risks (95% CI) of not having fluid at week 52 (compared to Rq4) were 1.34 (1.08-1.65), 1.07 (0.86-1.33), and 1.34 (1.08-1.66) for 2q4, 0.5q4, and 2q8, respectively, and the unadjusted percentages of those gaining 3 lines from week 12 to week 52 were 32%, 32%, 27%, and 30% in Rq4, 2q4, 0.5q4, and 2q8, respectively. Patients who had no fluid at week 12 were also likely to have no fluid at week 52: 80%, 85%, 79.2%, and 79% in Rq4, 2q4, 0.5q4, and 2q8, respectively. In patients who had no fluid at week 12, the unadjusted percentages of those gaining 3 lines from week 12 to week 52 were 31%, 32%, 34%, and 32% in Rq4, 2q4, 0.5q4, and 2q8, respectively. In this study, the most frequent ocular adverse events in the study population were conjunctival hemorrhage, eye pain, retinal hemorrhage, and reduced visual acuity.

**Conclusions:** Compared to Rq4, patients treated with IAI 2 mg were less likely to have fluid at week 12. IAI patients with fluid at week 12 were more likely than ranibizumab patients to be dry at week 52. There was no difference in BCVA between the wet and dry groups.

**Commercial Relationships:** Jeffrey L. Marx, Genentech (C), Parexel (C), Allergan (C); Darius M. Moshfeghi, None; Seeun M. Hariprasad, Bayer (C), Regeneron (C), Regeneron (R), Alcon (C), Alcon (R), Allergan (C), Allergan (R), OD-OS (I), Optos (C), Ocular Therapeutics (I); Jeffrey S. Heier, Acucela (C), Aerie (C), Alimera (F), Allergan (C), Bayer (C), Forsight Labs (C), Fovea (F), Genentech (C), Genzyme (C), Genentech (F), Genzyme (F), Thrombogenicics (C), Sequenom (C), Notal Vision (F), Novartis (F), Ophthotech (F), Ophthotech (C), Oraya (C), Paloma (F), Regeneron (F), Regeneron (C)

**Support:** Regeneron Pharmaceuticals, Inc., Bayer HealthCare

**Clinical Trial:** NCT00509795

**Program Number:** D0095

**Presentation Time:** 10:30 AM - 12:15 PM

**Impact of reticular pseudodrusen on macular function**


**Purpose:** To investigate the impact of reticular pseudodrusen on macular function using microperimetry.

**Methods:** Eighteen consecutive patients (18 eyes) with reticular pseudodrusen (group 1), and without medium/large drusen, underwent microperimetry. Eighteen age- and sex-matched subjects (18 eyes) with typical drusen and without pseudodrusen (group 2) also underwent microperimetry. Macular sensitivity was assessed by microperimetry and compared between the 2 groups.

**Results:** Mean age of patients with reticular pseudodrusen and with typical drusen was 77.3±6.8 and 75.0±9.9 year-old, respectively (p=0.4), and 61.1% and 61.1% were women, respectively. Mean best-corrected visual acuity was 0.14±0.09LogMAR and 0.13±0.09LogMAR (p=0.8), in group 1 and group 2, respectively. Microperimetry revealed a significant difference in overall mean macular sensitivity (“square 7x7”; 49 points) between group 1 and group 2 (5.9±1.7dB vs 8.8±2.4dB, p<0.001). Both mean central macular sensitivity (“square 3x3”; 9 points), and mean peripheral macular microperimetric sensitivity (overall “square 7x7” - central ”square 3x3”; 40 points), were significantly reduced in group 1 compared with group 2 (central macular sensitivity: 5.7±1.8dB vs 8.9±2.6dB, group 1 and group 2, respectively; p<0.001). In group 1, mean peripheral sensitivity was reduced when compared with mean central sensitivity (5.7±1.8dB vs 6.9±1.7dB, p=0.01), while, in group 2, mean sensitivity was similar in both peripheral and central macula (8.7±2.3dB vs 8.9±2.6dB, p=0.4).

**Conclusions:** We showed that eyes with reticular pseudodrusen present a greater extent of reduced sensitivity than eyes with typical drusen.

**Commercial Relationships:** Giuseppe Querques, None; Nathalie Massamba, None; Mayer Srour, None; Elise Boulanger-Scemama, None; Lea Querques, None; Eric H. Souied, BAUSCH + LOMB (C), NOVARTIS (C), BAYER (C), THEA (C), ALLERGAN (C)
Photoreceptor Abnormalities in Intermediate Age-Related Macular Degeneration

**Purpose:** To investigate the relationship between photoreceptor layers overlying and adjacent to large drusen in intermediate non-neovascular age-related macular degeneration (AMD).

**Methods:** Patients with AMD (n=41; ages 53-83 years) and elderly control subjects without eye disease (n=10; ages 51-79) were studied with SD-OCT (spectral-domain optical coherence tomography). Characteristics of large drusen (>125 µm) were measured and thickness of photoreceptor laminae overlying drusen and in retinal regions neighboring the drusen were quantified.

**Results:** There were 750 large drusen in 63 AMD eyes studied. The width of drusen sampled averaged 352 (SD=153) µm and height averaged 78 (SD=31) µm. There was significant reduction of the photoreceptor outer nuclear layer (ONL) thickness overlying 92% of the drusen. The thickness of the layer corresponding to photoreceptor inner and outer segments above drusen was also reduced, and the reduction was proportional to ONL thickness. At ~20% of normally laminated paradrusen locations sampled within ~300 µm of peak drusen height, ONL thickness was significantly increased compared to age- and retinal-location-matched normal values. Topographical analyses of the macula showed ONL thickening occurring in paradrusen areas as well as retinal locations distant from drusen.

**Conclusions:** Reductions in the photoreceptor laminae overlying drusen were detectable and this is consistent with histological studies revealing neuronal degeneration in AMD. ONL thickening in some macular areas of AMD eyes has not been previously reported and may be an early phenotypic marker of photoreceptor stress, as has been proposed for this finding in hereditary retinal degenerations. Photoreceptors; intrinsic autofluorescence (AF) of lipofuscin was exploited to image RPE cells. AF was excited with 532 nm light at levels 22-25 times lower than the ANSI maximum permissible exposure. AF emission was collected over a 150 nm bandwidth centered at 650 nm. Excitation source and confocal pinhole were positioned initially to correct for the longitudinal chromatic aberration (LCA) of the human eye. Focus was then further refined at each location for each patient by using the deformable mirror to step through several dioptric foci to determine the focus with maximum fluorescence. After focus optimization, the confocal aperture, under computer control, was placed algorithmically to the position of greatest intensity.

**Results:** Individual RPE cells were resolved in two AMD patients. Abnormal RPE cell topography was observed at areas that appeared unaffected clinically. Areas larger than single RPE cells (from two to tens of RPE cells in diameter) were observed that were devoid of lipofuscin fluorescence; photoreceptor reflectance in these areas was atypical.

**Conclusions:** RPE images in AMD patients were obtained through new methods that allowed us to compensate for LCA. Additional improvements, such as algorithmic focus control and compensation for eye movements will further improve the efficiency of imaging RPE cells in disease. Imaging of the RPE cell mosaic with AOSLO can now be used to answer questions about diseases affecting the RPE, such as AMD, and to evaluate treatments aimed at restoring RPE health.

**Commercial Relationships:** Ethan A. Rossi, Canon Inc. (F); David R. Williams, Bausch and Lomb (F), Polgenix (F), Canon (F), Welch Allyn (F), Pfizer (C), US 5,777,719 (P), US 5,949,521 (P), US 6,095,651 (P), US 6,379,005 (P), US 6,626,328 (P), US 6,948,818 (P), US 7,416,305 B2 (P), US 6,199,986 (P), US 6,299,311 (P), US 6,827,444 (P), US 6,511,180 (P), US 8,226,236 (P), US 8,413,680 (P), Alfredo Dubra, US Patent No: 8,226,236 (P); Lisa R. Latchney, None; Margaret A. Folwell, None; William Fischer, Canon (F), Carl Zeiss Meditec (F); Hongxin Song, Canon (F); Mina M. Chung, Canon (F)

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regression of choroidal neovascularization (CNV) due to changes in the retinal pigment epithelium (RPE) that clinically resemble geographic atrophy (GA). To understand whether this form of RPE atrophy is distinct from GA, we examined its microscopic features in vivo.

**Methods:** An 83-year-old patient with neovascular AMD who developed an atrophic RPE lesion after anti-VEGF injections underwent comprehensive eye examination and conventional imaging including fundus photography and fundus autofluorescence (FAF, Heidelberg Retina Angiograph). Adaptive optics scanning light ophthalmoscopy (AOSLO) was used to image the photoreceptor and RPE cells simultaneously. Near-infrared light (796 nm) was used to image photoreceptors; intrinsic autofluorescence (AF) of lipofuscin was exploited to image RPE cells (excitation 532 nm; emission 650 Å 150nm), using light levels more than 20 times below the ANSI maximum permissible exposure. Images were obtained within, at the margin, and outside of the lesion area. Two imaging sessions were conducted, three weeks apart.

**Results:** AOSLO reflectance imaging within the lesion showed cellular structures of a size and distribution consistent with cone photoreceptors. These cells did not exhibit the temporal variations in reflectivity characteristic of normal healthy cones. Fluorescence AOSLO imaging within the lesion showed collections of AF, not detected by conventional FAF, measuring 20-30 microns in diameter. Hyperautofluorescence was present just outside the lesion margin, and patterns of abnormal AF continued well outside the lesion.

**Conclusions:** AOSLO demonstrates that cones appear to be present, but injured, within areas of RPE atrophy after anti-VEGF antibody injections. The sparse collections of AF within the atrophy may represent enlarged, lipofuscin-laden RPE cells. These findings suggest that RPE atrophy developing after anti-VEGF therapy may be distinct from GA.

**Commercial Relationships:** Mina M. Chung, Canon (F); Hongxin Song, Canon (F); Lisa R. Latchney, None; Margaret A. Folwell, None; William Fischer, Canon (F), Carl Zeiss Meditec (F); Ethan A. Rossi, Canon Inc. (F)

**Support:** NIH # EY021786, Thome Memorial Foundation, and RPB

**Program Number:** 6285 Poster Board Number: D0101

**Presentation Time:** 10:30 AM - 12:15 PM

**The role of Optical Coherence Tomography (OCT) for the diagnosis, monitoring, and guiding of treatment for neovascular Age-related Macular Degeneration (nAMD): an evidence synthesis study**

Noemi Lois\(^1\), Augusto Azara-Blanco\(^2\), Graham Mowat\(^2\), Ray Mett C. Castillo de Chacon\(^1\), Andrew Elders\(^2\), Craig Ramsay\(^2\), Jennifer Burr\(^2\).

\(^1\)Ophthalmology Department, Grampian Univ Hosp/NS Trust, Aberdeen, United Kingdom; \(^2\)Health Services Research Unit, University of Aberdeen, Aberdeen, Scotland, United Kingdom; \(^3\)School of Medicine, University of St Andrews, St Andrews, United Kingdom.

**Purpose:** To determine the optimal role of OCT in diagnosing and monitoring nAMD (detecting disease activity and the need for further anti-VEGF treatment).

**Methods:** Systematic review. Major electronic databases and websites were searched. Studies were included if they reported the diagnostic performance of time domain or spectral domain OCT (or selected other tests) against a reference standard of ophthalmologist-interpreted fluorescein angiography in people with newly suspected or previously diagnosed nAMD. Risk of bias was assessed by two independent investigators using QUADAS-2. Summary receiver operating characteristic (SROC) curves were produced for each test given sufficient data.

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**Regenerative Medicine and Stem Cells**

**Poster Board Number:** D0100

**Presentation Time:** 10:30 AM - 12:15 PM

**Cellular Features of Retinal Pigment Epithelial Atrophy after Regression of Choroidal Neovascularization**

Mina M. Chung\(^1\), Hongxin Song\(^2\), Lisa R. Latchney\(^1\), Margaret A. Folwell\(^2\), William Fischer\(^1\), Ethan A. Rossi\(^2\).

\(^1\)Flaum Eye Institute, University of Rochester, Rochester, NY; \(^2\)Center for Visual Science, University of Rochester, Rochester, NY.

**Purpose:** Intravitreal injection of anti-VEGF antibodies has proven successful in treating neovascular age-related macular degeneration (AMD). However, some treated patients develop vision loss after...
Results: 3700 titles/abstracts were screened, and 120 (3.2%) were selected for full-text assessment. A total of 22 studies were included (17 on diagnosis, 7 monitoring, and 3 both). From 15 studies reporting OCT data, sensitivity and specificity ranged from 59% to 100% and 27% to 100%, respectively.

Conclusions: The reported diagnostic performance of OCT showed large variability. The methodological quality of most studies was sub-optimal.

Commercial Relationships: Noemi Lois, None; Augusto Azuara-Blanco, None; Graham Mowatt, None; Mayret M. Castillo de Chacon, None; Andrew Elders, None; Craig Ramsay, None; Jennifer Burr, None

Support: Supported by the Health Technology Assessment Programme, National Institute for Health Research, UK

Program Number: 6286 Poster Board Number: D0102
Presentation Time: 10:30 AM - 12:15 PM

Towards Automated Assessment of AREDS Severity Scale and Simple Scale Using RTVue® Spectral Domain Optical Coherence Tomography Tools
Qienyuan Zhou¹, Yulia Wolfson², Voraporn Chaikitmongkol²,³, Neil M. Bressler¹
Optovue, Inc., Fremont, CA; Retina Division, Wilmer Eye Institute, Johns Hopkins School of Medicine, Baltimore, MD; Department of Ophthalmology, Chiang Mai University, Chiang Mai, Thailand.

Purpose: To evaluate an automated drusen detection and quantification software tool from RTVue® Spectral Domain Optical Coherence Tomography (SD-OCT) (Optovue, Inc., Fremont, CA), comparing it to traditional manual colored photography drusen quantification, towards development of an automated assessment of the AREDS Severity Scale and Simple Scale.

Methods: After approval of the study protocol by a Johns Hopkins University School of Medicine Institutional Review Board, 18 eyes of 9 patients of a retina specialist (NMB) with a clinical diagnosis of the intermediate stage of AMD in both eyes, as defined by AREDS, who had received an Optovue 3D OCT and color fundus photographs as part of standard care on the same day were reviewed retrospectively. One eye was excluded due to difficulty in grading fundus photograph.

Drusen area calculation within the 6mm ETDRS grid was performed using both an automated algorithm of the OCT and manual grading of large drusen by two independent retina specialists (YW, VC) for each one of the 1, 3, and 6 mm ETDRS circles. The averaged results of the two graders were compared to those of the automated algorithm, and the intergrader variability was evaluated by Bland-Altman statistics.

Results: The mean (SD) drusen area in 1, 3, and 6 mm ETDRS circles was 0.14 (0.15), 1.10 (0.83), and 1.83 (1.17) mm², respectively, for the averaged manual grading and 0.13 (0.17), 0.73 (0.67), 1.24 (0.93) mm² for the automated OCT grading. The drusen area calculated automatically was consistently smaller than the manually calculated drusen area, with the difference increasing with increasing drusen area (best described as y=−0.2525x+0.2126, where y is the difference between OCT and the average of two graders and x is the mean of OCT and the average of two graders for the 6 mm ETDRS circle). Correlation (r²) recorded between the averaged graders drusen area and the automated drusen area calculations for the 1, 3, and 6 mm ETDRS circles was 0.002, 0.719, and 0.702, respectively.

Conclusions: The quantification of drusen area using automated RTVue® SD-OCT drusen detection and quantification tool yielded good agreement when compared to traditional manual grading.

Refinements of this tool may simplify the process of grading severity of AMD in clinical trials and clinical practice in the future.

Commercial Relationships: Qienyuan Zhou, Optovue, Inc. (E); Yulia Wolfson, None; Voraporn Chaikitmongkol, None; Neil M. Bressler, Abbott Medical Optics, Inc (F), Alimera Sciences (F), Allergan (F), Bausch &Lomb, Inc (F), Bayer (F), Carl Zeiss Meditec, Inc (F), ForSight Labs, LLC (F), Genentech, Inc (F), Genzyme Corporation (F), Lumenis, Inc (F), Notal Vislon (F), Novartis Pharma AG (F), Pfizer, Inc (F), Regeneron Pharmaceuticals, Inc (F), Roche (F), Thrombogencis (F)

Program Number: 6287 Poster Board Number: D0103
Presentation Time: 10:30 AM - 12:15 PM

Detachment of CNV from Bruch membrane due to contraction of fibrovascular membrane in AMD

Purpose: To investigate the cleft which developed after detachment of choroidal neovascularization(CNV) from Bruch membrane due to contraction of fibrovascular membrane in age-related macular degeneration(AMD) using spectral domain optical coherence topography(SD-OCT).

Methods: Two hundred twenty eight eyes of 225 cases with AMD were studied. These eyes were treated with anti VEGF drugs or PDT combined with VEGF antagonists. The appearance ratio of the cleft and the conformational characteristics of the cleft using SD-OCT were reviewed.

Results: Twenty three of 228 eyes(10%) had the cleft which developed after detachment of CNV from Bruch membrane.(11 of 80 eyes with occult CNV, 3 of 26 eyes with classic CNV, 4 of 109 eyes with PCV and 3 of 13 eyes with RAP.) In all cases with the cleft, CNV had fibrovascular changes in fundus examination and Retinal pigment epithelium (RPE) above the cleft adhered to CNV tightly and continuously in SD-OCT. Five eyes had RPE tear during follow-up. The thickness of the cleft was an average of 63.0 ± 41 μm and the thickness of CNV with fibrosis above the cleft was an average of 408 ± 251 μm.

Conclusions: CNV sometimes detached from Bruch membrane and developed the cleft between CNV and choroid. On the other hand, CNV adhered to RPE.

Commercial Relationships: Ryo Mukai, None; Taku Sato, Alcon Japan Ltd. (F); Shoji Kishi, None; Naoto Hanyuda, None
Support: None in the Support

Program Number: 6288 Poster Board Number: D0104
Presentation Time: 10:30 AM - 12:15 PM

Optical Coherence Tomography and fluorescein angiography in the diagnosis of choroidal neovascularization of age-related macular degeneration
Ramin Tadayoni¹, Vincent Gualino¹,², Salomon Y. Cohen¹,², Gabriel Quentel², Belkacem Haouachine¹,³, Ali Erginay¹, Pascale Massin¹, Eric Vicaut¹, Alain Gaudric². Ophthalmology, Lariboisiere University Hospital, Paris, France; Centre d’imagerie et de laser, Paris, France; Centre d’exploration de la vision, Rueil Malmaison, France; Clinical Research Unit, Lariboisiere University Hospital, Paris, France; Clinique du docteur Cave, Montauban, France.

Purpose: To determine the sensitivity and specificity of different retinal imaging combinations for the diagnosis of choroidal neovascularization (CNV) of age-related macular degeneration (AMD).

Methods: In a prospective observational study, 149 patients over 50 years with suspected, untreated, recent CNV related to AMD, were consecutively included in two different centers. Only data collected

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therapy.

Methods: Retrospective review of 30 patient records (male: 10, female: 20, mean age: 80 years) notable for a history of wet AMD having received at least one IV Bevacizumab injection a minimum of 4 weeks prior to initiating IV Aflibercept were reviewed. Aflibercept (2 mg IV injection) was administered by trained ophthalmologists once every 4 weeks to the study population for at least 3 months. An OCT machine (Cirrus HD-OCT Model 4000) was used to obtain high-resolution images of retinal thickness (RT) before each IV Aflibercept dose. One-way analysis of variance (ANOVA) within-subjects testing was performed using time as the independent variable (at pretreatment, 1, 2, and 3 month timepoints). RT was the dependent variable. A p value of <0.05 was considered the standard of statistical significance.

Results: Mean RT (n=30) was 317.93 microns before initiating IV Aflibercept therapy. Mean RT (n=30) was 297.53 microns prior to receiving the second injection and 280.47 microns prior to receiving the third injection. For patients receiving 4 or more injections the mean RT (n = 21) was 327.19 microns before beginning therapy and 305.52, 280.67, and 290.43 microns respectively during the following visits. Comparison between RT at all time-points achieved statistical significance (p<0.05).

Conclusions: AMD is a major cause of blindness and visual impairment in geriatric Americans. IV Aflibercept is a novel intervention developed for the treatment of wet AMD. Significant mean RT reduction after once-monthly administration of IV Aflibercept therapy for a minimum of 3 months was demonstrated in this study of 30 patients with AMD refractory to IV Bevacizumab. We recommend the use of IV Aflibercept in patients suffering from wet AMD whose disease is refractory to the current standard of care, Bevacizumab.

Commercial Relationships: Carmel Moazez, None; Kasra Attaran-Rezaei, None; Clive H. Sell, None; Shepard Bryan, None; Stephen De Souza, None; Alan J. Gordon, None; Henry M. Kwong, None; Rahul Reddy, None; Belinda Shirkey, None; Matthew C. Ziemianski, None

Program Number: 6290 Poster Board Number: D0106
Presentation Time: 10:30 AM - 12:15 PM

Inner Retinal Layers Damage in Age-related Macular Degeneration

Ulfah Rimayanti, Ken Yamane, Mifushal Akhyar Latief, Hideki Mochizuki, Junko Hirata, Yoshiaki Kiuchi, Ophthalmology and Visual Science Department, Hiroshima University, Hiroshima, Japan.

Purpose: To examine the presence of inner retinal layers damage in age-related macular degeneration (AMD)

Methods: One hundred and thirty three eyes with AMD and 72 normal eyes were included in this study. All subjects underwent ophthalmological examination including best corrected visual acuity (BCVA), slit lamp examination, intraocular pressure measurement, color fundus photograph. Fluorescein angiography and indocyanine green angiography examinations were performed on eyes with AMD. Ganglion Cell Complex (GCC) parameters (GCC average, superior, and inferior thickness, focal loss volume (FLV), global loss volume (FLV), and retinal nerve fiber layer (RNFL) thickness were measured using RTVue Spectral Domain Optical Coherence Tomography. The independent-samples t-test was used to compare the GCC parameters and RNFL thickness between AMD and normal eyes. One-way ANOVA was used to examine the relationships between treatment types (untreated, treated only with anti-vascular endothelial growth factor (VEGF), treated only with photodynamic therapy, combined therapy) and GCC parameters changes. The Spearman’s correlation test was used to determine the relationships between BCVA, duration...
of AMD and GCC parameters, RNFL thickness.

**Results:** There were significant decreased of GCC average, superior, and inferior thickness in eyes with AMD compared to normal eyes (all p<0.0001). As for the FLV and GLV, there were significant increased (all p<0.0001). There were no significant changes in RNFL average, superior, and inferior thickness. Furthermore, there were no relationships between treatment types and duration of disease to GCC parameters changes. In addition, there were significant negative correlations between FLV and BCVA, GLV and BCVA in eyes with AMD.

**Conclusions:** These findings indicated the presence of inner retinal layers damage in eyes with AMD, and it was not influenced by therapy.

**Commercial Relationships:** Ulfah Rimayanti, None; Ken Yamane, None; Miftahul Akhyar Latief, None; Hideki Mochizuki, None; Junko Hirata, None; Yoshiaki Kiuchi, None

**Program Number:** 6291 Poster Board Number: D0107

**Presentation Time:** 10:30 AM - 12:15 PM

**Comparison of spectral domain and time domain OCT for qualitative and quantitative fluid assessments in the Comparison of AMD Treatments Trials (CATT)**

Francisco A. Folgar1, Cynthia A. Toth1, Gui-Shuang Ying2, Maureen G. Maguire2, Glenn J. Jaffe1, 1Ophthalmology, Duke University, Durham, NC; 2Ophthalmology, University of Pennsylvania, Philadelphia, PA.

**Purpose:** To determine agreement of certified readers assessing spectral domain (SD) or time domain (TD) optical coherence tomography (OCT) for the presence of fluid and for thickness measurements of retinal layers in eyes with neovascular age-related macular degeneration (AMD) treated with ranibizumab or bevacizumab.

**Methods:** Paired SDOCT and TDOCT scans were obtained in a subset of patients during year 2 of the Comparison of AMD Treatments Trials (CATT). Two masked readers graded each scan and performed manual measurements independently. A senior reader arbitrated discrepant scores. Agreement on presence of fluid types was evaluated with kappa coefficients with 95% confidence limits (CL), and McNemar tests. Agreement on central foveal thickness measurements was evaluated with mean ± standard deviation (SD), mean difference (Δ) ± 2 SD (95% agreement limits), and intraclass correlation coefficients (ICC) with 95% CL.

**Results:** A total of 1213 pairs of OCT scans were assessed for 384 eyes. Agreement on readable fluid status was excellent for all fluid types: range 93-99%. Agreement on presence or absence of fluid varied among fluid types. Intraretinal fluid had 73% agreement (k=0.47, CI: 0.42-0.52) and was more frequent with TDOCT (p<0.001). Subretinal and sub-retinal pigment epithelium (RPE) fluid had 87% and 80% agreement, respectively, and were more frequent with SDOCT (both p<0.001). Presence of any fluid had 82% agreement (k=0.46, CI: 0.40-0.52) and was more frequent with SDOCT (p<0.001). Retinal thickness was 154 ±66 μm with SDOCT vs. 158 ±58 μm with TDOCT (Δ 5 ±67 μm), subretinal thickness was 11 ±37 μm with SDOCT vs. 10 ±35 μm with TDOCT (Δ 2 ±35 μm), and sub-RPE thickness was 133 ±105 μm with SDOCT vs. 126 ±97 μm with TDOCT (Δ 5 ±86 μm). Agreement on paired measurements was excellent for all layers: retinal thickness ICC=0.84 (CL: 0.83-0.86), subretinal thickness ICC=0.88 (CL: 0.86-0.89), and sub-RPE tissue thickness ICC=0.91 (CL: 0.89-0.92).

**Conclusions:** In CATT, manual thickness measurements were clinically similar between SDOCT and TDOCT, and measurements among paired scans had excellent agreement. Subretinal and sub-RPE fluid were detected more frequently with SDOCT. Lower-resolution imaging, with interpretation of dark areas as cystoid macular edema, may explain the greater frequency of intraretinal fluid detected with TDOCT.

**Commercial Relationships:** Francisco A. Folgar, None; Cynthia A. Toth, Genentech (F), Bioptigen (F), Physical Sciences Inc. (F), Unlicensed (P); Gui-Shuang Ying, None; Maureen G. Maguire, Inspire Pharmaceuticals (F), Amakem (F), Idx LLC (F), Merck (C); Glenn J. Jaffe, Heidelberg Engineering (C), Regeneron Pharmaceuticals (F), Neurotech USA (C), Abbott (C), Psivida (F), Pfizer (C), Bayer (C)

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**Clinical Trial:** ClinicalTrials.gov registration number NCT00593450

**Program Number:** 6292 Poster Board Number: D0108

**Presentation Time:** 10:30 AM - 12:15 PM

**Optical coherence tomographic correlates of angiographic subtypes of occult choroidal neovascularization**

Amirhossein Hariri1, Florian M. Heussen1,2, Muneessar Nittalal, Srinivas Sadda1. 1Doheny Eye Inst/Univ of Sthrn California, Los Angeles, CA; 2Charite - University Medicine Berlin, Berlin, Germany.

**Purpose:** Two angiographic subtypes of occult choroidal neovascularization (CNV), fibrovascular pigment epithelial detachment (FVPED) and late leakage of undetermined source (LLUS), have been well-described. The purpose of this study is to define and compare the optical coherence tomographic (OCT) correlates of these angiographic subtypes.

**Methods:** We retrospectively analyzed 17 consecutive patients with previously untreated occult with no classic choroidal neovascularization who had both fluorescein angiography (FA) and volume spectral domain (SD) OCT images obtained on the same visit. Planimetric grading was performed on the FA images by certified reading center CNV graders to precisely outline boundaries of the FVPED and/or LLUS lesion for each cases. SDOCT images were graded in a masked fashion and inner retinal pigment epithelium (RPE) and inner choroidal boundaries were manually segmented on all B-scans in order to generate a PED thickness map. FA images were registered with the OCT fundus image and PED thickness was correlated with the angiographic lesion present at each location in the fundus.

**Results:** Point-by-point comparison revealed that PED thickness was significantly different in areas of FVPED versus LLUS. Whereas the mean PED thickness in areas of FVPED was 65.78 ±46.87 μ, it was only 13.13 ±9.17 μ in areas on LLUS (p <0.001). Aside from differences in PED thickness, there were no apparent morphologic differences on OCT between areas of LLUS and FVPED, including internal reflectivity and RPE integrity.

**Conclusions:** Although they appear to be distinct angiographic subtypes, LLUS and FVPED appear to differ only based on the thickness or height of the RPE elevation, with areas of LLUS representing much shallower elevations of the RPE.

**Commercial Relationships:** Amirhossein Hariri, None; Florian M. Heussen, Novartis (C); Muneessar Nittalal, None; Srinivas Sadda, Allergan (C), Genentech (C), Regeneron (C), Optos (C), Carl Zeiss Meditec (C), Optos (F), Carl Zeiss Meditec (F), Optovue (F)

**Support:** Research to Prevent Blindness and Beckman Center for Macular Research.

**Program Number:** 6293 Poster Board Number: D0109

**Presentation Time:** 10:30 AM - 12:15 PM

**One-year macular volume change of the neurosensory retina in intermediate AMD by SDOCT semi-automated segmentation**

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ARVO 2013 Annual Meeting Abstracts by Scientific Section/Group – Retina

Eric L. Yuan1, Francisco A. Folgar1, Stephanie J. Chiu2, Sina Farsiu2,3, Cynthia A. Toth4,5,6. Ophthalmology, Duke University, Durham, NC; 2Biomedical Engineering, Duke University, Durham, NC.

Purpose: In non-advanced age-related macular degeneration (AMD), retinal thinning may occur over drusen, but it is unclear whether changes occur to the entire neurosensory retinal volume (NSRV) of the macula. We sought to compare NSRV of eyes with intermediate AMD vs. aged control eyes, and to correlate NSRV with future AMD progression.

Methods: Spectral domain optical coherence tomography (SDOCT) was obtained in 314 AMD eyes and 122 control eyes enrolled in the prospective observational AREDS2 Ancillary SDOCT Study. Semi-automated SDOCT segmentation of the neurosensory retina was performed from internal limiting membrane to outer border of the photoreceptor layer within a 5-mm diameter field centered on the fovea. Complete SDOCT segmentation and NSRV calculation were achieved in 269 AMD eyes and 118 control eyes at baseline. NSRV was compared between AMD and control eyes, and NSRV change was compared between baseline and year 1. In AMD eyes with noncentral geographic atrophy (GA), baseline NSRV was correlated to color fundus photography (CFP) measurement of GA area at years 2 and 4 of follow-up.

Results: Baseline NSRV (mean ± standard deviation) was 5.21 ±0.42 mm3 for 269 AMD eyes and 5.06 ±0.35 mm3 for 118 controls (p<0.001). One year NSRV was 5.16 ±0.37 mm3 for 250 AMD eyes and 5.02 ±0.32 mm3 for 99 controls (p<0.001). In paired baseline and year 1 scans, NSRV decreased significantly for AMD (-0.05 ±0.15 mm3, p<0.001) and controls (-0.03 ±0.06 mm3, p<0.001). There was no significant difference between AMD and controls for NSRV change (p=0.15) or percent of eyes with decreased NSRV (70% AMD vs. 74% controls, p=0.59) from baseline to year 1. In eyes with noncentral GA based on CFP measurement, smaller baseline NSRV was correlated with greater total GA area at year 2 (n=23 eyes, Spearman rho=-0.76 p<0.001), greater total GA area at year 4 (n=30 eyes, Spearman rho=-0.52, p=0.003), and greater change in GA area from baseline to year 4 (Spearman rho=-0.54, p=0.003).

Conclusions: Total macular volume of the neurosensory retina was greater in eyes with intermediate AMD than controls, but the volume decreased in both groups over 1 year. Structural or inflammatory changes may induce macular thinning in some early categories of AMD. In intermediate AMD, NSRV was negatively correlated with future GA area; therefore, NSRV may serve as an SDOCT biomarker that predicts progression of GA size.

Commercial Relationships: Eric L. Yuan, None; Francisco A. Folgar, None; Stephanie J. Chiu, Duke University (P); Sina Farsiu, Duke University (P); Cynthia A. Toth, Genentech (F), Biotigen (F), Physical Sciences Inc. (F), Unlicensed (P)

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Program Number: 6294 Poster Board Number: D0110
Presentation Time: 10:30 AM - 12:15 PM
Vitelliform-Like Lesions Associated with Type 1 Choroidal Neovascularization

Sabah Shah1,2, Vinnie P. Shah1,2, K Bailey Freund1,2.

Purpose: To describe the multimodal imaging findings of a vitelliform-like lesion (VLL) observed over type 1 (sub-RPE) choroidal neovascularization (CNV) in patients with neovascular age-related macular degeneration (AMD).

Methods: A retrospective review of 11 eyes of 11 patients with VLLs associated with type 1 CNV due to AMD. Patients were examined using multimodal imaging including spectral domain optical coherence tomography (OCT), fluorescein angiography (FA), fundus autofluorescence (FAF) imaging, and fundus photography. Baseline characteristics were noted and changes in visual acuity and imaging findings were evaluated following the initiation of intravitreal anti-VEGF therapy.

Results: Eleven eyes of 11 patients (10 female, 1 male) with VLLs associated with type 1 CNV were studied. Mean age at first detection of the VLLs was 71.2±10.8 years. The mean follow-up following VLL detection was 1.8±0.6 years. FA in all 11 eyes showed leakage and/or staining of underlying type 1 CNV, but not of the VLL itself, differentiating this material from type 2 (subretinal) neovascular tissue. In 6 eyes, the VLLs showed hypofluorescence and in 5 eyes the VLLs showed varying degrees of hyperautofluorescence. With OCT, all 11 eyes had evidence of hyper-reflective material in the subretinal space overlying type 1 CNV. Five eyes had an associated serous pigment epithelial detachment, 6 eyes had evidence of subretinal fluid, 2 eyes had subretinal hemorrhage, 2 eyes had subretinal fibrosis, and 1 eye had subfoveal RPE atrophy. Unlike eyes with typical vitelliform lesions, all 11 eyes with VLLs showed resolution of the subretinal material with reconstitution of the IS/OS junction following a mean of 12 injections. Mean visual acuity prior treatment was 20/85 and improved to 20/75 at the most recent follow-up.

Conclusions: Unlike most acquired vitelliform lesions occurring in the absence of CNV, VLLs associated with type 1 CNV show a favorable anatomic response to intravitreal anti-VEGF therapy with visual improvement in some eyes. VLLs appear to represent a form of exudation distinct from subretinal fluid, hemorrhage, and the material seen in Best macular dystrophy and acquired vitelliform lesions.

Color photograph (A), FAF image (B), FA (C) and OCT line scans (D & E) of a VLL overlying type 1 CNV prior to (D) and after (E) treatment with intravitreal anti-VEGF therapy.

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The purpose of this study was to determine if MI can predict the exact locations of growth at the margin of GA and predict the rate of growth outside the margin as well.

Methods: Patients with GA measuring from 1.25 mm² to 18 mm² were enrolled prospectively. OCT scans (Cirrus™ HD-OCT, Carl Zeiss Meditec Inc.) were analyzed at baseline and 52 weeks. Expert graders manually segmented OCT images of GA. For comparison to baseline, the 52-week follow-up scans were registered to the baseline scan coordinates using rigid transformation. MI values were studied within a margin of 180 microns around the boundary of GA. MI values in areas with progression of GA were compared using a one-sided t-test with MI values from areas that did not progress. ROC analysis was performed on MI values in the margin relative to lesion and background MI averages to determine sensitivity and specificity of prediction of growth. Average MI values in the margin were compared to overall growth rate to evaluate the prediction of growth outside the margin.

Results: 24 eyes were investigated, and no scans were excluded. A statistically significant elevation in MI (p<0.05) was seen in areas of growth in 22/24 cases (92%). Locations of growth in the margin at 52 weeks were predicted with 61% sensitivity and 61% specificity. MI values correlated significantly with overall growth rate, and high- and low-growth-rate subjects were identified with 80% sensitivity and 64% specificity.

Conclusions: These findings suggest that there is an increase in MI at the margins of GA prior to enlargement. Elevated MI may help predict areas of enlargement of GA, and may relate to overall rate of growth and be a useful screening tool for GA.
20 µm above the outer segmentation line.

**Results:** Initially, 30 patients were enrolled and 49 eyes with GA were imaged. At 6 and 12 months, the growth rates of GA correlated with the magnitude of the low lumiance visual acuity deficits (LLDs) measured at baseline. Lesions with faster growth rates had larger LLDs (p=0.007 and p=0.003 at 6 and 12 months, respectively). This correlation in eyes with visual acuity of 20/63 or better suggested a deficit in photoreceptor (PR) function within the central macula where the GA had not yet progressed. Outer retinal assessment using *en face* imaging revealed extensive areas of outer PR disruption extending beyond the borders of GA in most eyes, with a bilaterally symmetrical pattern evident in some patients. In some cases, these areas of outer PR disruption accurately predicted the progression of GA over 1 year. In other cases, the area of PR disruption was much larger than the area of progression. Eyes with reticular pseudodrusens displayed a speckled pattern that appeared diagnostic for this condition.

**Conclusions:** *En face* imaging of the IS/OS boundary can predict the growth of GA. Due to the bilateral symmetry of these findings, this imaging strategy may prove useful in identifying a genetic subset of patients in which PR loss precedes the appearance and progression of GA. Identification of these areas with PR disruption should be monitored in clinical trials designed to test treatments for non-exudative AMD.

**Commercial Relationships:** Renata Portella Nunes, Carl Zeiss Meditec Inc. (F); Zohar Yehoshua, None; Andrew A. Moshfeghi, Thrombogenics, Inc. (C), Allergan, Inc. (C), Alcon, Inc. (C), Bausch & Lomb, Inc. (C), Valeant, Inc. (C), Regeneron, Inc. (C), Genentech/Roche, Inc. (C), OptiSTENT, Inc. (I); Giovanni Gregori, Carl Zeiss Meditec (F), Carl Zeiss Meditec (P); Paul F. Stetson, Carl Zeiss Meditec Inc. (E), Carl Zeiss Meditec Inc. (I), Carl Zeiss Meditec Inc. (P); William J. Feuer, Abbott Medical optics (F), New World Medical (F); Philip J. Rosenfeld, Accudia (C), Advanced Cell Technology (F), Alexion Pharmaceuticals (F), Bayer Healthcare Pharmaceuticals (C), Boehringer Ingelheim (C), Chengdu Kanghong Biotech (C), GlaxoSmithKline (F), Oraya (C), Sanofi/Genzyme (C), ThromboGenics (C), Carl Zeiss Meditec (F)

**Clinical Trial:** NCT00935883

**Program Number:** 6298 Poster Board Number: D0114
**Presentation Time:** 10:30 AM - 12:15 PM

**Assessment of linearity of growth in time in geographic atrophy secondary to age-related macular degeneration**

**Purpose:** To analyze if there is linearity in the growth of geographic atrophy (GA) using different units of measurement.

**Methods:** We reviewed all visits of patients included in a prospective natural history study of GA, the GAIN study (NCT01694095), and those who attended at 6-month intervals (+/- 1 month) during 18 months were selected. Fundus autofluorescence was used to measure the area of atrophy. The progression was analyzed using slopes and growth was expressed in each of the following 5 metrics: size of atrophy in mm2, difference of growth between visits (diff mm2), growth of lesion size in percentage relative to the previous visit (%), square root (sqr) and difference of growth between visits expressed in square root (diff sqr). Patients were stratified in tertiles of baseline area of atrophy, and those in the extremes (small and large lesions) were compared in terms of the slope in the first and last periods (0-6 and 12-18 months) for each metric. We used the patients in the extremes to avoid confounding data from the medium sized lesions and from the intermediate period.

**Results:** The final sample included 26 eyes of 22 patients (72.7% females, with a median of 79 years old and a baseline size of atrophy of 4.48 mm2). The median size of lesions in the 1st and 3rd tertiles was 1.44 and 9.94 mm2, respectively. Absolute measures increased, while % of growth decreased (p<0.05). When mm2 or sqr were considered, there was a slower growth of atrophy (as identified by progressively decreasing slopes) with time, which was particularly marked in smaller lesions (p<0.05). When growth of atrophy is evaluated globally, a very high linear correlation coefficient is found (r>0.97, p<0.001); this analysis precludes the detection of the aforementioned subtle decrease in the speed of growth when measures are segmented in short periods of time.

**Conclusions:** The metrics in which progression of GA is measured have a large impact in its characterization and it cannot be assumed to be linear in all cases. Absolute measures (mm2, sqr) show a decreasing growth with time especially in small lesions, whereas spread of atrophy expressed in % decreases with time. These results may be useful in clinical trials, since a slowing down of the progression of growth may be expected in the natural history of GA and should not be attributed to a potential beneficial effect from interventional therapies.

**Commercial Relationships:** Jordi M. Mones, novartis (C), allergan (C), bayer (C), ophthotech (C), notalvision (C), allimera (C); Marc Biarnes, None

**Clinical Trial:** NCT01694095

**Program Number:** 6299 Poster Board Number: D0115
**Presentation Time:** 10:30 AM - 12:15 PM

**Enhanced Depth Imaging Optical Coherence Tomography of the Choroid in eyes with Geographic Atrophy secondary to Age-related Macular Degeneration**

**Purpose:** To compare the subfoveal choroidal thickness (SCT) in eyes with geographic atrophy (GA) secondary to age-related macular degeneration (AMD) with normal eyes using enhanced depth imaging optical coherence tomography (EDI-OCT).

**Methods:** A total of 42 eyes (42 patients, mean age: 77.4 ± 7.5 years) with GA and 40 eyes of 40 healthy subjects (mean age 74.6 ± 5.9 years) were examined by confocal scanning laser ophthalmoscopy (cSLO) and EDI-OCT (Spectralis HRA+OCT, Heidelberg Engineering, Germany). Two independent readers measured the SCT. Analysis included Bland-Altman statistics and correlation of SCT with age, gender and refractive error (RE, eyes with RE > -3 D have been excluded from the analysis), respectively. In the GA group, SCT was also correlated with both uni-multifocality and the total size of the atrophic area measured by semi-automated image analysis software (RegionFinder, Heidelberg Engineering).

**Results:** Mean SCT was significantly thinner in the GA group (154.2 ± 70.8 µm) compared to the control group (231.9 ± 60.3 µm) (p=0.001). Mean interobserver agreement for SCT measurements was 20.0 µm (95% confidence interval (CI) [-3.3; 11]) in both groups, there was a significantly negative correlation between SCT and age (p=0.004) while gender and RE (range -1.75 to +3.36 D) were not significantly correlated with SCT (p=0.95 and p=0.72) respectively. In the GA group, there was no significant correlation between SCT and neither total size of atrophy (mean 8.98 ± 7.48 mm2, p=0.46) nor uni-multifocality (p=0.98).

**Conclusions:** The results indicate that advanced dry AMD is associated with thinner choroid compared to normal eyes. This may
Commercial Relationships: Athanasios Bezatis, Heidelberg Engineering, Germany (F), Carl Zeiss Meditec, Germany (F), Optos, UK (F); Eva Becker, Heidelberg Engineering, Germany (F), Carl Zeiss Meditec, Germany (F), Optos, UK (F); Christian K. Brinkmann, Heidelberg Engineering, Germany (F), Carl Zeiss Meditec, Germany (F), Optos, UK (F); Steffen Schmitz-Valckenberg, Heidelberg Engineering (F), Optos (F), Carl Zeiss Meditec (F), Heidelberg Engineering (R), Genentech (C), Novartis (C), Novartis (R), Roche (R), Novartis (F); Rolf Fimmers, None; Monika Fleckenstein, Heidelberg Engineering, Germany (F), Heidelberg Engineering, Germany (C), Heidelberg Engineering, Germany (R), Carl Zeiss Meditec, Germany (F), Optos, UK (F), Optos, UK (C); Frank G. Holz, Acucela (C), Allergan (C), Genentech (F), Heidelberg Engineering (F), Zeiss (F), Novartis (F), Novartis (C), Optos (F), Merz (C), Bayer (F), Bayer (C), Boehringer Ingelheim (C)

Program Number: 6300 Poster Board Number: D0116
Presentation Time: 10:30 AM - 12:15 PM

A lack of delayed intraocular pressure elevation after intravitreal injections of ranibizumab for age-related macular degeneration


Purpose: To evaluate the delayed intraocular pressure (IOP) elevation after intravitreal injections of ranibizumab for age-related macular degeneration (AMD).

Methods: The charts of patients treated with intravitreal ranibizumab injections for exudative AMD and followed monthly for 12 months or longer were retrospectively reviewed. The treatment regimen included three consecutive monthly injections followed by a PRN dosing strategy. IOP was measured at every follow up visit with noncontact tonometer (NIDEK NT-4000 Non-Contact Tonometer). Delayed IOP elevation was defined as an IOP ≥22 mmHg on 2 consecutive visits with an increase from baseline >6 mmHg. In patients who received injection of ranibizumab to one eye, fellow untreated eyes served as controls. Eyes with glaucoma were also evaluated separately.

Results: A total of 111 eyes met inclusion criteria. Delayed IOP elevation was not found in any eyes in this study. The mean duration of follow up was 18.7±4.6 months. The mean number of injections was 4.4±1.4 for 12 months and 6.0±3.1 during the follow up period, both including the 3 initial injections. The mean IOP of all eyes at baseline was 12.9±3.1mmHg. The highest mean IOP during the follow up period was 12.9±3.0mmHg at month 21, which was not significantly different compared with the mean IOP at baseline (P=0.94). In the patients who received treatment to one eye, there was no significant difference in the mean IOP between the treated eyes and the control eyes. There were 9 eyes with AMD and glaucoma. The mean IOP was 13.0±4.4mmHg at baseline and the highest mean IOP during the follow up period was 13.0±4.0mmHg at month 23, which was not significantly different compared with the mean IOP at baseline (P=0.99). In the patients with glaucoma who received treatment to one eye, there was no significant difference in the mean IOP between the treated eyes and control eyes during the follow up period.

Conclusions: Repeated injection of ranibizumab was not associated with an increased risk for IOP elevation.

Commercial Relationships: Yusuke Ichiyama, None; Tomoko Sawada, None; Masashi Kakinoki, None; Osamu Sawada, None; Yoshitsugu Saishin, None; Hajime Kawamura, None; Masahito Ohji, Alcon (F), Novartis (F), Novartis (C), Pfizer (C), Santen (F), Santen (C), Shionogi (C), Carl Zeiss (C), Bayer (C), Senju (C)
Support: None in the Support

Program Number: 6301 Poster Board Number: D0117
Presentation Time: 10:30 AM - 12:15 PM

Long-term effect of multiple intravitreal anti VEGF injection on intraocular pressure

Yoon Jeon Kim, Kyung Rim Sung, Yoo-Ri Chung, Kyoung Sub Lee, Soo Geun Joe, Joo Young Lee, June-Gone Kim, Young Hee Yoon. Asan Medical Center, Seoul, Republic of Korea.

Purpose: To evaluate the longterm effect of multiple intravitreal anti-vascular endothelial growth factor (VEGF) injections on intraocular pressure (IOP) in eyes with neovascular age related macular degeneration (AMD) and retinal vein occlusion (RVO).

Methods: Patients who underwent multiple (more than 3 times) intravitreal anti-VEGF injections and were followed more than 12 months after last injection were consecutively enrolled. Clinical information such as baseline demographics, underlying disease, baseline IOP, and frequency of anti-VEGF injections were obtained via medical record review. IOP elevation was defined as increase of 5mmHg higher than baseline measurement on 2 consecutive visits. The frequency of IOP elevation was determined, and hazard ratio of each putative risk factor for IOP elevation was calculated using Cox proportional hazard model.

Results: Six hundred and thirty nine eyes with neovascular AMD and 95 eyes with RVO were included in the analysis. Twenty eyes with neovascular AMD (3.0%) and 7 eyes with RVO (7.4%), showed IOP elevation after multiple anti-VEGF injections. In 27 eyes experiencing IOP elevation, IOP at the last follow up was 13.9±2.3 mmHg, which was not significantly different from the baseline IOP, 13.4±3.0 mmHg (P = 0.53). In neovascular AMD patients, history of IOP elevation associated with intravitreal steroid injections (34.65% P = 0.002), and history of glaucoma (4.20% P = 0.0285) were significant risk factors according to multivariate Cox proportional hazards. In RVO patients, history of glaucoma (7.217, P = 0.047) was a significant risk factors. In cox proportional hazard analysis of total participants incorporating underline disease as another variable, history of IOP elevation associated with intravitreal steroid injections (25.154, P = 0.002), history of glaucoma (5.294, P = 0.047) was a significant risk factors for IOP elevation after multiple anti-VEGF injections.

Conclusions: The incidence of IOP elevation after multiple intravitreal anti-VEGF injections was low, and elevated IOP was normalized without medication in most of cases in our study.

Commercial Relationships: Yoon Jeon Kim, None; Kyung Rim Sung, None; Yoo-Ri Chung, None; Kyoung Sub Lee, None; Soo Geun Joe, None; Joo Young Lee, None; June-Gone Kim, None; Young Hee Yoon, Allergan (R), Bayer (C), Alcon (R)
Support: None in the Support

Program Number: 6302 Poster Board Number: D0118
Presentation Time: 10:30 AM - 12:15 PM

Effect of an Intravitreal Anti-VEGF Injection on the Dynamics of the Anterior Segment

Jonathan Naysan1, Tushar Suthar1, Ronni M. Lieberman2, Jonathan Jonisch1, 2. 1Ophthalmology, North Shore - Long Island Jewish, Great Neck, NY; 2Ophthalmology, Mount Sinai University Medical Center, New York, NY; 3Ophthalmology, Long Island Vitrreoretinal Consultants, Great Neck, NY.

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Purpose: Intravitreal injections of various pharmacologic agents are now standard of care in a number of retinal vascular diseases. Optical Coherence Tomography (OCT) allows imaging of the anterior segment, specifically the angle structures, anterior chamber, and cornea. This study investigates the effects of a single intravitreal anti-VEGF injection on the dynamics of the anterior segment structures.

Methods: A chart review was done looking for patients who had received a single intravitreal injection of either Lucentis® (ranibizumab), Avastin® (bevacizumab), or Eylea® (aflibercept), in addition to anterior segment imaging of the same eye. Nine eyes were identified. Each eye was injected with equal volumes (0.05mL). Using the Visante Optical Coherence Tomography (OCT) machine, imaging of the anterior segment was performed 5 minutes before and after the injection. The angle opening distance (AOD) and trabeculiris space area (TISA) at 500µm and 750µm anterior to the scleral spur were measured both pre and post injection. The scleral spur angle (SSA), and central corneal thickness (CCT) were also obtained. None of the patients carried the diagnosis of glaucoma or anterior segment anomalies.

Results: Of the 9 patients, 7 were injected into the left eye and 2 in the right. Six were injected with Lucentis, 2 with Avastin, and 1 with Eylea. The mean pre injection AOD(500µm) was 0.385mm and post injection 0.369mm with a mean difference of -0.0165mm (-4.2%, p=0.19) after injection. The mean pre injection AOD(750µm) was 0.542mm and post injection 0.536mm with a mean difference of -0.0064mm (-1.2%, p=0.35). The TISA(500µm) mean pre injection was 0.145mm² and post injection was 0.133mm² with a mean difference of -0.012mm² (-8.3%, p=0.029). The TISA(750µm) mean pre injection was 0.26mm² and post injection was 0.133mm² with a mean difference of -0.13mm² (-49%, p<0.001). The SSA decreased by an average of 2.2% (p=0.28). The CCT showed a 0.2% increase after injection (p=0.32).

Conclusions: A statistically significant decrease in the TISA at both 500µm and 750µm after an anti-VEGF intravitreal injection is seen. While the AOD and SSA both decreased overall, they did not reach statistical significance. Intravitreal injections may have an effect on the dynamics of the anterior segment, specifically the angle structures. Further studies are warranted on the effects of intravitreal injections on the angle dynamics.

Commercial Relationships: Jonathan Naysan, None; Tushar Suthar, None; Ronni M. Lieberman, None; Jonathan Jonisch, None

Program Number: 6303 Poster Board Number: D0119
Presentation Time: 10:30 AM - 12:15 PM

Intraocular pressure monitoring in patients with ranibizumab development
Anna Plyukhova, Maria A. Karpilova, Aleksey V. Kuznetsov, Irina V. Andreeva, Olga A. Gabina, Maria V. Budzinskaya, Valery P. Eritchev, Sergey E. Avetisov. State Research Institute of Eye Diseases of Russian Academy of Medical Sciences, Moscow, Russian Federation.

Purpose: To report the rate of intraocular pressure elevation following repeated intravitreal injections (IVI) of anti-VEGF agents or dexamethasone intravitreal implants and to determine the risk factors.

Methods: A prospective study of 220 eyes undergoing IVI of ranibizumab (n=179), bevacizumab (n=22), or dexamethasone implant (n=19) was carried out. A total of 1340 IVI were performed. Intraocular pressure (IOP) was measured by standard Goldman applanation during the follow-up. Ocular hypertension (OHT) following these injections was diagnosed for an IOP superior to 25mmHg and investigated with respect to number of injections, pre-existing glaucoma, diabetes and YAG capsulotomy. Sub-groups analysis according to the different treatments were carried out.

Results: After a mean of 5.8 IVI, 8.4% (n=18) had IOP elevation above 25mmHg and required medical treatment (3% of them peaked above 30mmHg). Patients with pre-existing glaucoma experienced higher rates of OHT were compared to patients without pre-existing glaucoma (21.7mmHg +/-2.4 versus 17.23mmHg +/-4.5, p=0.06). No significant difference was found in diabetes subgroup (n=40, p=0.32), nor in YAG capsulotomy subgroup (n=12, p=0.8) compared to the control group. The peak of IOP was significantly correlated with the total number of IVI (p=0.01, R=0.19). The mean highest IOP was 17.2mmHg in ranibizumab group, 18.8mmHg in bevacizumab group and 19.9mmHg in dexamethasone intravitreal implant. No difference was found between these molecule subgroups (Kruskal-Wallis, p=0.38)

Conclusions: Serial intravitreal injections may lead to persistent IOP elevations that require IOP lowering therapies. This risk is correlated with the number of injections in our study and must be checked during the follow-up. Pre-existing glaucoma could be a risk factor but larger prospective studies are needed to verify these results.


Purpose: To compare the posture-induced intraocular pressure (IOP) changes after endovitreal injection of ranibizumab in AMD patients and a combination of AMD and glaucoma.

Methods: We examined 71 patients (71 eyes) with exudative form of AMD, of whom 11 in conjunction with primary open-angle medical treatment compensation form glaucoma in one case, after antiglaucoma surgery. Each eye received a single intravitreal injection of 0.5 mg ranibizumab. The IOP was measured minute prior to the injection 1, 30 and 180 minutes after using the iCare ONE home tonometer(Finland)

Results: 1 and 2 of IOP elevation patients was detected in a minute after injection of ranibizumab, up to 60 mm Hg and smooth its decline to 30 minutes. By 180 minutes after drug administration level IOP returned to normal only in patients in group 1. In patients with combined pathology after 3 hours IOP remained above baseline. These differences between the groups were statistically significant.

Conclusions: Ranibizumab treatment causes an increase IOP in both groups, followed by a decline, and these variations are comparable. In the group with comorbidity level of IOP does not reach baseline, though, and within the age norm.

Commercial Relationships: Anna Plyukhova, Novartis (R); Maria A. Karpilova, None; Aleksey V. Kuznetsov, None; Irina V. Andreeva, None; Olga A. Gabina, None; Maria V. Budzinskaya, Novartis (F); Valery P. Eritchev, None; Sergey E. Avetisov, None

Program Number: 6304 Poster Board Number: D0120
Presentation Time: 10:30 AM - 12:15 PM
Persistent ocular hypertension following intravitreal injections

Purpose: To compare the posture-induced intraocular pressure elevation following repeated intravitreal injections (IVI) of anti-VEGF agents or dexamethasone intravitreal implants and to determine the risk factors.

Methods: A prospective study of 220 eyes undergoing IVI of ranibizumab (n=179), bevacizumab (n=22), or dexamethasone implant (n=19) was carried out. A total of 1340 IVI were performed. Intraocular pressure (IOP) was measured by standard Goldman applanation during the follow-up. Ocular hypertension (OHT) following these injections was diagnosed for an IOP superior to 25mmHg and investigated with respect to number of injections, pre-existing glaucoma, diabetes and YAG capsulotomy. Sub-groups analysis according to the different treatments were carried out.

Results: After a mean of 5.8 IVI, 8.4% (n=18) had IOP elevation above 25mmHg and required medical treatment (3% of them peaked above 30mmHg). Patients with pre-existing glaucoma experienced higher rates of OHT were compared to patients without pre-existing glaucoma (21.7mmHg +/-2.4 versus 17.23mmHg +/-4.5, p=0.06). No significant difference was found in diabetes subgroup (n=40, p=0.32), nor in YAG capsulotomy subgroup (n=12, p=0.8) compared to the control group. The peak of IOP was significantly correlated with the total number of IVI (p=0.01, R=0.19). The mean highest IOP was 17.2mmHg in ranibizumab group, 18.8mmHg in bevacizumab group and 19.9mmHg in dexamethasone intravitreal implant. No difference was found between these molecule subgroups (Kruskal-Wallis, p=0.38)

Conclusions: Serial intravitreal injections may lead to persistent IOP elevations that require IOP lowering therapies. This risk is correlated with the number of injections in our study and must be checked during the follow-up. Pre-existing glaucoma could be a risk factor but larger prospective studies are needed to verify these results.

Commercial Relationships: Emilie Agard, None; Hussam El Chehab, None; Ikrame Douma, None; Guillaume Ract-Madoux, None; Claude Dussart, None; Corinne Dot, None

Clinical Trial: EUDRACT : 2010-A01168-31

Program Number: 6305 Poster Board Number: D0121
Presentation Time: 10:30 AM - 12:15 PM
Evaluating safety and efficacy of intravitreal Ranibizumab injection in AMD patients and recommendations to improve the standards of AMD service
Yasir Khan, Minji Jennifer Kim, Swan Kang, Sheena George. Medical Retina, Western Eye Hospital, Imperial College London, London, United Kingdom.
Purpose: Guidelines on the use of Ranibizumab for treatment of wet AMD recommends frequent follow-up and prompt initiation of treatment which has posed challenges for AMD services. The aim of this study was to evaluate the efficacy and safety of intravitreal injection of Ranibizumab for patients with wet ARM and to assess the length of time between referral and first treatment.

Methods: Retrospective analysis was performed on 160 eyes of 149 patients undergoing repeat Ranibizumab injections attending two-stop AMD service clinic at Western Eye Hospital, London, over 12 months period. Patients with wet AMD (classic, predominantly classic and occult lesions involving the central fovea) with visual acuity range of 0.3 to 1.2 logMar were included in study. Patients fulfilling treatment criteria received 3 consecutive monthly Intravitreal Ranibizumab injections (loading dose) and then were followed up on a monthly basis. Patients were re-injected, if increase in CRT on OCT or drop in visual acuity were noted on follow up visit (PrONTO trial).

Results: 62% of patients were female and 37% were male with average age of 82.5 years. An average of 5.1 injections (range 3-10) was administered during the first year and no case of endophthalmitis occurred. Average number of days from initial referral to AMD clinic assessment was 12 days and an average time from initial assessment to first injection was 7 days. Therefore the average time interval from initial referral to first treatment was 19 days. The mean visual acuity improved by 8.5 letters and 29% of patients improved their visual acuity by 15 or more letters. Average central retinal thickness on OCT was 341.5μm at initial assessment and reduced to 250.9μm at 12 month.

Conclusions: Intravitreal Ranibizumab injections appear to be a safe and efficacious intervention for patients with wet AMD leading to stabilisation of vision, in a condition that otherwise leads to severe loss of central vision. One-stop AMD service was introduced to achieve rapid referral and prompt treatment intervention. On line referral pathway was implemented which reduces time interval from referral to treatment to within 2 weeks.

Commercial Relationships: None

Program Number: 6306 Poster Board Number: D0122

Presentation Time: 10:30 AM - 12:15 PM

The UNVEIL (Utilizing raNibizumab intraVitrEal Injection in real-world setting) study interim results: Effectiveness and safety of ranibizumab in the treatment of neovascular age-related macular degeneration under real-life conditions in patients from Africa, Asia and the Middle East

Mohamed Mahgoub1, Naresh K. Yadav2, Viktoria Mester3, Kgaogelo E. Legodi4, Hakyoung Kim5, Eddy Wu6, Sasha Hristoskova7, Shelley DiTommaso8

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Purpose: A 12-month, multicenter, open label, single cohort, prospective observational study evaluating the effectiveness and safety of ranibizumab in the treatment of neovascular age-related macular degeneration (nAMD) in a diverse population from Africa, Asia and the Middle East under real-life conditions. The study was initiated in September 2010 and will complete in March 2013

Methods: Patients with nAMD received ranibizumab 0.5 mg injections in accordance with the prescribing information in participating countries. Treatment decisions, follow-up visits and assessments were at the physician’s discretion. The primary endpoint was mean change in best-corrected visual acuity (BCVA) from baseline (BSL) to Month 3. Secondary endpoints included the proportion of patients with ≥15 letters of VA gain, mean change in central retinal thickness (CRT) from BSL to Months 3 and 12, and safety. The 3-month related objectives and safety were included in the interim analysis.

Results: 385 patients were evaluated in the analysis. The majority of patients were Asians (88.1%) including 246 (63.9%) patients from India and 90 (23.4%) from South Korea. 61% of patients were males. The mean age was 66.8 years. The mean duration of nAMD was 0.6 years. 314 (81%) patients were nAMD treatment naïve. At BSL, the mean BCVA and CRT were 70.2 (17.4 standard deviation (SD)) letters and 354.7 (144.7 SD) μm, respectively. At Month 3, the mean gain in BCVA was 7.7 (13.9 SD) letters and mean reduction in CRT was 97.7 (145.0 SD) μm, both were statistically significant compared to BSL (p<0.001). The proportion of patients with ≥15 letters gain was 33.6%. Most commonly observed adverse events were vitreous floaters (4 patients, 1%), transient vision blurred (3, 0.8%), and upper respiratory tract infection (2, 0.5%)

Conclusions: The interim analysis results showed that ranibizumab treatment resulted in significant vision gain and CRT reduction at Month 3 and was well tolerated under real-life conditions in a diverse group of nAMD patients from Africa, Asia and the Middle East. The findings are in accordance with the efficacy and safety profile of ranibizumab observed in controlled randomized clinical trials

Commercial Relationships: Mohamed Mahgoub, Novartis (R); Naresh K. Yadav, None; Viktoria Mester, NOVARTIS (R); Kgaogelo E. Legodi, None; Hakyoung Kim, None; Eddy Wu, Novartis Pharma AG (E); Sasha Hristoskova, Novartis Pharma AG (E); Shelley DiTommaso, Novartis Pharma AG (E)

Support: Novartis Pharma AG

Program Number: 6307 Poster Board Number: D0123

Presentation Time: 10:30 AM - 12:15 PM

Role of biomechanical properties of fibrous coat of the eye in intraocular pressure changes in patients after intravitreal ranibizumab injections. Pilot study

Ekaterina Chikun, Maria A. Karpilova, Aleksey V. Kuznetsov, Irina V. Andreeva, Olga A. Gabina, Anna Plyukhova, Maria V. Budzinskaya, Valery P. Erichev, Sergey E. Avetisov

State Research Institute of Eye Disease of Russian Academy of Medical Sciences, Moscow, Russian Federation.

Purpose: The purpose of the present research was to analyze the influence of biomechanical properties of fibrous coat of the eye on intraocular pressure (IOP) in patients after intravitreal ranibizumab injections.

Methods: The study involved 60 patients (60 eyes) with wet age-related macular degeneration without history of glaucoma or ocular hypertension. 0.05 ml (0.5 mg) of ranibizumab was injected into the vitreous. IOP was measured before and 1 minute after the injection with the Icare ONE tonometer (Finland). Biomechanical properties of the cornea such as corneal hysteresis (CH) and corneal resistance factor (CRF) were examined two weeks after the last injection (after IOP normalization without medication) with an Ocular Response Analyzer (Reichert ORA, USA).

Results: One minute after injection IOP in all patients was elevated by 14,0±0.39 to 36,9±1.5 mm Hg. In 7 patients IOP after injection was more than 35 mm Hg, CH and CRF in these eyes were 7,25±0,33 and 10,2±0,7 respectively. In 5 other patients IOP after injection was less than 15 mm Hg, CH and CRF were 9,88±0,33 and 9,9±0,66 respectively. Difference in CH was statistically significant (p=0,021).

Conclusions: Viscoelastic property of fibrous coat of the eye is

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characterized by CH. Lower CH determines elevated IOP after intravitreal ranibizumab injection.

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**Purpose:** To determine the rate of intraocular hemorrhage following intravitreal anti-vascular endothelial growth factor (anti-VEGF) injection among patients with age-related macular degeneration (AMD) taking systemic anticoagulant medication(s) at the time of injection versus patients with AMD not taking systemic anticoagulation.

**Methods:** Retrospective consecutive case series of all patients treated with anti-VEGF injection for the treatment of neovascular AMD at the Penn State Hershey Eye Center in 2004-2010. The study included 1710 anti-VEGF injections performed in 228 eyes of 191 patients. Each injection was analyzed according to whether or not the patient was taking systemic anticoagulant medication(s) at the time of injection.

**Results:** Intraocular hemorrhage occurred following intravitreal anti-VEGF injection in 4 eyes (0.25%). Vitreous hemorrhage occurred in 3 patients taking systemic anticoagulation. Subretinal hemorrhage occurred in 1 patient not on anticoagulant therapy. The odds of intraocular hemorrhage were 1.9 times higher for injections performed in patients on systemic anticoagulation compared to injections performed in patients not on systemic anticoagulation; this difference is not statistically significant (odds ratio=1.9; 95% CI [0.2, 18.5]; p-value=0.56).

**Conclusions:** The rate of intraocular hemorrhage following intravitreal injection of anti-VEGF therapy among patients with AMD is low and there is no significant difference between patients taking systemic anticoagulant medication(s) at the time of injection versus patients not on anticoagulation.

### Commercial Relationships: Joanna Olson, None; Ingrid U. Scott, None; Denise Kerchner, None; Allen Kunselman, Merck (I)

**Program Number:** 6310 Poster Board Number: D0126

**Presentation Time:** 10:30 AM - 12:15 PM

**Microbial spectrum of endophthalmitis following intravitreal injection versus pars plana vitrectomy**

Michael Dollin, Philip P. Storey, John D. Pitcher, James Vander, Jason Hsu, Sunir J. Garg, Wills Eye Institute, Philadelphia, PA.

**Purpose:** To compare causative organisms in endophthalmitis following intravitreal injection (IVI) to endophthalmitis following pars plana vitrectomy (PPV).

**Methods:** Retrospective review of all available bacterial cultures in patients who developed endophthalmitis following IVI or PPV between January 1, 2009, and October 1, 2012, from one large vitreoretinal practice. Data were analyzed using Fisher’s exact test (two-tailed).

**Results:** Bacterial cultures from 34 cases of endophthalmitis following IVI, and 17 cases of endophthalmitis following PPV, were reviewed. In the IVI group, 14 cases (41.2%) were culture positive. Seven of these cases showed growth of bacteria associated with oral flora: Streptococcus viridans, Streptococcus mitis, Streptococcus salivarius, Streptococcus sanguinis, Enterococcus faecalis (2 cases), and Lactobacillus. In the PPV group, 8 cases (47.1%) were culture positive. The most common organisms in this group were Staph species, and none of the cultures grew bacteria associated with oral flora. Patients who developed endophthalmitis after IVI were significantly more likely than patients developing endophthalmitis after PPV to grow bacteria associated with oral flora (P = 0.023).
Conclusions: Endophthalmitis following IVI has a higher likelihood of being due to oral flora compared to endophthalmitis following PPV. Caution should be taken to avoid introduction of oral flora onto the eye during IVI.

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Program Number: 6311 Poster Board Number: D0127
Presentation Time: 10:30 AM - 12:15 PM
Index of Non Circularity as a Predictor for Progression in Eyes with Geographic Atrophy (GA)

Purpose: Given that baseline area and configuration of GA are associated with its progression rate, we hypothesized that a non circular configuration has a higher growth rate. Index of non circularity was developed on color photographs and was a strong predictor of progression rate of GA. The purpose of this study is to evaluate the index in a sample of autofluorescence images submitted for the Age Related Eye Disease Study 2 (AREDS2).

Methods: Among 63 eyes with GA that had incident or baseline GA with 2 years of follow up, the perimeter and area of GA was measured from autofluorescence images (Heidelberg) using planimetry. A Non-Circularity Index (NCI) was calculated based upon the ratio of the measured area of GA (actual area) to the area of GA expected for a given perimeter (expected area) NCI = actual area/expected area; range 0.0 to 1.0; a value of 1.0 indicates a circular shape and departure from 1.0 indicates non circularity or an irregular shape. The relationship between progression rates of GA area by autofluorescence imaging and NCI were analyzed in this pilot sample.

Results: The mean area of GA at baseline was 5.27 mm² (+/- 0.81 95% CI). Baseline NCI was categorized as 0-0.25 (n=22), 0.26-0.50 (n=23), 0.51-0.75 (n=13), and 0.76-1.0 (n=5). The mean progression rates of GA for these NCI categories were 2.16, 1.87, 1.25, and 0.93 mm²/yr respectively (p<0.01 ANOVA).

Conclusions: In this pilot sample, NCI is moderately associated with progression rate of GA. Using semi automated software for GA segmentation, availability of NCI as an automated output may be helpful prognostic factor and might be considered as a parameter to assist with clinical trial eligibility.

Commercial Relationships: Ronald P. Danis, Allergan (C), GSK (C), KangHong (C), Oraya (C), Thrombogenics (C), EyeKor LLC (I), Topcon (C); Amitha Domalpally, None; Ellie Corkery, None; Ruth A. Shaw, None; Ashwini R. Narkar, None; James White, None
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Program Number: 6312 Poster Board Number: D0128
Presentation Time: 10:30 AM - 12:15 PM
Predictors for the progression of geographic atrophy in patient with age-related macular degeneration: fundus autofluorescence study with modified fundus camera
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Purpose: We aimed to determine the association between abnormal fundus autofluorescence (FAF) features on images obtained from a modified fundus camera (mFC) (Topcon, Paramus, New Jersey, USA) and the progression of geographic atrophy (GA) in patients with age-related macular degeneration (AMD).

Methods: Consecutive serial FAF images of 103 eyes from 103 patients with GA were enrolled. All FAF images were obtained with an mFC (excitation, approximately 500-610 nm; emission, approximately 675-715 nm). Two examiners quantified the areas of GA (mm²) at baseline and at 1-year follow-up using customized segmentation program in Matlab (Mathworks 7.0, Natick, MA, USA) and the reproducibility of the quantifying process was accessed by calculating interclass correlation coefficient (ICC). The mean value of two GA areas measured by each examiner was used to calculate the difference between size at baseline and size at 1-year follow up. Patterns of abnormal FAF in the junctional zone were classified into None or minimal change, Focal, Patchy, Banded, and Diffuse by two other examiners. Multiple regression analysis was used to evaluate the relationship between GA enlargement and abnormal FAF, and binary logistic regression was used to determine predictors of GA enlargement.

Results: The reproducibility of quantification for the areas of GA was statistically significant (ICC 0.95, p < .05). No correlation was found between GA enlargement and abnormal FAF features in multiple regression analysis. Binary logistic regression analysis did not reveal significant risk factor for GA enlargement. However, when the Diffuse pattern of abnormal FAF was compared to pooled data from other patterns of abnormal FAF, the Diffuse pattern was a strong risk factor for GA enlargement (OR = 9.39; p < 0.05).

Conclusions: FAF image acquisition by mFC appears to be adaptable for evaluation in accordance with published classification system. Based on these classification systems, the Diffuse FAF pattern on baseline FAF images indicate a higher risk of GA progression than other patterns in patients with AMD. The identification of high-risk characteristics with mFC is a broadly available method that will provide additional information for predicting the disease course.

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Program Number: 6313 Poster Board Number: D0129
Presentation Time: 10:30 AM - 12:15 PM
Directional kinetics of geographic atrophy progression in age-related macular degeneration with foveal sparing
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Purpose: In eyes with advanced dry age-related macular degeneration (geographic atrophy - GA) the fovea may be spared for some time despite atrophy enlargement. The purpose of this study was to determine directional spread in the context of a natural history study in eyes with foveal sparing.

Methods: In the context of the Fundus Autofluorescence in Age-related Macular Degeneration (FAM) Study (NCT00393692), patients with GA and foveal sparing were examined longitudinally with confocal scanning-laser-ophthalmoscopy (cSLO) fundus autofluorescence (FAF, exc. 488nm, em. > 500nm) and near-infrared reflectance (IR) imaging (Spectralis HRA+OCT or HRA2, Heidelberg Engineering). Peripheral vs. central spread was analyzed based on measurements in processed cSLO images. Linear mixed effect models were used to model the development of the area of GA and the sparing of the central macula over time. In addition, a similar model was used to describe the development of the radius of both
Results: A total of 46 eyes of 42 patients aged 77.4 ± 9.1 years were analyzed over a median follow-up time of 11.6 months (min 2.5, max 71.9 months). The mean size of the entire atrophic lesions was 13.3 ± 6.0 mm² and of the residual foveal islands was 0.82 ± 0.61 mm² at baseline, respectively. Mean enlargement of the area of GA was 2.36 ± 0.22 mm²/year while the area of the preserved foveal retina showed a mean regression of -0.23 ± 0.05 mm²/year. Analysis of the radius of both areas revealed a peripheral progression of 0.17 ± 0.02 mm/year and a central regression of -0.08 ± 0.01 mm/year.

Conclusions: The results indicate that centrifugal vs. centripetal spread of GA can be quantified based on standardized image analysis and that the directional extension over time differs significantly. Although protective factors underlying the foveal sparing phenomenon are yet unknown, the kinetics suggests that local factors are operative in topographic atrophy progression. Natural history data on the preservation of a residual foveal island are helpful to model the disease process and to design interventional clinical trials aiming at prolonging foveal survival and, thus, central visual acuity.

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