# The Seventeenth Annual John T. Flynn Resident-Fellow Research Day
Edward S. Harkness Eye Institute, 7th Floor Amphitheatre
Thursday, June 15, 2017
11:00 A.M. – 3:30 P.M.

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Abstract Title: Cone Function in USH2A-associated Retinal Degeneration is More Attenuated in Patients with Hearing Loss

PURPOSE:
Mutations in Usherin 2A (USH2A) can cause Usher syndrome (USH), which manifests as retinitis pigmentosa (RP) with bilateral neurosensory hearing loss, or autosomal recessive non-syndromic RP (NSRP). Few studies have characterized natural disease phenotype for patients with USH2A-associated retinal degenerations. Thus, we performed a retrospective analysis comparing electroretinography (ERG) data, retinal structure, and distribution of severe mutations between NSRP and USH patients harboring at least two mutations in USH2A.

METHODS:
A total of 20 RP patients with two or more pathogenic mutations in USH2A were included, specifically ten USH patients and ten age-matched NSRP patients. To evaluate visual function prognosis, 30 Hz-flicker ERG recordings were compared between groups. Ellipsoid zone (EZ)-line length on SD-OCT and autofluorescent (AF) ring diameters on fundus AF (FAF) imaging were also compared.

RESULTS:
NSRP patients had higher mean 30 Hz-flicker amplitudes of 17.0 ± 5.9 µV (mean ± SE) compared to USH patients, 2.1 ± 0.6 µV (p = 0.04). The proportion of total alleles containing a severe mutation was 45% in the USH group compared to 15% of NSRP patients, with an odds ratio of 4.6 (confidence intervals: 1.1, 20) (p=0.04). There was no statistically significant difference in EZ-line length or AF ring diameters between groups.

DISCUSSION/CONCLUSIONS:
Our data suggests USH manifests as a more severe phenotype compared to NSRP caused by mutations in the same USH2A gene, as assessed by ERG. A genetic threshold in which mutation burden relates to visual and auditory phenotype may exist.
The fate of rescued rods in a diseased environment

PURPOSE:
Retinitis pigmentosa is the leading cause of inherited blindness. While gene therapy has the capacity to rescue diseased cells (usually rods), current methods generate retinas that are a mix of treated, rescued and untreated, dying rods. To determine whether the dying rods negatively impact rescue, we developed mouse models that allowed us to treat defined fractions of diseased rods.

METHODS:
We created two RP mouse models to test whether dying, untreated rods negatively impact treated, rescued rods. In one model, treated and untreated rods were segregated. In the second model treated and untreated rods were diffusely intermixed, and their ratio controlled to achieve low-, medium- or high-efficiency rescue.

RESULTS:
We found that dying rods did not trigger the death of rescued photoreceptors, even when the rescued cells are greatly outnumbered. On the other hand, the rescued photoreceptors did exhibit long-term defects in their outer segments, which were less severe when more rods were treated.

DISCUSSION/CONCLUSIONS:
In summary, our study suggests that even low-efficiency gene therapy may achieve stable survival of rescued photoreceptors in RP patients, albeit with OS dysgenesis.
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Name of Author(s): Joaquin O. De Rojas, MD; Kaspar Schuerch, MD; Priya M. Mathews, MD; Thiago Cabral, MD; Albert Hazan, MD; Janet Sparrow, PhD; Stephen H. Tsang, MD, PhD; Leejee H. Suh, MD

Abstract Title: Evaluating structural progression of retinitis pigmentosa after cataract surgery

PURPOSE:
To determine whether cataract surgery accelerates disease progression in retinitis pigmentosa (RP).

METHODS:
Retrospective cohort study featuring 70 eyes of 40 patients with RP were categorized as having had phacoemulsification with intraocular lens implantation versus no cataract surgery at a single tertiary-level institution. Spectral domain optical coherence tomography (SD-OCT) was used to measure the ellipsoid zone (EZ) width, which has been demonstrated to be a reliable marker of RP severity, at baseline and throughout follow-up (median 768 days). RP progression was calculated as the loss of EZ width over time for all patients. Additional post-operative data was collected for the cataract surgery group, including pre- and post-operative best-corrected visual acuity, incidence of macular edema, posterior capsular opacification, epiretinal membrane, and intraocular lens subluxation.

RESULTS:
Multivariable analysis including age, baseline EZ width, mode of inheritance, and cataract surgery status showed that there was no significant difference in RP progression between the cataract surgery and control groups ($P=0.23$). Mode of inheritance was associated with RP progression, with autosomal recessive RP progressing at 148 microns/year and autosomal dominant RP progressing at 91 microns/year ($P=0.003$). Visual acuity improved in almost all eyes that underwent surgery (17/19, 89%), and remained stable in remaining eyes (2/19, 11%). There was a high incidence of post-surgical posterior capsular opacification (18/19, 95%). There were no serious complications such as lens subluxation or endophthalmitis.

DISCUSSION/CONCLUSIONS:
Our findings suggest that cataract surgery is a safe and effective means of improving visual acuity in RP patients and that it does not seem to be associated with faster disease progression as measured using SD-OCT.
Abstract Title: Progression and Outcomes of Fellow Eye After Unilateral Treatment for Retinopathy of Prematurity

PURPOSE: In the ET-ROP study 20.9% of infants had asymmetric disease with high-risk prethreshold disease in only one eye. The eyes in this category had a lower rate of unfavorable outcome (1.5%) than those in which bilateral treatment occurred (8.1%). It is the practice in some centers to treat the fellow eye in such babies so as to avoid the need for repeat general anesthesia. We undertook to investigate if a similar percentage of babies in our NICU developed ROP of sufficient severity to lead to only one eye having Type 1 ROP at the time of treatment, and to determine how often and when the fellow eye converted to treatment-requiring ROP from a lesser category.

METHODS: An IRB-approved, retrospective chart review was performed of patients developing treatment-requiring ROP in one eye. Patients were analyzed for time to develop treatment-requiring ROP in the second eye, and management course and outcomes.

RESULTS: A total of 774 babies were screened by the ophthalmology service at Columbia University Medical Center in New York, NY, USA, from 2011 – 2015. We identified 33 patients who underwent laser treatment for ROP. Of these, 8 babies (24%) received their initial laser treatment in only one eye. Of the 8 infants treated with laser unilaterally, 2 babies (25%) underwent treatment for ROP in the second eye. One reached Type 1 ROP in the second eye 2 weeks later and received laser treatment. The second was treated with laser in the fellow eye outside standard criteria of Type 1 ROP 1 week later. Six of the infants (75%) never required fellow eye treatment and all six untreated eyes had complete regression of ROP. One baby received bilateral off-label bevacizumab injections prior to unilateral laser treatment and the fellow eye did not require laser.

DISCUSSION/CONCLUSIONS: In our NICU a similar percentage of babies had asymmetric treatment-requiring ROP as reported in the ET-ROP study. Of the two that later went on to receive treatment in the fellow eye, both developed disease within two weeks of initial treatment, suggesting that when progression occurs, it is usually rapid. This can be helpful for clinicians screening for ROP as well as reduce morbidity from excessive laser treatment. Further evaluation of the long-term outcomes in these patients may help guide clinical care.
Name of Author(s): James Lin MD, Jonathan S. Chang MD, Jason Horowitz MD, Stanley Chang MD

Abstract Title: Physiological outcomes after silicone oil removal

Purpose: We performed a retrospective study to examine the long-term IOP lowering effects of SOR, along with factors that affected visual outcomes following SOR.

Methods: We reviewed longitudinal data from a university-based retina practice, including patients who underwent silicone oil tamponade for retinal detachment repair with subsequent SOR. Maximum IOP up to 2 months prior to SOR (pre-op IOP) was compared to IOP at time points up to 2 years post-SOR using the paired t-test. Physiological outcomes such as membrane peeling were examined in its effects on visual acuity (VA) and central retinal thickness (CRT).

Results: Overall, the mean IOP was significantly lower up to 1 month after SOR compared to pre-op IOP (12.7 vs. 17.6, p=0.001). Similarly the lasting effect of lowered IOP was seen at 3-6 months post-SOR at an average of 14.2 mmHg (p=0.003). At >2 years, the mean IOP was 10.5 mmHg (p=0.0001). Of the 40 patients who underwent SOR, 11 patients (28%) underwent SOR secondary to elevated IOP (>21 mmHg). When compared to pre-SOR, VA began to improve at 3-6 months (p=0.05), lasting up to 1 year (p=0.005) after SOR. Those who had concurrent membrane peeling did not seem to have a difference in CRT (p=0.3). Likewise, membrane peeling did not have an effect on VA (p=0.6). Centistokes of oil, intraoperative membrane peeling, and membranes present post-SOR did not predict final VA or CRT.

Conclusions: The effect of SOR in significantly lowering IOP among all patients is demonstrated regardless of whether SOR was performed secondary to elevated IOP. While VA is improved up to 1 year after SOR, it does not appear that membrane peeling has a significant effect on vision or retinal thickness. This latter observation may be explained by the relatively poorer prognosis of retinal pathology requiring silicone oil.
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Authors: Jesse T. McCann, MD, PhD, K. Bailey Freund, MD; Jason D. Horowitz, MD

Title: Understanding the Retinal Vasculature using Insights from Optical Coherence Tomography Angiography

Purpose
Optical coherence tomography angiography (OCTA) is a new technique that uses motion flow data to aid in visualization of perfusion without the use of intravenous contrast by comparing the difference in backscattered OCT signal between multiple OCT B scans of the same cross-section. It presents a significant innovation for the visualization of macular conditions. Many OCTA image algorithms contain a significant amount of en face OCT data in their composition, and projection artifacts often limit the view of superimposed vascular layers. Unlike fluorescein angiography, flow can be localized to the layers of the retina. Structural and functional imaging of the retinal circulation with OCTA and understanding of the flow between the capillary plexi can be understood by examining the formation of collaterals.

Methods
18 eyes of 18 patients presenting for evaluation of branch retinal vein occlusion had 3-, 6-, and 8-mm cuts of en face OCT and OCTA performed of the macula in addition to fluorescein angiography (IVFA). Image analysis using ImageJ was combined with three-dimensional modeling to correlate structure with flow in imaging of retinal layers after vein occlusions with attention to the superficial, intermediate, and deep capillary plexi.

Results
Collateral formation in branch retinal vein occlusion can now be resolved in a three-dimensionally. Collaterals in all eyes were found to pass through the deep capillary plexus in all eighteen eyes, suggesting a bias towards venous drainage in the intermediate and deep capillary plexi.

Conclusions
Current models of retinal vascular circulation show parallel capillary arrangement through the superficial, intermediate, and deep capillary plexi. Multi-layered collateralization suggests that retinal circulation can be divided between the predominantly arterial superficial capillary plexus and the venous plexus consisting of the intermediate and deep capillary layers.
PURPOSE:
Using standard screening techniques, sickle retinopathy reportedly occurs in 10% of adolescents with sickle cell disease (SCD). We performed a prospective, observational clinical study to determine if ultra-widefield fluorescein angiography (UWFA), spectral-domain optical coherence tomography (SD-OCT) and optical coherence tomography angiography (OCT-A) detect more frequent retinopathy in adolescents with SCD.

METHODS:
Setting: Institutional.
Subjects: Sixteen adolescents with SCD, ages 10-19 years, (mean age 14.9 years) and 5 age-equivalent controls (mean age 17.4 years).
Observation Procedures: Examinations including acuity, standard slit-lamp biomicroscopy, UWFA, SD-OCT and OCT-A were performed.
Main Outcome Measures: Sickle retinopathy defined by biomicroscopic changes, Goldberg stages I-V, Penman scale, flow void on OCT-A, or macular thinning on SD-OCT.

RESULTS:
While 22/32 SCD eyes (68.8%) had retinopathy on biomicroscopy, by UWFA 4/24 (16.7%) SCD eyes had peripheral arterial occlusion (Goldberg I), and 20/24 eyes (83.3%) had peripheral arteriovenous anastomoses (Goldberg II) in addition. No patients had Goldberg stages III-V. By SD-OCT and OCT-A, thinning of the macula and flow voids in both the superficial and deep retinal capillary plexus were found in 6/30 (20%) eyes.

DISCUSSION/CONCLUSIONS:
All 24 eyes with adequate UWFA studies demonstrated sickle retinopathy. SD-OCT and OCT-A, which have not been previously reported in the adolescent population, detected abnormal macular thinning and flow abnormalities undetected by biomicroscopy. These findings suggest that pediatric sickle retinopathy may be more prevalent than previously suspected. If these findings are confirmed with larger cross-sectional and prospective analyses, these approaches may enhance early screening for sickle retinopathy.
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Authors:  Aliaa Abdelhakim MD PhD, Muhammad Anwar MS, Lauran Rosko BS, James Todaro MD, Takayuki Nagasaki PhD, Robert Ludwig MS, Martha Welch MD, Bryan Winn MD

Title: Role of Oxytocin and Secretin in Ocular Surface Inflammation

Purpose: Inflammatory diseases of the ocular surface occur with high prevalence. Previous studies have shown that combined administration of oxytocin and secretin down-regulated gut inflammation elicited by experimental colitis in rodents. In this study, we investigate the presence of the oxytocin and secretin receptors (OXTR and SCTR) on the corneal and conjunctival surfaces as possible modulators of inflammatory ocular surface disease.

Methods: Using fluorescently labeled anti-OXTR and anti-SCTR antibodies, we localized OXTR and SCTR by immunostaining of paraffin sections in rodent and human eyes, as well as in cell culture using immortalized SV40-HCEC cells derived from human cornea. Western blotting was used to confirm the presence of migrating bands corresponding to OXTR and SCTR from ocular-surface derived cell lysate.

Results: OXTR was expressed abundantly within the superficial layer of the human corneal and conjunctival epithelia. This localization pattern was also observed in the from rat eye, indicating conservation of OXTR expression between these two species. Moreover, OXTR was abundantly present in SV40-HCEC and was visualized in a peripheral manner consistent with its known membranous localization. Addition of a blocking peptide abrogated the fluorescence signal, confirming specificity of the anti-OXTR antibody. Anti-OXTR Western blotting using SV40-HCEC lysate confirmed the presence of the full-length protein migrating at ~ 46 kDa, consistent with that of OXTR. We also visualized specific immunolabeling for SCTR in the human and rat cornea. Intense staining with the anti-SCTR antibody was also observed using SV40-HCEC cells in vitro. Western blot analysis using SV40-HCEC lysate confirmed that the anti-SCTR immunofluorescent signal was specific, revealing a band corresponding to the size of SCTR at ~48 kDa.

Conclusions: OXTR and SCTR are present on ocular surface tissues in humans and rodents, showing that expression of these receptors are conserved. Given the high incidence of ocular inflammatory disease and previous studies showing the anti-inflammatory roles of OXTR and SCTR, our findings suggest a similar anti-inflammatory role for these receptors on the ocular surface.
Name of Author(s): Mathieu F. Bakhoum, MD, PhD, Jesse D. Sengillo, Eugenia C. White, Wei-Pu Wu, Marcelle M. Morcos, MD, K. Bailey Freund, MD, Henry D. Perry, MD and Stephen H. Tsang, MD, PhD

Abstract Title: Mitochondrial A3243G mutation results in endothelial corneal dystrophy

PURPOSE: The mitochondrial DNA (mtDNA) point mutation A3243G leads to a spectrum of syndromes ranging from maternally inherited diabetes and deafness (MIDD) to mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS). We tested whether corneal endothelial dystrophy is present in patients harboring the mtDNA point mutation A3243G.

METHODS: Patient Population: Four patients (eight eyes) diagnosed with mtDNA point mutation A3243G pattern macular dystrophy, MIDD or MELAS. Exclusion criteria included prior intraocular surgery, a prior diagnosis of corneal dystrophy, a positive family history of Fuchs’ endothelial corneal dystrophy and contact lens wear.
Observation Procedures: Slit-lamp corneal examination and specular microscopy were performed. Patients who were previously diagnosed solely based on clinical history and examination were genetically tested for the mtDNA point mutation A3243G with pyrosequencing.
Main Outcome Measures: Corneal endothelial cell size and polymegathism, corneal endothelial cell count and central corneal thickness.

RESULTS: Corneal endothelial changes observed using slit-lamp examination were primarily mild to rare guttata. Specular microscopy showed mainly polymegathism along with guttata. The average coefficient of variation (COV) of cell size was 41.6 ± 4.3%. When compared to the average population, the average COV was significantly higher than predicted for the patients’ age. One patient had a pre-descemet’s opacity.

DISCUSSION/CONCLUSIONS: In patients with the mtDNA point mutation A3243G, endothelial corneal dystrophy is a highly penetrant phenotype. This previously uncharacterized corneal dystrophy is mainly associated with polymegathism along with mild guttata. The prevalence of this mtDNA point mutation in the Caucasian population is about 0.24%. This observation underscores the role of mitochondria in the pathogenesis of endothelial corneal dystrophies.
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Authors: Albert S. Hazan, MD, Jonathan S. Chang, MD
Title: Refractive Changes Following Scleral Buckle Surgery for Rhegmatogenous Retinal Detachment Based on Type of Implant Used

Purpose: To evaluate refractive changes after scleral buckle surgery for rhegmatogenous retinal detachment, and compare outcomes of radial, segmental and encircling scleral buckle techniques.

Methods: Retrospective chart review patients undergoing rhegmatogenous retinal detachment (RRD) treated with primary scleral buckle at Columbia University Medical Center. Preoperative and post-operative refraction, pre-operative and postoperative best corrected visual acuity (BCVA), and reoperation rates were recorded. Configuration of retinal detachment and type of element used was also compared. Change in spherical equivalent (SE change) was compared between patients undergoing radial, segmental and encircling scleral buckle surgery.

Results: A total of 47 eyes were reviewed. There were 9 patients who received radial scleral buckles, 20 who received segmental scleral buckles and 18 who received encircling scleral buckles with complete refractive data. There was a greater myopic shift in encircling scleral buckle repair of RRD (mean pre-operative to post-operative SE change of -3.05D) when compared to segmental (SE change -0.42D p < 0.001) and radial (SE change -0.19D p= 0.0003) scleral buckle repair. No significant difference was noted between circumferential and radial scleral buckles (p=0.66). There was no significant difference between the 3 groups in terms of preoperative BCVA, postoperative BCVA and reoperation rates (all p-values >0.1).

Conclusions: Radial and segmental techniques of scleral buckle demonstrated significantly less refractive changes than encircling buckles, with no differences in post-operative BCVA or retinal attachment status. For patients with high refractive demands such as young patients or post-refractive surgery patients, a segmental or radial buckle may be a better option than an encircling buckle for RRD repair.
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Name of Author(s): Jonathan Fay, MD, George Florakis, MD, Danielle Trief, MD
Leejee Suh, MD

Abstract Title: A method for imaging and evaluating corneal vascularization

PURPOSE: There is great clinical interest in the prevention and treatment of corneal neovascularization. One limitation in the study and management of corneal neovascularization is a lack of validated methods to quantify it and follow changes over time. In this study we propose a method for the clinical evaluation of corneal neovascularization.

METHODS: A standardized protocol was used to study a patient with corneal neovascularization. Color slit lamp images were obtained using broad beam illumination at 10x magnification. Using Image J software (National Institute of Health, Bethesda, MD), a red-free filter was applied to the images. Three independent observers manually identified the corneal limbus then circumscribed areas of vessels extending beyond the limbus. The degree of corneal neovascularization was reported as the percent surface area of cornea involved.

RESULTS: The protocol was applied to 36 images obtained at two time points and assessed by three independent observers. The percent surface area involved at a single time point was 43.5% (95% CI 41.0%-46.0%). Percent surface area involved ranged from 42% to 46% among three observers. Difference in intra-observer percent surface area calculation was no greater than 8% with standard deviation ≤ 0.05%.

DISCUSSION/CONCLUSIONS: We describe a method for evaluating corneal neovascularization that is reproducible with good inter Observer agreement. This method utilizes readily available tools and is simple and non-invasive. Limitations include the two-dimensional evaluation of a three-dimensional structure and that vessel caliber is not assessed. Further studies may demonstrate the clinical utility of this method with regard to monitoring the progression or treatment of corneal neovascularization.
**Abstract Title:** Sustained Long-Term Improvement in Visual Acuity in Patients with Keratoconus and Post-LASIK Ectasia Undergoing Collagen Cross-Linking

**PURPOSE:**
Previous studies have demonstrated that collagen cross-linking is an effective treatment to halt the progression of keratoconus (KCN) and post-LASIK ectasia (PLE). The purpose of this study was to determine if the benefit of collagen cross-linking extends beyond vision stabilization, and possibly result in sustained improved visual acuity.

**METHODS:**
This is a retrospective analysis of 56 eyes with KCN/PLE undergoing collagen crosslinking following the Dresden protocol. Best spectacle corrected visual acuity (BSCVA) of both eyes was recorded at baseline and all follow-up visits. A change of 0.1 logMAR was considered equivalent to 1 line in the Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity chart. Continuous outcomes were compared with student’s \( t \)-test (paired and unpaired), and binary variables were compared with chi-squared analysis.

**RESULTS:**
There was a significantly greater proportion of patients who showed some degree of improvement in visual acuity at 3, 6, 12, 18, 24, and 30 months in eyes undergoing CXL treatment versus the fellow untreated eye (\( p < 0.05 \) for all). There was a substantial improvement (defined as at least 2 lines improvement in vision from pre-operative BSCVA) in the CXL-treated eyes compared to the fellow untreated eyes at 1 year [8/32 (25.0%) versus 1/30 (3.3%), \( p = 0.03 \)] and 2 years [11/17 (64.7%) versus 0/11 (0%), \( p = <<0.001 \)]. At three years, 3/8 (37.5%) of CXL eyes showed an improvement of three or more lines versus 0/6 (0%) of the fellow untreated eyes (\( p = 0.10 \)).

**DISCUSSION/CONCLUSIONS:**
Our results suggest that collagen cross-linking not only halts the progression of KCN/PLE, but may substantially improve visual acuity which is sustained for years. The benefits of collagen cross-linking likely extend beyond current indications and should be considered for treatment of refractive error and other corneal disorders as well.
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Name of Author(s): Gene Kim, MD; C. Gustavo De Moraes, MD, MPH; Portia E. Sirinek, MD; Dana M. Blumberg, MD, MPH; Lama A. Al-Aswad, MD, MPH; Christopher Girkin, MD, MSPH; Felipe A. Medeiros, MD, PhD; Robert N. Weinreb, MD; Linda M. Zangwill, PhD; Alon Skaat, MD; Luna Xu, MD; Jeffrey M. Liebmann, MD

Abstract Title: Optic disc hemorrhage and subsequent central visual field loss in the African Descent and Glaucoma Evaluation Study (ADAGES)

PURPOSE: Optic disc hemorrhage (DH) is a significant predictor of visual field (VF) progression. We investigated the association between DH and subsequent global vs. central VF loss on standard automated perimetry.

METHODS: 406 eyes of 246 participants were included from the ADAGES cohort. Stereoscopic disc photos were taken annually for up to 13 years and reviewed for DH presence by two masked investigators. 24-2 VF tests were performed every 6 months, while 10-2 tests were performed in the last 5 years of follow-up. Rates of VF progression after DH detection were assessed using mixed effects linear models with 3 outcomes: (i) 24-2 mean deviation (MD), (ii) 24-2 central mean deviation (CMD, based on total deviation of points within the central 10 degrees), and (iii) 10-2 MD.

RESULTS: 24 eyes (6%) of 20 patients (8%) had at least one DH and at least four subsequent 24-2 and 10-2 VFs. Based on 24-2 MD rates, there was a non-significant difference between DH and non-DH eyes (difference between groups $\beta=-0.06$ dB/yr, $p=0.303$). However, DH eyes progressed significantly faster than non-DH eyes based on 24-2 CMD rates ($\beta=-0.16$ dB/yr, $p=0.012$) and 10-2 MD rates ($\beta=-0.59$ dB/yr, $p=0.026$).

DISCUSSION/CONCLUSIONS: DHs often occur in the inferotemporal sector, where RNFL defects are associated with macular damage. We found that DH is a predictor of subsequent focal, central VF progression which can be missed with global 24-2 MD. Clinical DH identification should prompt more intensive surveillance of the central VF, and can be enhanced by 10-2 VF testing.
PURPOSE:
Descemet’s membrane endothelial keratoplasty (DMEK) is replacing Descemet’s stripping automated endothelial keratoplasty (DSAEK) as the endothelial keratoplasty of choice because of proven better post-op corrected and uncorrected visual acuities. However, ultrathin-DSAEK, defined as a donor graft < 100 microns thick, may be comparable to DMEK; this is yet to be evaluated in the United States. The purpose of this study was to compare best-corrected visual acuity (BCVA) and refractive outcomes after DMEK or UT-DSAEK.

METHODS:
A retrospective chart analysis was performed for endothelial keratoplasty procedures from 1/1/2010 through 1/6/2017 with concurrent cataract extraction/posterior chamber intraocular lens placement at our institution. Pre- and post-operative BCVA, spherical equivalent, difference between acquired and target refractions, hyperopic shifts, and any complications were compared between the two groups.

RESULTS:
A total of 30 patients who underwent cataract surgery combined with DMEK (n=16) or UT-DSAEK (n=14) were included in the analysis. Pre-operative logMAR BCVA was same between DMEK and UT-DSAEK (0.30 vs 0.36 respectively, P=0.36). At post-op month 6, no significant differences were found in logMAR BCVA (0.067 vs 0.068, P=0.97), spherical equivalent (-0.34 vs -0.27, P=0.83), or hyperopic shift (+0.24 vs +0.62, P=0.26).

DISCUSSION/CONCLUSIONS:
Our data suggest no difference in BCVA between groups and a trend towards more hyperopia after UT-DSAEK vs DMEK. Compared to the literature, we calculated a less hyperopic shift after DMEK or UT-DSAEK, and even a myopic shift in a few patients.
Abstract Title: Baseline 24-2 Central Visual Field Damage is Predictive of Global Progressive Field Loss

Purpose: Central visual field (VF) damage in glaucoma patients can significantly hinder daily activities. The present study investigates whether the presence of localized baseline damage to the central ten degrees of VF is predictive of faster global mean deviation (MD) progression.

Methods: This prospective cohort study analyzed eyes from the multicenter African Descent and Glaucoma Evaluation Study (ADAGES) with established glaucoma and VF loss and a minimum of five 24-2 VFs were eligible. Baseline central 24-2 damage was defined as any of the 12 central-most points with total deviation (TD) values at P<0.5% on two consecutive examinations. Progression was determined using two criteria: (i) MD rates of change with mixed effects linear models and (ii) >-5 dB MD loss over the entire follow-up with Cox proportional hazards survival analysis.

Results: 1,111 eyes of 777 patients were studied. Mean rate of MD change of the entire sample was -0.21dB/yr (95% CI: -0.25 to -0.18, P<0.001). Eyes with baseline central damage progressed faster than those without (difference: $\beta_{central} = -0.29$ dB/yr, 95% CI: -0.37 to -0.21, P<0.001) and were more likely to experience MD loss greater than 5 dB [HR=6.53 (95% CI: 2.63 to 16.2, P<0.001)]. These differences remained significant after matching for baseline severity (P=0.011).

Discussion/Conclusions: The presence of central VF damage increases the velocity of global progression six-fold. Detection of central VF damage aids in stratification of high-risk patients who may need intensive surveillance and aggressive treatment.
**Title:** Is Macular Pucker Associated with More Severe Glaucoma?

**Purpose:** Both macular pucker (MP) and glaucoma affect the elderly and impact visual function. Data suggests that both conditions may be associated with inflammatory mediators and glial proliferation. This study investigates the possible relationship between MP and glaucoma severity.

**Methods:** The records of all patients undergoing vitrectomy and membrane peel for MP from 2010 to 2016 at Columbia University Medical Center were reviewed. Inclusion criteria required a preoperative diagnosis of bilateral primary open angle glaucoma and severe unilateral MP that distorted the macula anatomically. Patients with uveitis, history of intraocular surgery other than uncomplicated cataract extraction, or coexisting optic nerve and macular pathologies were excluded. For inclusion, patients must have had automated perimetry program 24-2 and Cirrus OCT optic disc cube 200x200 scans within 12 months of surgery. Two glaucoma specialists masked to the presence of the ERM independently evaluated disc photographs and assessed the relative degree of optic nerve cupping between eyes. Inter-eye comparisons between optic nerve parameters (Cirrus disc rim area, average cup to disc ratio, vertical cup to disc ratio), visual field index (VFI), and mean deviation (MD) were made using the Wilcoxon matched pairs signed rank tests.

**Results:** Eight subjects were enrolled. The mean patient age was 72 yrs and 62.5% were women. All were European-derived. The two specialists independently agreed on the glaucoma asymmetry for all cases; in 7/8 cases the MP occurred in the eye with the worse glaucoma. The MP eye had statistically significantly lower VFI (80.9 vs 93.0 %, p = 0.01), and higher average cup to disc ratio (0.78 vs 0.71, p = 0.04). The rim area between the two eyes approached statistical significance (0.79 vs 0.97, p = 0.06) as did the mean deviation (7.2 dB vs 4.3 dB, p=0.10).

**Discussion:** This pilot study explores a potential association between macular pucker and glaucoma severity, which had not been examined previously. The two share similarities in theories of pathogenesis including reactive gliosis and inappropriate cytokine activation. Our data suggests that it is reasonable to suspect that in eyes with unilateral MP and glaucoma, the MP eye is associated with the more severe glaucoma. While one may suspect the visual field data could be confounded by the presence of MP, the optic nerve parameters should remain relatively unaffected.

**Conclusion:** In eyes with unilateral MP and glaucoma, MP occurs more commonly in the eye with worse glaucomatous disease.
The Seventeenth Annual John T. Flynn Resident-Fellow Research Day  
Edward S. Harkness Eye Institute, 7th Floor Flanzer Amphitheatre  
Thursday, June 15, 2017

Author: Kristen E. Dunbar M.D., Tavish Nanda M.D., Ashley A. Campbell M.D., Ryan M. Bathras, and Michael Kazim M.D.

Title: Asymmetric Exophthalmos in Patients with Thyroid Eye Disease and Compressive Optic Neuropathy: A Clinical and Anatomical Investigation

INTRODUCTION: Worsening proptosis is believed to occur in more severe TED and is a factor in several clinical severity indices. Despite the paucity of data, however, it is also generally held that greater proptosis in TED may provide relative protection from CON, by expanding orbital volume and reducing pressure on the optic nerve. The objective of this study is two-fold; (1) to investigate the possible phenomenon of spontaneous decompression in patients with bilateral TED-CON who demonstrate asymmetric proptosis and (2) to examine the orbital anatomy of patients who developed significant clinical asymmetry.

METHODS: This study is an institutional review board approved retrospective study of 67 patients (134 orbits) with bilateral TED-CON evaluated by a single practitioner (M.K.) at the Harkness Eye Institute at Columbia University Medical Center. TED-CON was suspected based on a constellation of clinical findings, including decreased visual acuity and the addition of either an afferent pupillary defect (APD), visual field defect, or reduced color vision. Diagnosis was confirmed by the improvement in these clinical findings following systemic steroids or orbital decompression surgery. Asymmetry for exophthalmos, measured on Hertel, was defined as >2mm. Asymmetric CON was defined first, as the presence of an RAPD. Those without an RAPD were evaluated according to the formula \( y = -0.69 - 0.31 \times \text{motility} - 0.2 \times \text{mean deviation} - 0.02 \times \text{color vision} \) as previously established for the diagnosis of TED-CON (sensitivity 83%, specificity 81% for a value >0). A difference in the formula result >1.0 between eyes was considered indicative of significant asymmetric CON. Using a contouring program (Pinnacle Systems v.2–v.10) patients with asymmetric CON were further evaluated, including orbital volume (OV), fat volume (FV), muscle volume (MV), FV/OV ratio, MV/OV ratio, MV/FV ratio, orbital length and diameter, globe size, and the percent of the globe posterior to an artificial demarcation drawn from the most anterior zygomatic border.

RESULTS: 29/67 patients demonstrated asymmetric CON by RAPD. 12/67 demonstrated asymmetric CON by the formula, resulting in 41/67 patients with asymmetric CON. With a cutoff point >1.0, all orbits demonstrated a color plate difference >30% (avg. 46.6%) and/or a MD on HVF difference >2.2 (avg. 6.34) between eyes. In total, 21/67 patients demonstrated significant asymmetric proptosis (>2mm), but only 12 also demonstrated asymmetric CON. Of those, only 5 demonstrated greater proptosis in the eye with less CON. On CT scan, none of the orbits with CON asymmetry demonstrated significant anatomic differences between eyes.

CONCLUSION: Despite commonly held assumptions, the results of the current study suggest that proptosis is not relatively protective in TED-CON. In total, only 5/67 (7.4%) had less severe CON in the eye with worse proptosis. Although there was no apparent anatomic predisposition for developing CON asymmetry, other variations including intra-orbital design, optic nerve size, and blood supply cannot be excluded.
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Authors: Ashley A. Campbell, MD, Tavish Nanda, Susel Oropesa, Michael Kazim, MD

Title: Age-Related Changes in the Clinical Phenotype of Compressive Optic Neuropathy in Thyroid Eye Disease

Introduction
The most important factor in determining the clinical phenotype of thyroid eye disease (TED) is the age of the patient. This study compares the age-related clinical features of TED-compressive optic neuropathy (TED-CON) to those with non-compressive disease (TED-NC).

Methods
A retrospective case series review of 165 orbits from 121 patients with TED-CON were compared to an age and gender-matched cohort of 88 orbits from 44 patients with TED-NC. Clinical features including exophthalmos, dyschromatopsia, restricted ocular motility, visual acuity, and mean deviation on 24-2 Humphrey Visual Field (MD-HVF) were compared in five age groups. A previously validated formula used to mathematically predict the presence or absence of compressive optic neuropathy was applied, and the sensitivity and specificity of the formula was measured in each age group.

Results
Exophthalmos, dyschromatopsia, restricted ocular motility and MD-HVF vary significantly across age groups in patients with TED-CON. Conversely, visual acuity did not demonstrate an age-related difference. There was a significant difference between the TED-CON and the TED-NC groups when comparing the two groups by decade. The predictive formula used to determine the presence of compressive optic neuropathy had high sensitivity and specificity (74%-90%) in all age groups.

Conclusions
A large case series of TED-CON patients demonstrates that the clinical phenotype of TED-CON varies significantly by decade when examining exophthalmos, dyschromatopsia, ocular motility restriction, and MD-HVF. These clinical characteristics are also significantly different when compared to a population of patients with TED-NC.
**Name of Author(s):** Sanjai Jalaj, MD; Bryan Winn, MD; Lora Glass, MD

**Abstract Title:** Lower Eyelid Movement in Downgaze

**PURPOSE:**
Lower eyelid movement in downgaze has not been well examined in the literature. Specifically, the method of measuring lower eyelid movement, and the degree to which the lower eyelid retracts with downgaze, have yet to be clearly elucidated. The purpose of this research is to define and measure the average amount the healthy lower eyelid moves on downgaze by attempting to measure it directly.

**METHODS:**
46 lower eyelids of 23 healthy adult individuals 18 years of age or older were directly measured in millimeters from primary position to downgaze, and from upgaze to downgaze. The authors excluded those with a history of acquired or congenital eyelid disease, thyroid eye disease, myasthenia gravis, neurologic disease, history of eyelid surgery, intraocular surgery, strabismus surgery, orbital surgery, botulinum toxin or filler injections periocularly, or those with any other cause of anatomic pathology of the lids such as chemical or thermal injury.

**RESULTS:**
The average age of participants was 56.2 years old (SD ± 13.6). The average amount of lower lid movement from primary gaze to downgaze was 3.2mm (SD ± 0.67). The average amount of lower lid movement from upgaze to downgaze was 5.5mm (SD ±1.0).

**DISCUSSION/CONCLUSIONS:**
The amount of lower eyelid movement on downgaze is easily measurable. The authors have defined a reference average in a healthy population. This measure, analogous to upper eyelid levator function, may be useful in characterizing lower eyelid pathology.
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Name of Author(s): Stacy Scofield-Kaplan, MD, Kristen Dunbar, MD, Gregory Stein, MD, Michael Kazim, MD

Abstract Title: Improvement in Eccentric and Primary gaze ocular alignment in Thyroid Eye Disease-Strabismus Surgery by the addition of Tenon’s recession

PURPOSE: To evaluate the improvement in primary and eccentric gaze in thyroid eye disease patients undergoing horizontal strabismus surgery with Tenon recession.

METHODS: This is an Institutional Review Board-approved retrospective analysis of patients with thyroid eye disease (TED) undergoing horizontal strabismus surgery for esotropia. The study included all patients from 2007 to 2016 operated on by a single surgeon at Columbia University Medical Center. Surgical success was defined as the ability to fuse at both near and distance either without prismatic correction or with less than 10 PD of correction. Measurements of ocular alignment were also made in eccentric fields of gaze.

RESULTS: Thirty-six patients with TED and restrictive horizontal strabismus underwent unilateral or bilateral medial rectus recession to relieve diplopia. Overall the success rate was 86% and a re-operation rate of 8.3%. The improvement in horizontal deviation in primary and eccentric gaze was statistically significant (P<0.001), but the change in vertical deviation in the five cardinal positions of gaze was not statistically significant. There was coincidental postoperative change in vertical deviation, which was not proportional to the preoperative horizontal deviation or the amount of horizontal recession.

DISCUSSION/CONCLUSIONS: The addition of Tenon recession to TED-horizontal strabismus surgery led to statistically significant improvement in ocular alignment in both primary, and eccentric gaze. This is the first study of TED-strabismus surgery to analyze the post-operative results in positions outside of primary and reading gaze. Due to the preoperative incommitance of ocular deviations in this subset of patients it has been routine to expect persistent postoperative eccentric misalignment. We postulate that the release of scar tissue by the addition of Tenon recession contributes to these improvements.
Abstract

Title: T-shaped Wedge Resection of the Upper Eyelid

PURPOSE:
The classically described pentagonal wedge resection is a method of upper lid reconstruction following full-thickness defects of the upper lid. This method involves a full-thickness lid resection in the shape of a pentagon. The triangular portion of the excision extends above the upper lid crease, resulting in a vertical skin incision superior to the lid crease. We describe a t-shaped pentagonal wedge resection, which restores the structural integrity of the upper eyelid while respecting relaxed skin tension lines.

METHODS:
A retrospective chart review was performed on patients who underwent a t-shaped wedge resection by a single surgeon between January 1, 2014 and June 1, 2017. In this procedure, a lid crease incision is made. A full-thickness rectangle of upper eyelid is then excised up to the level of the upper eyelid crease. An additional triangle of posterior lamella is excised superior to the eyelid crease, creating a pentagon while leaving the anterior lamella undisturbed. The eyelid margin is repaired using a vertical mattress suture through the Meibomian gland orifice line and an interrupted suture through the lash line. The tarsus is repaired using several interrupted partial thickness dissolvable sutures. The skin medial and lateral to the defect inferior to the eyelid crease is undermined to allow for redistribution of the wound along the eyelid crease. The skin is closed using multiple interrupted skin sutures. Post-operative complications, patient satisfaction, and post-operative appearance were assessed.

RESULTS:
Four patients underwent t-shaped wedge resection. The indication for surgery was a full-thickness upper eyelid defect following Mohs surgery for basal cell carcinoma. The width of the defect ranged from 5mm to 8mm. Post-operative complications included transient ptosis secondary to eyelid edema and transient foreign body sensation. Post-operative patient satisfaction was high and post-operative appearance was acceptable in all patients.

DISCUSSION/CONCLUSIONS:
The modified pentagonal wedge resection using a t-shaped resection is an effective alternative to the classically described pentagonal wedge resection. This procedure restores the structural integrity of the upper eyelid while also rendering a more natural appearance.
Name of Author(s): Dov B Sebrow, MD, Raksha Urs PhD, Ronald H Silverman PhD

Abstract Title: 3D Ultrasound Imaging of Orbital Vessels

PURPOSE:
While we have demonstrated color-flow images of the orbital vasculature derived from ultrafast plane-wave ultrasound, individual planes fail to convey 3D anatomy. We now describe a technique for generating 3D volumetric images of orbital blood flow.

METHODS:
While acquiring data at 1000 planes/sec, we manually pivoted an 18 MHz linear array probe to sweep out a volume centered on the optic nerve. Color flow images of each plane were then merged in ImageJ to produce a 3D model.

RESULTS:
The central retinal artery and vein, short posterior ciliary arteries and choroid were visualized after a 3-second scan. Processing time from data acquisition to 3D image was ~20 minutes.

DISCUSSION/CONCLUSIONS:
While 2D depiction of flow is useful, appreciation of 3D anatomy is difficult or impossible from single scan planes. We demonstrated that our current signal-processing strategy can readily be extended to 3D, potentially impacting assessment of occlusions and other vascular pathologies of the eye and orbit.
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Authors: Nailyn Rasool, MD, John Merriam, MD, Stephen Brooks, MD

Title: Tensile strength of periorcular soft tissues: clinical implications for wound closure.

Purpose:

The difference in strength of suturing techniques has been described well in both orthopedic and abdominal surgery but less in the ophthalmic literature. It is thought that the tensile strength of suture should meet but not greatly exceed that of the tissue. Optimal horizontal suturing distances in maintaining apposition against a load have been investigated in meniscal tears but not yet in the ophthalmic literature. We investigated the effect of distance and depth of sutures upon tensile strength, the regional differences in facial tissue and the effect upon tensile strength and the effect of differing lid lacerations upon tensile strength.

Methods:

One cadaveric head with intact facial tissue was used for the study. A 4.0 cm horizontal lesion was made through epidermis and dermis on each cheek. 2-0 polysorb sutures on a tapered needle were used to suture across one end of the lesion, and a 7.0 cm noose was created upon which a force-gauge was used to determine how much force it would require to tear through the tissue. Differing distances and depths were tested including distances of 1mm, 2mm and 3mm respectively. rom the cheek as well as depths of 1mm, 2mm and 3mm at a distance of 2mm. The tensile strength difference between eyebrow and cheek were performed using the same technique with 2-0 polysorb sutures 2mm adjacent to the wound. Similarly, tensile strength measurements of the eyelid by layer were performed through full thickness lid, tarsus and anterior lamellae. The results were analyzed using the t-test to determine whether distance and depth affected the tensile strength of the suture.

Results:

The mean force for sutures placed at a distance of 2mm with a depth of 1mm was 1482.9, 2mm was 2697.2 and 3mm was 3310.8. There was a statistically significant increase in tensile strength of the effect of tissue depth between each of the tested measurements. Additionally, at a depth of 2mm, sutures at a distance of 1mm had a tensile strength of 793.4, 2mm of 1476.9 and 3mm of 2304.8. There was a statistically significant increase in tensile strength of the effect of tissue distance between each of the tested measurements. The tensile strength of brow was 1476.8 compared to 2697.2 of the cheek. Lastly, the rupture force at the eyelid by layer was greatest for sutures through full thickness lid (2206), then tarsus (1624) and least for anterior lamella (1150).
Conclusions:

The study demonstrated that sutures placed deeper and further away from the wound edge provided greater tensile strength. In addition, the tensile strength of cheek is significantly greater than that of the eyebrow and tarsus has a much higher rupture force than anterior lamella. Our results demonstrate that tissue tensile strength may also vary directly with depth and length of suture bite. In part this may be secondary to capturing a greater volume of tissue. This is likely due to the greater volume of tissue within the substance of the suture. This simple yet practical knowledge may enable a better understanding of tissue biomechanics on the face and regional differences but also help inform proper surgical technique and suture selection.
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Thursday, June 15, 2017

Name of Author(s): Dan A. Gong, MD, Jonathan S. Chang, MD

Abstract Title: Difference-in-Differences Analysis of the Association between Physician Payment Disclosure Laws and Industry Payments to Ophthalmologists, 2013-2014

PURPOSE:
The implementation of the Physician Payments Sunshine Act (PPSA) was intended to increase transparency of physician relationships with industry, but its impact on the number and amounts of industry payments has not been previously studied. This study evaluates the association between the implementation of the PPSA and industry payments to ophthalmologists.

METHODS:
This study used physician-level Open Payments Database payment records from August-December 2013 and 2014. A difference-in-differences analysis compared changes in industry payments to ophthalmologists in years 1 and 2 of the PPSA implementation in 5 states and the District of Columbia with prior payment disclosure laws to changes in 13 contiguous states newly affected by the PPSA. Additional state- and physician-fixed effects were included to control for time-invariant state- and physician-level characteristics.

RESULTS:
Among the studied states, 4,634 ophthalmologists had $4.69 million payments in 2013 and $5.98 million payments in 2014. Mean number of payments per physician among states with prior physician payment disclosure laws was 3.35 in 2013 and 3.31 in 2014; among newly affected states, the mean number of payments per physicians was 5.26 in 2013 and 4.96 in 2014. The implementation of the PPSA was associated with a 0.40 reduction in the number of payment records per physician (p=0.016). No association existed for payment amounts.

DISCUSSION/CONCLUSIONS:
Implementation of the PPSA was associated with a reduction in the mean number of industry payments per ophthalmologist from 2013 to 2014.