YALE EYE CENTER- POSTERS PRESENTED AT CSEP 2014

Embolus extravasation is a mechanism of microvascular recanalization in human retinal artery occlusions

Abstract Number: 241 - B0049

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Purpose: Recently an alternative mechanism of emboli clearance in the cerebral microcirculation involving the engulfment of emboli by the endothelium, followed by their translocation through the vessel wall, leading to recanalization and blood flow reestablishment was identified in mice (C. K. Lam, T. Yoo, B. Hiner, Z. Liu, J. Grutzendler, Embolus extravasation is an alternative mechanism for cerebral microvascular recanalization., Nature 465, 478-82 (2010)). The specific aim of the study was to examine whether the mechanism, which was termed angiophagy, is not limited to the brain but also occurs in the microvasculature of the retina.

Methods: To explore the potential presence of angiophagy in humans, we reasoned that, given its accessibility for imaging, the retina would be one of the few places where detection of angiophagy in vivo might be possible. To search for microvascular occlusions, we retrospectively reviewed all fundus photographs and fluorescein angiographies from patients with retinal artery occlusion from the Yale Eye Center from 2002 through 2013. 193 were selected for the study, and nine patients with retinal arterial emboli were identified. Longitudinal retinal photography was used to determine whether the emboli were located within the vessels or in the adjacent perivascular space. Fluorescein angiography was used to identify whether the vessels were occluded or recanalized.

Results: Careful examination of nine cases in which multiple imaging time points had been acquired revealed three patients with emboli that seemed to have moved to the adjacent perivascular spaces, and the corresponding previously occluded microvessels were recanalized. Recanalization of vessels was confirmed by fluorescein angiograms revealing perfusion both proximal and distal to the once occluded area. Additional corroboration of vessel recanalization was the resolution of an adjacent area of ischemia, as evidenced by changes in the typical pattern of abnormal retinal ischemia.

Conclusions: In humans, longitudinal in vivo retina photography and angiography demonstrate that, similar to the observations in mice, vessel recanalization can occur in association with transvascular embolus extrusion. Thus, angiophagy is a ubiquitous mechanism of microvascular recanalization with potentially broad implications in vascular occlusive disorders and could constitute a novel therapeutic target.
An international multi-center investigation of macular holes: the European Vitreo-Retinal Society Macular Hole Study

**View Session Detail**

**Abstract Number:** 314 - B0292

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**Purpose:** To investigate factors associated with outcome of macular hole repair.  
**Methods:** An international collaborative multi-center non-randomized clinical study spanning 4 continents. Symptoms, signs, techniques, dyes, tamponades, post-operative positioning, success rate and complications were evaluated.  
**Results:** 4207 cases of idiopathic macular hole were enrolled by 140 retina specialists from 28 countries. 85.7% of holes closed following vitrectomy and 59% gained at least 3 lines of visual acuity. After multivariate regression, predictors for hole closure include earlier stage, shorter duration of hole and staining (p<0.001). There was no statistically significant difference among dyes including ICG, trypan blue, brilliant blue and other dyes. Staining improved anatomical outcome, but it did not affect visual outcome. There was no statistically significant difference in success rate among a variety of tamponades. Factors associated with better visual outcome include: hole closure, better baseline visual acuity, earlier stage and shorter duration of hole (p<0.001). 6% of cases had Inverted ILM flap technique that was associated with good anatomical and visual outcome. Retinal tear was noted in 3.2% of cases.  
**Conclusions:** Early repair of macular hole was associated with a better visual outcome. Staining improved anatomical success but not visual success. There was no statistically significant difference among dyes. Inverted ILM flap technique may be a promising technique for large macular holes.

Kainate Receptors Mediate Signaling in Both Transient and Sustained OFF Bipolar Cell Pathways in the Mouse Retina

**View Session Detail**

**Abstract Number:** 4527

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Purpose: A fundamental question in sensory neuroscience is how parallel processing is implemented at the level of molecular and circuit mechanisms. In the retina, it has been proposed that distinct OFF cone bipolar cell types generate fast/transient and slow/sustained pathways by the differential expression of AMPA- and kainate-type receptors, respectively. However, the functional significance of these receptors in the intact circuit during light stimulation remains unclear. Here, we evaluated the contribution of AMPA and kainate receptors to light-evoked responses of OFF bipolar cells in the whole-mount mouse retina.

Methods: We measured light-evoked (λmax 395 nm) glutamate release from bipolar cells in the mouse retina in vitro, by two-photon fluorescence imaging of a glutamate sensor (iGluSnFR) expressed on postsynaptic amacrine and ganglion cell dendrites. We perturbed AMPA and kainate receptor function using non-selective (DNQX: 100 μM) or selective blockers (AMPA: 100 μM GYKI 52466, 100 μM GYKI 53655; kainate: 50 μM UBP310, 1 μM ACET); L-AP4 (20 μM) was used to block the ON pathway. To validate and complement imaging experiments, excitatory currents were recorded from ganglion and bipolar cells with targeted whole-cell recordings.

Results: Light-evoked glutamate release persisted at all OFF levels of the inner plexiform layer in the presence of DNQX but was abolished by subsequent application of L-AP4, indicating that cross-over inhibition from DNQX-resistant ON pathways can drive release from bipolar terminals throughout the OFF layers. In subsequent recordings we first applied L-AP4 to isolate OFF responses mediated by the cone→OFF bipolar cell synapse. In both transient and sustained OFF layers, cone-driven glutamate release from bipolar cells was blocked by antagonists to kainate receptors, but not AMPA receptors. Electrophysiological recordings from bipolar and ganglion cells confirmed the essential role of kainate receptors for signaling in both transient and sustained OFF pathways. Kainate receptors mediated contrast responses at temporal frequencies up to 20 Hz, exceeding the limits implied by the time constant for recovery from desensitization measured previously (0.5 - 1.5 s).

Conclusions: Light-evoked responses in all mouse OFF bipolar pathways depend on kainate, not AMPA, receptors.

Autophagy over the lifespan: using fetal, stem cell, and adult RPE cultures to model the pathogenesis of AMD

Abstract Number: 371 - C0142

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Purpose: Dysfunctional autophagy in the retinal pigment epithelium (RPE) has been implicated as a potential therapeutic target in age-related macular degeneration (AMD). To explore how autophagy changes over the lifespan and in response to photoreceptor outer segments (POS), we compared induced pluripotent stem cell RPE (iPS-RPE), human fetal RPE (hfRPE), and adult donor RPE (ad-RPE).

Methods: RPE was cultured from 16-week human fetuses and cadaveric eyes. Stem cell-derived RPE was prepared from human embryonic stem cells (hESC-RPE) and induced pluripotent stem cells (iPS-RPE). LC3 conversion (immunoblotting) and changes in autophagy-related gene expression (qRT-PCR) were used to monitor autophagy. Relative maturity of RPE cultures was assessed using a panel of signature and maturation genes (qRT-PCR). Autophagy was manipulated with an inhibitor, Spautin-1, and inducer, Rapamycin. iPS-RPE were challenged with porcine POS daily for up to 1 month, and monitored with confocal-immunomicroscopy. The health of RPE cultures was assessed by the transepithelial electrical resistance (TER).

Results: Autophagic flux (LC3 conversion) increased from stem cell to 53-year-old ad-RPE, but was reduced in 90-year-old RPE. Rapamycin stimulated RPE autophagy, but Spautin-1 inhibited autophagy only partially—the strongest effect was on 90-year-old ad-RPE. qRT-PCR revealed quantitative differences in the expression of autophagy- and maturation-related genes. In iPS-RPE, the expression level of most maturation genes was similar to hfRPE, but some were at the level of less mature hESC-RPE. However, iPS-RPE and ad-RPE exhibited substantially higher levels of autophagy-related genes than hfRPE. In iPS-RPE, continuous feeding of POS over three weeks lowered TER to physiologic levels. One-week exposure to POS had little effect on iPS-RPE autophagy gene expression, but did result in the accumulation of autofluorescent granules.

Conclusions: The characteristics of autophagy depended on the culture model: autophagy gene expression in iPS-RPE more closely resembled ad-RPE than hfRPE. Pending the examination of more donors, partial inhibition by Spautin-1 suggests that a non-canonical autophagy pathway is replaced in old age by the canonical pathway. The accumulation of lipofuscin-like granules induced by POS indicates that complementary RPE cultures will be a valuable aid to explore targets for therapeutic agents for AMD.

Primary Epithelial Malignancies of the Lacrimal Gland: Trends in Survival

Abstract Number: 5445 - A0019

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Purpose: To determine the trends in incidence, treatment, and survival of primary epithelial malignancies of the lacrimal gland in the United States from 1988 to 2010 using a systemic review of the National Cancer Institute Surveillance, Epidemiology and End Results (SEER) database.

Methods: One hundred and thirty-two cases of primary epithelial malignancy of the lacrimal gland were identified in the Surveillance, Epidemiology, and End Results (SEER) program database in the
United States from 1988 to 2010. Survival rates were calculated by the Kaplan-Meier method and significance was determined using chi-squared testing.

**Results:** There were 132 cases of primary epithelial lacrimal gland tumors with histopathologic confirmation in the SEER database. The most common tumor types were adenoid cystic carcinoma (51.5%), mucoepidermoid carcinoma (17.4%), adenocarcinoma in situ (15.1%). The majority of tumors (61%) presented as locally invasive disease. The remainder, were confined to a tumor capsule (35%) or metastatic at presentation (4%). Most tumors were 2-4 cm in size at diagnosis (68%), with 19% less than 2cm and 13% greater than 4cm (13%). Surgery was the treatment of choice in 90% of patients, with 58% receiving radiation therapy (RT). There was a statistically significant improvement in survival among patients undergoing surgery versus those without surgical treatment (8.24 years vs. 1.0 year; p< 0.0001). Those undergoing radiation therapy fared poorer (2.25 years vs. 8.94 years; p = 0.02). Patients with advanced disease were significantly more likely to be treated with radiation therapy alone (70% regionally invasive or metastatic vs. 45% locally invasive; p<0.01). Patients with a history of prior malignancy had worse survival (5.3 years vs. 9.6 year; p = 0.014). There was no significant gender, age, or race predilection. There has been no significant improvement in survival between the 1988-1997 group and the 2004-2010 group (9.6 years vs. 8.36 years, p=0.77).

**Conclusions:** Surgery confers a statistically significant improvement in survival among patients diagnosed with primary epithelial tumors of the lacrimal gland and should remain an important tool in disease management. The SEER data demonstrates that there has been no significant improvement in survival among patients diagnosed with primary epithelial malignancies of the lacrimal gland during the period of data collection.

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**Medicare Payment and Cataract Surgical Volume**

**Abstract Number:** 6097 - A0224

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**Disclosure Block:** Dan Gong, None; Jun Lin, None; James C. Tsai, None

**Purpose:** The extent to which Medicare payment impacts cataract surgical volume has not been well quantified. This project studies the Medicare payment-surgical volume elasticity for complex (CPT 66982) and non-complex (CPT 66984) cataract surgeries and determines whether reduced Medicare payment shifts the composition of cataract surgery type from non-complex to complex.

**Methods:** [i] Payment data (2005-09) from the Medicare Physician Fee Schedule and [ii] surgical volume data from Medicare Part B Carrier Summary Data Files were matched by Medicare Part B carriers. A fixed effects regression model was used to analyze associations between Medicare payment and cataract surgical volume, controlling for [a] stable carrier-specific characteristics causing regional variations in cataract surgical volume, [b] national trends in cataract surgical volume, and [c] national trends in cataract surgery composition including those secondary to increased alpha-blocker use. Shifts between procedures were based on changes in the proportion of total cataract surgeries performed that were complex. All analyses adjusted for Medicare beneficiary population and inflation.

**Results:** From 2005 to 2009, 658,265 complex cataract surgeries at an average payment of $830.37 (in 2005 $) and 11,593,725 non-complex cataract surgeries at an average payment of...
$606.70 (in 2005 $) were performed across 55 Medicare carriers. For every 1% decrease in Medicare payment for complex cataract surgery, surgical volume increased by 1.30% (p<0.001). For every 1% decrease in non-complex cataract surgery payment, surgical volume increased by 0.45% (p=0.03). When payment for both procedures decreased by 1%, the proportion of complex cataract surgeries increased by 0.83% (p<0.001). An ophthalmologist performing ten CPT 66982 surgeries at $800 and ninety CPT 66984 surgeries at $600 who experiences a 10% reduction in Medicare payment will recoup more than half (51.6%) of “lost income” from decreased payment by performing more procedures.

**Conclusions:** Our study demonstrates that reduced Medicare payments are associated with significant increases in cataract surgical volume with greater responses seen for complex cataract surgeries. Moreover, decreased payment leads to a shifting effect from lower-paid non-complex to higher-paid complex procedures. These behavioral offsets are critical for national policymakers to understand when attempting to contain healthcare costs through payment reform.

**DSAEK Descemetorhexis in Two Patients with Anterior Segment Fibrosis after Multiple Intraocular Surgeries**

**View Session Detail**

**Abstract Number:** 2023 - C0042

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**Purpose:** To report clinical and histopathologic findings of the posterior cornea in two patients with a history of multiple intraocular procedures and to describe a surgical approach for descemetorhexis in these cases.

**Methods:** Interventional case series.

**Results:** Two patients developed unilateral bullous keratopathy following pars plana vitrectomies, cataract surgeries, and glaucoma filtering surgeries with multiple anterior chamber drainage devices. Both underwent Descemet’s stripping automated endothelial keratoplasty that was complicated by difficult descemetorhexis due to fibrotic posterior corneal tissue seen intraoperatively that was consistent with stromal downgrowth on histopathologic analysis. In these cases, descemetorhexis necessitated unconventional instruments including a reverse cystotome and intraocular scissors. Both patients developed detachments of the endothelial grafts and subsequent re-bubbling procedures.

**Conclusions:** Patients with bullous keratopathy secondary to multiple surgeries and anterior segment surgical implants may pose intraoperative challenges due to thickened and scarred posterior corneal tissue. It is imperative for surgeons performing endothelial keratoplasty on such patients to consider unique approaches to descemetorhexis as described herein or alternative techniques such as endothelial keratoplasty without Descemet stripping, penetrating keratoplasty, and deep lamellar endothelial keratoplasty.
Quality of Life in Age-Related Macular Degeneration Comparing Aflibercept, Photodynamic Therapy and Pegaptanib Sodium Treatment Groups

Abstract Number: 3950 - C0252

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Disclosure Block: Laura Hall, None; Shabnam Pakneshan, None; Ron A. Adelman, None

Purpose: To examine quality of life (QOL) in age-related macular degeneration (AMD), particularly across those receiving aflibercept (Eylea®), photodynamic therapy (PDT), pegaptanib sodium (Macugen®), and no treatment.

Methods: The Visual Function Questionnaire (VFQ-25) was administered to AMD patients. Subgroup analysis was performed per NEI algorithms and correlations between visual acuity (VA) and subgroup outcomes were calculated. Additional analyses regarding questions on treatment side effects were performed on patients recently switched to aflibercept from bevacizumab (Avastin®) and/or ranibizumab (Lucentis®).

Results: The study included 93 patients: 18 treated with PDT, 9 with pegaptanib, 12 with aflibercept, 25 with aflibercept after being switched from ranibizumab and/or bevacizumab, and 29 with no treatment (14 of those received AREDS). The no treatment group had better mean VA acuity and less severe disease. Mean age was 88 years. Values reported are on a scale of 0-100: higher values indicate better functioning. The overall QOL score yielded a mean of 71.2 for all patients, 60.3 PDT, 63.9 pegaptanib, 80.2 all aflibercept, 81.6 aflibercept after switch, and 71.2 no treatment (p=0.02). There is a strong correlation between visual acuity and QOL (r=0.63). The two lowest subgroup scores were perception of general vision (51.0 all patients, 37.8 PDT, 35.6 pegaptanib, 69.5 all aflibercept, 71.2 aflibercept after switch, and 47.9 no treatment, p<0.01) and driving (p=0.18). The highest scores were in the ocular pain, color vision, and social functioning subgroups. Other significant analyses included the following subgroups: dependency (p<0.01), mental health (p<0.01), peripheral vision (p=0.01) and social functioning (p=0.04). Visual acuity also strongly correlated to near vision and driving and moderately correlated to distant activities, peripheral vision, color vision and role difficulties. Of the 25 patients who were switched to aflibercept, 44% felt that their change in vision was better versus worse (4%) or no change (52%); and 56% felt that the switch was a positive experience versus negative (4%) or no change (40%).

Conclusions: There has been a significant improvement in quality of life for AMD patients since the introduction of anti-VEGF agents. Patients experience markedly less dependence with increased social functioning and mental health.

Long Term Efficacy of Intravitreal Bevacizumab for Macular Edema Secondary to Retinal Vein Occlusions

View Session Detail
Abstract Number: 3918 - C0220

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Purpose: To evaluate the long-term effect of Bevacizumab on macular edema secondary to central and branch retinal vein occlusions.

Methods: Retrospective study of 12 consecutive patients with macular edema secondary to retinal vein occlusions with a minimum of 3-years of follow up. Patients were evaluated at baseline using Optical Coherence Tomography (OCT) and Fluorescein Angiography and given intravitreal injections of Bevacizumab. Patients were followed with OCT and further injections were administered on follow up visits if persistent edema was noted (as needed therapy). Patients who received any other concurrent treatment modality were excluded from this study. The primary end points included visual acuity and central macular thickness (CMT) at 3- and 5- years. Statistical analyses were performed with paired T-tests.

Results: A total of 12 patients (mean age 59) were included. All patients had at least 3-years of follow up and 6 patients had 5-years of follow up. There was an improvement in logMAR visual acuity of -0.24 (p=0.02) after 3 years and -0.19 (p=0.47) after 5 years. There was a statistically significant reduction in mean CMT from 374 to 254 microns (difference=120, p=0.001) after 3 years, and from 470 to 304 microns (difference=166, p=0.01) after 5 years.

Conclusions: As needed intravitreal injections of Bevacizumab lead to a significant reduction in macular edema after three years and after five years. Intravitreal injections of Bevacizumab improved visual acuity after three years.

Using Genotype Analysis to Predict Duration of Disease and Response to Therapy in Wet Age-Related Macular Degeneration

Abstract Number: 2231 - A0022

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Purpose: Recent studies have demonstrated the utility of genotype assessment to predict future choroidal neovascularization (CNV) in patients with early age-related macular degeneration (AMD). In this study, relevant genetic markers were evaluated for utility in predicting visual prognosis,
treatment requirements, and time to resolution in patients with advanced AMD and CNV.

**Methods:** DNA specimens from 51 subjects with angiographically-confirmed CNV were genotyped for single nucleotide polymorphisms (SNPs) in genes known to be associated with CNV: CFH, CFHR4, CFHR5, F13B, C2, C3, CFB, and ARMS2. Retrospective chart review was performed to collect age, gender, race, smoking status, date of initial conversion to wet AMD, and time to first resolution of wet disease. Visual acuity, central foveal thickness (CFT) and cube average macular thickness (CAT) by optical coherence tomography, and treatments were recorded at each visit. Linear regression analysis was used to assess the effect of genotype and demographic variables on these outcomes over time.

**Results:** The C-A SNP at rs1750311 (CFHR5) was significant for improved visual acuity over time (p=0.0063). Non-white race (p=0.0353) and SNPs at rs2274700 (CFH, p=0.0176, 0.0032) were associated with decreased CFT over time. SNPs at rs1092253 (CFHR5) were associated with increased CFT (p = 0.0015, 0.0005). CAT increased over time in patients with G-T at rs2990510 (F13B, p=0.0296) and decreased in patients with A-G at rs698859 (F13B, p=0.0100). Greater numbers of monthly anti-VEGF injections were required for patients with SNPs at RS1061170, RS9332739, and RS2990510 (p = 0.033, 0.0256, 0.0355). Fewer treatments were required for patients with SNPs at RS69885 and RS299050 (p = 0.0017, 0.0114). Non-smokers required fewer injections than patients who previously smoked (p = 0.0009). Shorter time to resolution was seen with SNPs at rs641153 (CFB, p=0.0918) and rs2274700 (CFH, p=0.0267, 0.0421). Hypertension was also associated with shorter time to resolution (p=0.0003). Longer time to resolution was seen with C-A at rs1750311 (CFHR5, p=0.013).

**Conclusions:** Genotype analysis in patients with newly-diagnosed CNV revealed SNPs associated with certain outcomes of vision, macular thickness, treatment requirement, and time to first resolution. Genotype assessment can aid the ophthalmologist in discussing expectations in patients with wet AMD.

**Predictive Factors for Visual Acuity Loss after Focal/Grid Photocoagulation for Diabetic Macular Edema**

**Abstract Number:** 1790 - A0227

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**Disclosure Block:** Daniel Lee, None; Ryan K. Wong, None; James K. Kempton, None; John J. Huang, Allergan (Code R (Recipient))

**Purpose:** Macular edema accounts for the majority of vision loss in those with diabetic retinopathy. Though focal/grid laser photocoagulation remains the standard for treatment, many studies are showing the benefit of other modalities, such as intravitreal corticosteroids or anti-vascular endothelial growth factor (VEGF) agents. With an array of treatment choices, it is at times difficult to determine which modality to use. We aim to identify prognostic factors for response to laser photocoagulation treatment of diabetic macular edema (DME).

**Methods:** A retrospective chart review was conducted on patients referred for DME to the West Haven Veteran’s Administration Hospital from January 2010 to January 2013. Inclusion criteria
included: patients treated with focal/grid laser photocoagulation for clinically significant macular edema. Exclusion criteria included: lack of followup, previous vitrectomy, history of intraocular surgery or previous treatment for DME within the previous 4 months prior to treatment, or any concomitant ocular pathology know to also cause macular edema (epiretinal membrane, vein occlusion, tractional detachment). Data was collected on the following at baseline: visual acuity, age, renal function (eGFR), diabetic retinopathy stage, smoking status, HbA1c, blood pressure, and BMI. Endpoints were visual acuity at 4 month followup and 1 year followup. 

Results: 15/56 (27%) patients and 24 eyes qualified for the study. Tables 1 and 2 demonstrate that worse renal function (eGRF) was a predictive factor for vision loss (change of 0.1 logMAR) following focal/grid laser photocoagulation at both the 4-month followup (p=.04) and the 1-year followup (p=0.02). Baseline visual acuity, age, diabetic retinopathy stage, smoking status, HbA1c, systolic blood pressure, mean arterial blood pressure, and BMI were not predictive of visual acuity worsening following treatment.

Conclusions: Though a larger study will need to validate our data, the results suggest a possible predictive role of renal function for treatment failure following focal/grid laser photocoagulation for DME. Though laser photocoagulation still remains the proven standard for treatment, this information could be useful in determining which patients should forgo laser photocoagulation for alternative treatments such as corticosteroids or anti-VEGF agents.

Orbital Volume Augmentation Using Expandable Hydrogel Implants in Acquired Anophthalmia and Phthisis Bulbi

View Session Detail

Abstract Number: 2783 - A0262

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Disclosure Block: Esther Lee, None; Carlo Rob Bernardino, None; Flora Levin, None

Purpose: Insufficient orbital volume following enucleation or evisceration can result in post-enucleation socket syndrome (PESS), and long-standing phthisis can result in orbital volume deficiency similar to PESS. Patients may achieve volume augmentation using a variety of available implants, but there continues to be little consensus regarding the ideal choice of orbital implant. Hydrogel is a hydrophilic, self-expanding material that offers many advantages of the ideal implant. While it has been used successfully for congenital anophthalmia and microphthalmia, we present our initial experience with hydrogel implants in cases of acquired anophthalmia and phthisis bulbi.

Methods: This is a retrospective review of the clinical records of all adult patients who received an expandable spherical hydrogel implant or injectable hydrogel pellets for orbital volume augmentation in cases of orbital atrophy following enucleation or phthisis bulbi at the Emory Eye Center between 2004 and January 2007 and the Yale Eye Center between 2009 and 2011. 

Results: Nine women and five men were included in the study. The average age was 51.2 years old, with a range of 35 to 76 years. Follow-up spanned from 2 to 31 months, with a mean follow-up time period of 15.1 months. Four patients received spherical hydrogel implants and 10 patients
underwent hydrogel pellet injections. An average of 9 pellets (range 5-16) were placed in each patient over an average of 1.7 injections (range 1-3). Most commonly, five pellets were injected per session, as was the case for 13 of the 17 total treatment sessions. All patients experienced an overall subjective improvement in cosmesis. Post-operative complications included two cases of pellet migration, one subcutaneously and one anteriorly, due to insufficiently posterior implant placement, as well as one hospital admission for pain after injection of 10 pellets in one sitting.

**Conclusions:** Hydrogel implants offer several advantages over other existing options for orbital volume augmentation, as they are easy to place, well-tolerated, volume-titratable, and, to the extent that our follow-up shows, appear safe and durable. Further studies will be necessary to assess the longer-term use of these implants, but our experience suggests they are a promising means of treating orbital atrophy in acquired anophthalmia or phthisis bulbi.

**Impact of laser trabeculoplasty and cataract surgery on ab interno trabeculectomy (Trabectome) outcomes**

**Abstract Number:** 3173 - A0343

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**Purpose:** To report the impact of laser trabeculoplasty and phacoemulsification on outcomes of Trabectome.

**Methods:** Single-center retrospective study of 189 consecutive cases of Trabectome surgery that had 12-months of follow up. Trabectome surgeries were either Trabectome only (Tome) or combined with phacoemulsification cataract extraction and intraocular lens implantation (Tome+CE/IOL). Two groups were compared: eyes with no history of laser trabeculoplasty (NoLT) and eyes with a history of laser trabeculoplasty (LT) prior to Trabectome surgery. Outcomes included: intraocular pressure (IOP) reduction, glaucoma medication reduction, and secondary glaucoma procedures.

**Results:** 189 Trabectome cases qualified for analysis: 129 cases of primary open angle glaucoma (POAG), 40 cases of normal tension glaucoma (NTG), and 20 cases of pseudoexfoliation glaucoma (PXG). 172 cases were Tome+CE/IOL and 17 cases were Tome. The mean preoperative IOP was 19.2±5.6mmHg and 21.8±10.4mmHg in the NoLT (n=147) and LT groups (n=42) respectively. At 12 months, the mean IOP decrease was -4.0±6.2mmHg (16%) in the NoLT group and -4.5±9.6mmHg (15%) in the LT group. Glaucoma medication reduction did not differ between the two groups. Laser trabeculoplasty type did not affect outcomes. 4.8% of NoLT eyes and 15.2% of LT eyes required secondary glaucoma procedures (p=0.04). Applying OHTS criteria, an IOP reduction of at least 20% was achieved in 47% of NoLT eyes and 38% of LT eyes. Linear regression compared outcomes among POAG, NTG, and PXG eyes. PXG eyes with or without prior laser trabeculoplasty had significantly greater IOP reduction (-9.9±12.0mmHg, 34%) and glaucoma medication reduction (-1.5±1.4 drops, 59%) compared to NTG (-2.3±3.6mmHg, 13%, p<0.001; -0.7±1.2 drops, 36%, p=0.05) and POAG eyes (-3.8±6.4mmHg, 14%, p<0.001; -0.9±1.2 drops, 35%, p=0.03).

**Conclusions:** Trabectome was effective in decreasing IOP in eyes either with or without previous
laser trabeculoplasty. Both Tome and Tome+CE/IOL resulted in a moderate decrease in IOP and a
decrease in glaucoma medications. Eyes with previous laser trabeculoplasty had higher rates of
secondary procedures after Trabectome. PXG eyes had the most significant reduction in IOP and
glaucoma medications and may be good candidates for Trabectome.

Co-culture of stem cell derived retinal progenitors and retinal pigment epithelium promotes tissue maturity

View Session Detail

Abstract Number: 3995 - D0054

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Purpose: To restore vision, stem cell therapies for retinal degenerations must address the loss of
both photoreceptors and retinal pigment epithelium. To explore the effects of each tissue layer on
the other's maturation, we co-cultured human embryonic stem cell derived retinal progenitor cells
(hESC-RPC) with retinal pigment epithelium (hESC-RPE).

Methods: Cultures were derived from the H9 human embryonic stem cell line using modifications of
previously published techniques. To generate hESC-RPC, H9 were seeded as clusters to
polycaprolactone (PCL) scaffolds and cultured in retinal differentiation media. hESC-RPE were
expanded as monolayers on laminin-coated Transwell filters in serum-free media, and adapted to
the retinal differentiation media for co-culture. In the co-culture group, hESC-RPC cultures were
placed on top of hESC-RPE monolayers during the retinal differentiation protocol. For controls,
cultures were maintained separately in retinal differentiation media. Transepithelial electrical
resistance (TER) was monitored over time to assess RPE integrity and function. After 2-4 weeks, co-
cultured tissue layers were separated and compared to controls by RT-PCR and
immunofluorescence.

Results: Neural retinal marker mRNAs were expressed by hESC-RPC in both monoculture and co-
culture. Co-cultures expressed several of these markers at higher levels, including Crx and
Rhodopsin. Immunofluorescence revealed multilayered clusters positive for markers including Otx2,
Crx, and Recoverin. In co-cultures, these markers localized to the surface opposing the RPE. An
RT-PCR array for monitoring RPE maturation showed that co-cultured hESC-RPE was more mature.
In addition, co-cultured hESC-RPE maintained a high TER in retinal differentiation medium, while in
controls the TER decreased after 2-4 weeks.

Conclusions: Co-culture increases the maturation of both hESC-RPC and hESC-RPE, underlining
the interdependence of these tissues. Secretions of the RPE and contact with the RPE could
supplement or replace media as promoters of RPC differentiation, facilitating the creation of a
transplantable tissue.
Role of the starburst network in direction selectivity and beyond

Abstract Number: 3522

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Presentation Description: The talk will review recent results on the synaptic function of the starburst network in direction selectivity and the functional properties of cholinergic and GABAergic neurotransmission in the inner plexiform layer of the mammalian retina.