COLUMBIA
OPHTHALMOLOGY

The Nineteenth Annual John T. Flynn Resident-Fellow Research Day
Edward S. Harkness Eye Institute, 7th Floor Flanzer Amphitheatre
Thursday, June 20, 2019

Name of Author(s): **Aliaa Abdelhakim**, Eyup Karahan, Ceren Durmaz, Tongalp Tezel_

Abstract Title: Thinning of the Retinal NFL after Anti-VEGF Treatment is due to the Relief of the Mechanical Compression on Axoplasmic Flow induced by Intraretinal Cystoid Fluid Pockets

PURPOSE:
To evaluate the mechanical compression of intraretinal cystic fluid pockets on the axons within overlying retinal nerve fiber layer (RNFL) and the release of this effect with anti-VEGF treatment

METHODS:
RNFL thickness and reflectance measurements were done at pre-selected areas (at the cystic peak, the nasal and temporal edges of the cystic area, 500 µm, 1500 µm, 2500 µm nasal to the nasal edge of the intraretinal cystic area, and 1500 µm temporal to the temporal edge of the intraretinal cystic area) before and after anti-VEGF injection in 6 eyes with diabetic macular edema and 5 eyes with macular edema secondary to branch retinal vein occlusion. Correlations between the spatial fluctuations of RNFL thickness after anti-VEGF treatment and change in dimensions of the intraretinal cysts were sought. Data was corrected to overall retinal thickness induced by the treatment and the impact of the anti-VEGF treatment on axoplasmic flow was determined by the change in RNFL reflectance.

RESULTS:
Post-injection RNFL thickness decreased significantly at peak point of cyst, at its nasal edge and 500 µm nasal to the cyst border ($p=0.038$, $p=0.026$ and $p=0.006$, respectively). There was no significant thinning at 1500 and 2500 µm nasal to nasal point of the cyst ($p=0.594$ and $p=0.722$ respectively) indicating a local mechanical effect. There was also no thinning at temporal edge of the cyst or 1500 µm distance to temporal edge of the cyst. ($p=0.328$, $p=0.167$, respectively) indicating the slowing down of the axoplasmic flow beyond the point of mechanical compression. Anti-VEGF treatment resulted in a decrease in RNFL density ($p=0.033$, at peak point of the cyst, $p=0.021$ at its nasal edge, $p=0.021$, 1500 µm temporal. The proximity of the apex of the cysts to RNFL before the anti-VEGF treatment was the only significant determinant affecting the degree of change in RNFL thickness after anti-VEGF therapy was ($p=0.001$).

DISCUSSION/CONCLUSIONS:
Intraretinal cystic pockets mechanically compress the overlying axons and result in axonal stasis. This local effect can be relieved with anti-VEGF treatment. Thus, thinning of the RNFL thickness after anti-VEGF injections is not because of a RNFL atrophy but due to the relief of compression-induced by intraretinal cysts. Axonal stasis and compressional atrophy of the axons in long-standing macular edema may contribute to functional loss, and necessitate early decompression treatment especially in patients with inner retinal ischemia and/or low axonal reserve.

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Name of Author(s): **Carolina Adams, MD**; Shelby Leach OD; Yocheved S. Kresch OD; Steven E. Brooks, MD.

Abstract Title: Actual Visual Demands of Children in the Classroom- Implications for Vision Screening Guidelines

PURPOSE:
There is little information regarding the level of visual acuity children need to meet the typical demands of a classroom, yet such information is critical to developing appropriate visual screening guidelines as well as optimal classroom standards. This study sought to determine the actual visual requirements found in typical classrooms, in terms of logMAR demands and contrast sensitivity levels.

METHODS:
Careful measures of classroom dimensions with specific attention to viewing distances were made in several public and private school classrooms, at various grade levels, in New York City. Measurements were also made of typical text dimensions shown to students on smart boards and white boards. These measurements were used to calculate minimum and average logMAR demands at various seating locations within the classrooms. Estimations of letter vs. background contrast were made using photographic comparison to Pelli-Robson charts.

RESULTS:
Five schools (14 classrooms total) were evaluated at several grade levels. Classroom dimensions varied significantly from school to school, ranging from 8ft x 10ft to 23ft x 23ft. Based on the typical optotype sizes shown to students in each class, the seats closest to the front and center of the rooms required minimum logMAR acuities of 0.71 to 1.66 (mean=0.93±0.20). Seats at the right and left of the front row required minimum logMAR acuities of 0.48 to 0.99 (mean=0.71±0.16). Seats in the center of the back row required logMAR acuities of 0.1 to 0.8 (mean=0.46±0.21), while those at the right and left of the back row required logMAR acuities of 0.13 to 0.69 (mean=0.43±0.17). Contrast was high for black markers on white boards (CS=0.00), but varied from 0.15 to 0.60 on smart boards. Optotype dimensions did not vary with grade level (p=0.5).

DISCUSSION/CONCLUSIONS:
Our data suggest that actual visual demands vary greatly from classroom to classroom across schools, and within a given classroom. Contrast levels also vary greatly, and were highest with black markers on a white board and lowest on smart boards in rooms with high levels of ambient room light. This data, combined with visual acuity data obtained from large scale pediatric vision assessments, can be used to help determine appropriate acuity thresholds for ophthalmic or optometric referral, as well as inform schools regarding optimization of visual content in the classroom.

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Name of Author(s): **Joah Aliancy MD,** James Lin MD, Amal Hussnain MD, Jonathan Chang MD, Jason Horowitz MD, Stanley Chang MD

Abstract Title: Visual outcomes and intraocular pressure changes following silicone oil removal

PURPOSE:
Elevated intraocular pressure (IOP) is a complication of silicone oil tamponade for retinal detachment repair, and commonly an indication for silicone oil removal (SOR). We performed a retrospective clinical study to examine the IOP lowering effects of and visual outcomes following SOR.

METHODS:
We reviewed longitudinal data from a university-based retina practice from 2010-2018, including patients who underwent silicone oil tamponade for retinal detachment repair with subsequent SOR. Patients were separated into two groups based on whether they were on glaucoma medications pre-operatively; paired t-tests were used to determine a change in glaucoma medications post-operatively within these two groups. Maximum IOP up to 2 months prior to SOR (pre-op IOP) was compared to IOP at time points <1 month and 3-6 months post-SOR using the paired t-test. Snellen visual acuity (VA) prior to SOR was compared to visual acuity up to 6 months post-SOR using the paired t-test.

RESULTS:
Pending

CONCLUSIONS: While VA was not significantly improved in long term follow up after SOR, the effect of SOR in significantly lowering IOP among all patients is demonstrated regardless of whether SOR was performed secondary to elevated IOP. This supports that silicone oil may be sub-clinically present in the anterior chamber in all patients with silicone oil tamponade, with its total removal contributing to decreased IOP.

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Name of Author(s): **Norimitsu Ban,** and Tongalp H. Tezel

Abstract Title: COMPERATIVE ANAYSIS OF GLIOSIS INDUCED BY COVERING OF MACULAR HOLES WITH A PATCH OF RETINAL AUTOGRAFT VS. AMNIOTIC MEMBRANE

PURPOSE:
To compare the glia activation and wound healing response induced by covering the macular holes with a retinal auto graft or a patch of human amniotic membrane (hAM).

METHODS:
Freshly enucleated (≤ 24hrs) human cadaver eyes were obtained from a local eye bank. Sensory retina was dissected under sterile conditions and 6.0 mm circular retinal explants were cut on a Teflon sheet. 1.0 mm circular defects were created at the center of the explants with a trephine. Retina explants with a central defect mimicking macular hole were placed in in a tissue culture well. Explant were either left uncovered, or covered with a 3.0 mm circular retinal autograft, or a 3.0 mm circular hAM graft (AmnioGraft®, TissueTech, FL). Retina explants were maintained in the culture medium for up to 3 days. Western blotting, PCR and immunohistochemistry for glial activation markers (GFAP, vimentin, osteopontin (SPP1), BMP7, serpin a) around the macular hole were used to compare the wound healing response between groups.

RESULTS:
Covering the macular hole for 72 hours with hAM or retinal autograft increased GFAP (2.02x vs. 1.86x), vimentin (2.07x vs. 3.52x) and Serpin A (2.09x vs. 3.45x, respectively) expression significantly compared to uncovered macular holes. While retinal autograft and hAM graft-covered retina expressed comparable amounts of BMP7 similar to uncovered explants, only hAM coverage boosted up the osteopontin (SPP1) expression (1.61x). No significant change in gliosis markers was detected in the retinal autograft. Immunostaining for GFAP revealed retinal glia migrating from the edges of the retinal defect using the hAM as a scaffold.

DISCUSSION/CONCLUSIONS:
Covering the macular hole with hAM graft or a retinal autograft activates wound healing by boosting up gliotic response and creating a scaffold for glia migration. Higher activation of gliosis with hAM as well as the safety and ease of obtaining it makes it a preferable patch for the treatment of failed chronic macular holes.

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Name of Author(s): Mark P. Breazzano, M.D.

Abstract Title: Utility of Ophthalmologic Screening for Patients with *Candida* Bloodstream Infections: A Systematic Review

Recently published in *JAMA Ophthalmology*:

- Breazzano MP, Day HR Jr, Bloch KC, Tanaka S, Cherney EC, Sternberg P Jr, Donahue SP, Bond JB 3rd. Utility in ophthalmologic screening for Candida blood stream infections: a systematic review. *JAMA Ophthalmol*. 2019; Apr 18.

PURPOSE:
The Infectious Diseases Society of America recommends ophthalmologic examinations for everyone with positive *Candida* blood culture results (candidemia) to screen for endophthalmitis, a practice that remains controversial because of multiple concerns for its limited usefulness and potential for harm. The purpose of this study is to determine guideline efficacy by reconciling discrepancies in the incidence of endophthalmitis and evaluating outcomes of studies assessing ophthalmologic screening for candidemia.

METHODS:
PubMed literature searches, including the search terms *candidemia*, *fungemia*, *chorioretinitis*, and *endophthalmitis*, identified longitudinal studies prior to 2018 of
patients who underwent ophthalmologic evaluations in the setting of positive fungal blood culture results regardless of symptoms or clinical status. Additional studies not captured by these queries were found by manually scanning references within the articles captured by the queries. Ambiguous studies of patients with concomitant bacterial or viral infections were excluded.

RESULTS:
Thirty-eight applicable studies of 7,472 patients who underwent ophthalmologic screening for candidemia or fungemia were identified. Criteria were compared with the conventional definition of endophthalmitis based on present (concordant) or absent (discordant) frank vitreous involvement. Concordant (59 of 6693 [0.9%]) and discordant (114 of 779 [14.6%]) endophthalmitis incidence rates differed by 13.8% (95%CI, 11.4%-16.4%; P < .001). None of the concordant endophthalmitis cases reported direct, intraocular, microscopic evidence of Candida or other fungal organisms. Outcomes were available for 19 patients with concordant endophthalmitis; 6 died within 4 weeks of screening. The rate of substantial vision loss was associated ($\varphi = 0.58$; 95%CI, 0.01-0.86; P = .046) with additional invasive intervention (3 of 6 [50.0%]) compared with medical management alone (0 of 6).

DISCUSSION/CONCLUSIONS:
In this systematic review without meta-analysis, inconsistent definitions of endophthalmitis accounted for discrepancies of its incidence and over-reporting among patients with candidemia, contributing to bias and resulting in the construction of guidelines. As few as 3 of 7472 patients had potential improvement, while routine examination overall could lead to additional interventions and harm in this population. These findings suggest that indiscriminate screening based on candidemia alone does not appear to be supported by the literature and should be reevaluated for inclusion as a recommendation from the Infectious Diseases Society of America.

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Name of Author(s): **Thalmon R. Campagnoli,** Cecile Truong, Tarun Sharma, Stanley Chang

Abstract Title: Swept-Source Optical Coherence Tomography Angiography (SS-OCTA) for Diabetic Retinopathy

PURPOSE:
While fluorescein angiography (FA) is the standard of care to evaluate vascular changes in patients with diabetic retinopathy (DR), it is an invasive procedure and associated to even life-threatening side effects. The images on FA are two-dimensional, not depth-resolved, and time-consuming (~ 10 minutes duration). Alternatively, Swept-Source Optical Coherence Tomography Angiography (SS-OCTA) is an emergent technology that provides non-invasive, high-resolution, ultra-fast (~ 4-6 seconds per eye) and depth-resolved three-dimensional images of the retinal and choroidal vasculature, therefore bringing a unique opportunity to investigate with superior detail both diabetic retinopathy and diabetic choroidopathy.
The purpose of the current study is to assess if SS-OCTA can provide as good qualitative and quantitative information as FA in eyes with DR with or without clinically-significant macular edema (CSME), and describe these findings.

METHODS:
Setting: Institutional, prospective observational study
Subjects: 30 age-matched patients with CSME, 15 patients with severe non-proliferative diabetic retinopathy (NPDR) without CSME and 15 patients with proliferative diabetic retinopathy (PDR) without CSME are proposed to be studied
Observation Procedures: Examinations including visual acuity, standard slit-lamp, indirect biomicroscopy, colored wide-field fundus pictures, FA and SS-OCTA have been performed
Main Outcome Measures: Evaluation and comparison of superficial and deep retinal capillary plexuses and choriocapillaris in FA and SS-OCTA images.

RESULTS:
SS-OCTA demonstrated superior vascular features in eyes with DR in comparison to FA imaging.

DISCUSSION/CONCLUSIONS:
SS-OCTA shows to be a superior technology for capillary-level vascular changes information in DR eyes in comparison to FA imaging. SS-OCTA provides non-invasive, higher-resolution and depth-resolved three-dimensional images in a much faster acquisition (~ 4-6 seconds per eye) manner of the retinal and choroidal vasculature.

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Name of Author(s): **Maryam Ghiassi M.D MHS**, Spencer Langevin M.D , Brian Marr M.D

Abstract Title: A Retrosepctive Chart Review of Orbital Lymphoma Treatment Modalities and Rate of recurrence

PURPOSE:
The purpose of the study is to conduct a retrospective analysis of patients presenting with primary intraorbital lymphoma (PIOL) or secondary intraorbital lymphoma (SIOL), in order to determine their response to different treatment modalities, recurrence rates, and survival curves.

METHODS:
A retrospective chart review will be done on adult patients diagnosed with orbital lymphoma treated at Columbia University Medical Center (CUMC). We will determine the orbital lymphoma primary location site, the presence or absence of systemic disease, treatment course, timeframe to recurrence, and survival to date. We will compare the efficacy of treatment modality and survival curve.

RESULTS:
27 patients with known orbital lymphoma with appropriate follow up were identified. 17 patients had marginal zone B cell lymphoma of which, 11 presented with conjunctival lesions, 5 orbital, and 1 with an eyelid lesion. 76% of patients only had focal disease at the time of presentation. 58% of patients had no recurrence with treatment.
In total, only 26% of patients (7/27) had systemic disease at the time of presentation of which 57% had recurrence of disease after initial treatments.

DISCUSSION:
Patients with orbital lymphoma are treated with a variety of modalities. It is important to closely monitor patients for signs of recurrence. However, patients with local disease, once treated did not show any signs of systemic recurrence and the lymphoma was confined to the orbit. Only 28% of patients had any sign of recurrence after treatment during the duration of the study. There was higher rate of orbital recurrence after treatment. This is due to the fact that systemic disease is mainly treated with systemic chemotherapy.

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Name of Author(s): **Kyle J. Godfrey MD**, Paula W. Feng MD, Gabriella Schmuter BS, Andrea Tooley MD, Michael Kazim MD

Abstract Title: Identification of Age-Stratified Clinical Features of Active Thyroid Eye Disease

PURPOSE:
Thyroid eye disease (TED) is a phenotypically heterogeneous, biphasic, autoimmune, inflammatory disease that presents variably at different ages. Because disease activity guides treatment decisions, it is valuable to better understand how TED manifests and evolves during the active phase based on patient age. The purpose of this project is to elucidate which clinical features of TED feature most prominently in patients as a function of age, and to understand how these features evolve over the course of the active phase.

METHODS:
An IRB-approved, retrospective analysis of consecutive TED patients evaluated over a three-year interval was performed. Inclusion criteria were patients diagnosed with active TED who had at least two comprehensive evaluations during the active phase of disease. Exclusion criteria included prior treatment with corticosteroids, radiotherapy, or immunomodulatory agents, prior surgery, or inactive disease at presentation. Clinical data was collected from the VISA Classification System. Patients were then divided into four age cohorts: 25 years and under, 26-45 years, 46-65 years, and over 65 years of age. Average values for graded clinical features were compared during an interval of suspected disease activity (0-6 months) vs. period of suspected disease inactivity (18-24 months). Statistical analysis was performed on these groups using analysis of variance (ANOVA) and student's t-test. Significance was estimated at *p* value of 0.01 to account for multiple comparisons.

RESULTS:
240 consecutive charts were reviewed. 145 patients met inclusion criteria. Younger patients generally demonstrated shorter active phase TED (12.8, 14.1, 15.6, and 14.5 months, youngest to oldest age groups, respectively). Younger patients also generally demonstrated a shorter interval between the onset of endocrinopathy and the onset of TED (0.4, 2.6, 2.1, and 6.6 years to onset, youngest to oldest age groups, respectively). The features noted to change significantly between the active and quiescent phase of the disease for the youngest patients (under age 25) were exophthalmometry, diurnal variation of symptoms and eyelid erythema; in the oldest patients (over age 66) the only feature was upper eyelid edema. For patients aged 26-65, features likely representing active phase disease included diurnal variation, eyelid erythema, gaze evoked pain, eye pain at rest, and lower eyelid edema.

DISCUSSION/CONCLUSIONS:
Clinicians should consider age when evaluating clinical activity in TED. TED patients at the ends of the age spectrum may demonstrate less significant clinical signs and symptoms, and shorter active phase disease marked by select clinical features. The clinical features representing active TED (those changing significantly between the active and inactive phase of the disease) may be limited to exophthalmos, diurnal variation, and eyelid erythema in the youngest patients, and upper eyelid edema in the oldest patients.

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Name of Author(s): **Dan Gong, M.D.;** Jonathan S Chang M.D.; Miriam Barbany M.D.; Borja F Corcostegui M.D.; Mehmet Fatih Kağan Değirmenci, M.D.; Hiroto Ishikawa M.D., Ph.D.; Zaid Mammo, M.D.; Emin Ozmert, M.D.; Tommaso Rossi M.D.; Stanley Chang M.D._

Abstract Title: Comparison of US and International Ophthalmic Drug Pricing

PURPOSE:
To compare US and international drug pricing for commonly prescribed intravitreal and topical ophthalmic medications.

METHODS:
For twenty-five commonly used ophthalmic medications (three intravitreal, twenty-two topical), we obtained 2017 Q4 US average wholesale price (AWP), drug acquisition cost or consumer pricing through US government health insurance plans (Veterans Affairs (VA), Medicaid, Medicare Part B, Medicare Part D) and commercial drug plans (CVS Caremark and Navitus Health Solutions), online pricing without insurance through a large US warehouse retailer (Costco), and international drug pricing through government-sponsored health plans in Canada, Italy, Spain, Turkey, and Japan.

RESULTS:
For intravitreal medications in the United States, aflibercept and ranibizumab were priced similarly to each other and more expensive than dexamethasone implants. Pricing of aflibercept and ranibizumab through government health insurance plans in Canada, Italy, Spain, Japan, and Turkey were less expensive by as much as 85.2% compared to the United States. For topical medications in the United States, pricing varied significantly both across different classes of medications but also between non-branded and branded medications. Drug acquisition costs through the VA and Medicaid were inexpensive on average, but pricing through a hospital-employee drug insurance plan offered the smallest range (between $2.35 and $60.00). In all five non-US countries studied, each topical medication with the exception of cyclosporine emulsion and difluprednate was less expensive than $100, and 94.4% of topical medications in these countries had a non-branded or branded option less expensive than $50.

DISCUSSION/CONCLUSIONS:
In the United States, for topical more than intravitreal medications, significant price variation exists across both different drug pricing systems and different medications. Price differentials between non-branded and branded medications can be significant. Internationally, topical medications exhibited a more limited and lower price range compared to drug pricing in the United States.

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Name of Author(s): **S. Amal Hussnain, MD**[1]; Tarun Sharma, MD, FRCSEd; Donald C. Hood, PhD; Stanley Chang, MD

Abstract Title: Schisis of the Retinal Nerve Fiber Layer in Epiretinal Membranes

PURPOSE:
To describe schisis of the retinal nerve fiber layer (sRNFL) associated with epiretinal membranes (ERMs) seen on spectral domain optical coherence tomography (SD-OCT) prior to vitreoretinal surgery. Areas of sRNFL (size and location) were noted during preoperative planning. SD-OCT scans were obtained to study the inner retinal morphology postoperatively.

METHODS:
Pre- and post-operative SD-OCT and en-face images of 41 eyes with ERMs that had undergone vitrectomy by a single surgeon were analyzed to record the presence of sRNFL. The extent of sRNFL was classified as focal or diffuse. Other characteristics such as involvement of the papillomacular bundle and areas of fibrillary protrusion of sRNFL above the ILM were documented. Color fundus photographs were reviewed to correlate with the SD-OCT images.

RESULTS:
Mean patient age and length of follow-up were 69.3 years (range 52-82 years) and 6.8 months (range 0.25-21 months), respectively. Mean pre-operative and post-operative central thicknesses were 477μm and 387μm, respectively ($p<0.0001$). sRNFL was observed in 51.2% (21/41 eyes), and was classified as diffuse (>1 disc diameter) in 90.5% (19/21 eyes). Protrusion of sRNFL through the ILM was present in 76.2% (16/21 eyes) and occurred in areas of dehiscence of the adjacent internal limiting membrane (ILM). sRNFL was best visualized on SD-OCT and *en-face* imaging at the vitreoretinal interface (VRI) and sometimes correlated with areas of retinal whitening. sRNFL resolved in all cases post-operatively.

DISCUSSION/CONCLUSIONS:
sRNFL was a relatively common occurrence in ERMs, correlated frequently with areas of dehisced ILM intra-operatively, and resolved post-operatively in all cases.

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Name of Author(s): Rosen RB, Andrade Romo JS, **Krawitz BD**, Mo S, Fawzi AA, Linderman RE, Carroll J, Pinhas A, Chui TYP

Abstract Title: Earliest Evidence of Preclinical Diabetic Retinopathy Revealed Using Optical Coherence Tomography Angiography Perfused Capillary Density

PURPOSE:
To compare perfused capillary density (PCD) in diabetic patients and healthy controls using optical coherence tomography angiography (OCTA).

METHODS:
Forty controls, 36 diabetic subjects without clinical retinopathy (NoDR), 38 with nonproliferative retinopathy (NPDR), and 38 with proliferative retinopathy (PDR) were imaged using spectral-domain optical coherence tomography. A 3 × 3-mm full-thickness parafoveal OCTA scan was obtained from each participant. Following manual delineation of the foveal avascular zone (FAZ), FAZ area, perimeter, and acircularity index were determined. Seven consecutive equidistant 200-μm-wide annular segments were drawn at increasing eccentricities from the FAZ margin. Annular PCD (%) was defined as perfused capillary area divided by the corresponding annulus area after subtraction of noncapillary blood vessel areas. Nonparametric Kruskal-Wallis testing with Bonferroni correction was performed in pairwise comparisons of group PCD values.

RESULTS:
The NoDR group demonstrated consistently higher PCD compared to the control group in all 7 annuli, reaching statistical significance (36.6% ± 3.30% vs 33.6% ± 3.98%, P = .034) at the innermost annulus (FAZ margin to 200 μm out). The NPDR and PDR groups demonstrated progressively decreasing PCD. Differences in FAZ metrics between the NoDR and control groups did not reach statistical significance.

DISCUSSION/CONCLUSIONS:
Relative to healthy controls, increased PCD values in the NoDR group likely represent an autoregulatory response to increased metabolic demand, while the decrease in PCD that follows in NPDR and PDR results largely from an incremental loss of capillary segments. These findings, consistent with previous studies, demonstrate the potential of OCTA as a clinical tool for earlier objective detection of preclinical diabetic retinopathy.

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Name of Author(s): **Spencer T Langevin, M.D**., Brian P Marr, M.D., Alex J Rai Ph.D.

Abstract Title: Isolation and Characterization of Exosomes from Uveal Melanoma Patients: Do they Contain Biomarkers to Detect Metastases and Guide Future Therapy?

PURPOSE:
To isolate and characterize exosomes that are present in Uveal Melanoma (UM), and determine their potential for identifying early metastatic disease to improve outcomes.

METHODS:
Sampling of cell lines and body fluids including blood and urine from UM patients with primary and metastatic disease. An optimized procedure which included sequentially increasing centrifugal spins was used to obtain different populations of subcellular constituents. Proteomic analysis was then performed on the exosome fraction to identify the proteins present.

RESULTS:
Over 600 proteins were identified in exosomes from 92.1 (UM) cells with and without treatment with Crizotinib (a c-Met-Inhibitor). Approximately 150 proteins were unique to each group and 450 were common. We then further identified 32 high-value biomarker candidates, validated antibodies to ten of these candidates, and detected some of these by western blot in the exosomes of 92.1 (UM) cell culture media and in serum and urine of UM patients.

DISCUSSION/CONCLUSIONS:
From the proteomic analysis of exosomes in UM patients we demonstrate the effect of crizotinib on the selective packaging and distribution of proteins within exosomes, and have developed a list of protein biomarkers potentially useful for clinical management of UM patients.

With the biomarkers identified we will obtain blood and urine samples in patients with and without metastatic disease to quantify these proteins and determine which ones correlate best with clinical status.

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Name of Author(s): **Jose Ronaldo Lima de Carvalho Jr**, Sara Ragi, Karen Sophia Park, Janet R. Sparrow, Stephen H. Tsang.

Abstract Title: Multimodal imaging of patients with Best Vitelliform Macular Dystrophy (BVMD): a 4-year follow-up study.

PURPOSE:
To test the hypothesis that imaging biomarkers can be used to measure outcome in upcoming Best Vitelliform Macular Dystrophy (BVMD) treatment trials.

METHODS:
A retrospective analysis of 31 patients (59 eyes) from 27 families with a clinical and genetic diagnosis of dominant BVMD was performed. Three eyes were excluded from analysis due to poor image quality. SD-OCT, SW-AF and NIR-AF images were taken at the same visit. A second set of imaging was performed in 15 patients (30 eyes). The diameter of the lesion measured by the two different autofluorescence techniques were correlated with the measurements made by SD-OCT. Central macular thickness (CMT), foveal height of the lesion (HL) and foveal outer nuclear layer (ONL) thickness were measured by SD-OCT. Likewise, ONL thickness at temporal (T-ONL) and nasal (N-ONL) limits of the lesion and at 500μm from the border of the lesions (5T-ONL and 5N-ONL) towards the healthy retina were evaluated. In addition, the area of the macular lesion was manually measured on both SW-AF and NIR-AF. Comparative statistics was used to calculate differences between the calculated means. The Pearson correlation coefficient was used to evaluate the relationships between each imaging modality.

RESULTS:
Among 59 eyes, one eye classified in the pre-vitelliform stage did not exhibit a lesion after 2 years of follow-up but revealed a hypoautofluorescent signal on NIR-AF that was not observed on SW-AF. The mean follow-up time was 4.11±0.54 years. Significant positive correlations were found among SD-OCT, SW-AF, and NIR-AF when used to measure lesion diameter ($P<0.001$). Distinct regions of the lesions, namely T-ONL, N-ONL, 5N-ONL, decreased in thickness by -3.83±2.26μm/year, -5.03±2.01μm/year, -5.11±2.69μm/year, respectively, over time. No progression was observed in the diameter and area of the lesion as measured by each imaging modality.

CONCLUSIONS:
NIR-AF appears to have greater sensitivity to the early pre-vitelliform stage in BVMD. As significant changes were observed in the ONL of the lesions over time, our data suggests that ONL measurements may be used as an anatomical outcome measure for clinical trials. Future studies should include parameters such as microperimetry, which may additionally serve as a form of functional outcome measure for BVMD.

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Name of Author(s): **Yuchen Lin**, Christine L. Xu, Mark P. Breazzano, Stephen H. Tsang

Abstract Title: Progression of *KIZ*-associated autosomal recessive retinitis pigmentosa using quantitative analysis with multimodal imaging

PURPOSE:
KIZ is a centrosomal substrate of Polo-like kinase-1 (PLK1) that mediates mitotic chromosome stabilization. The purpose of this study is to evaluate the progression of autosomal recessive retinitis pigmentosa (RP) due to mutations in *KIZ* using multimodal imaging and a quantitative analytical approach.

METHODS:
Four patients carrying nonsense or missense mutations in *KIZ* were clinically evaluated with comprehensive history and examination, visual field testing, electroretinography (ERG), spectral-domain optical coherence tomography (SD-OCT), short-wavelength autofluorescence (SW-AF) imaging, and fundus photography. Serial measurements of peripheral retinal pigment epithelium (RPE) atrophy area with SW-AF, as well as the ellipsoid zone (EZ) width using SD-OCT were performed.

RESULTS:
All patients experienced typical RP symptoms of night blindness followed by visual field constriction. Symptoms began around age 30. Fundus examination and ERG revealed classic RP characteristics, and SD-OCT demonstrated outer retinal atrophy. The RPE atrophy area increased annually by 4.91%. The average annual reduction rate of the normalized EZ line distance was greater temporally (9.90%) than nasally (5.90%), P=0.009.

DISCUSSION/CONCLUSIONS:
Nonsense and missense mutations in *KIZ* give rise to a non-syndromic recessive RP phenotype without apparent extra-ocular features. RPE atrophy appears to gradually increase along with a progressive loss of EZ, particularly involving the temporal relative to nasal retina.

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Thursday, June 20, 2019

Name of Author(s): **Michelle M. Maeng MD**, Ranjodh S. Boparai MD, Kyle J. Godfrey MD, Andrea A. Tooley MD, Kristen E. Dunbar MD, Michael Kazim MD

Abstract Title: Comparing Manual and Auto-Segmentation Techniques for Determining Three-Dimensional Orbital Cavernous Hemangioma Volume on Magnetic Resonance Images

PURPOSE:
Accurately determining orbital tumor volume is important for therapeutic planning, monitoring disease progression, and assessing tumor response to therapy. Commonly, three-dimensional tumors are monitored in a two-dimensional subjective fashion, posing challenges for accuracy. Various segmentation techniques exist for estimating three-dimensional tumor volume based on two-dimensional images. The purpose of this study is to compare manual and auto segmentation techniques of MRI scans of orbital cavernous hemangiomas.

METHODS:
Fourteen patients with orbital cavernous hemangiomas were included in the study. Pre-treatment T2-weighted MR images at a single timepoint were analyzed by two observers using a manual segmentation method (ellipsoid), an auto segmentation method (GrowCut 3D slicer, www.slicer.org), and a parameter-dependent segmentation method (*k*-means clustering, ImageJ). For the ellipsoid method, maximal cross-sectional measurements in transverse (TV), antero-posterior (AP) and cranio-caudal (CC) planes were obtained, multiplied and divided by two ((TV x AP x CC) / 2) (Figure 1A – 1B). For the GrowCut method, observers assigned seed pixels to the foreground, i.e., tumor, and background, i.e., non-tumor (Figure 2A). The segmentation then compared characteristics of seed pixels to neighboring pixels and assigned them to tumor or non-tumor (Figure 2B – 2D). For *k*-means clustering, observers selected a region of interest that included both orbits, and selected the number clusters (Figure 3A). The segmentation then partitioned voxels until each cluster contained voxels that were similar in signal intensity and location and dissimilar to voxels in other clusters (Figure 3B – 3E). The primary outcome of the study was inter-observer reliability, represented as concordance correlation coefficients (CCC). CCC values of 1 indicated perfect correlation, with values closer to 0, indicating worse correlation.

RESULTS:
Using the ellipsoid method, the average tumor volumes calculated by the two observers were 1.68ml (SD 1.45) and 1.48ml (SD 1.19). Using the GrowCut method, the average tumor volumes calculated by the two observers were 3.00ml (SD 2.46) and 6.34ml (SD 3.78). Using *k*-means clustering segmentation, the average tumor volumes calculated by the three observers were 2.31ml (SD 1.83) and 2.12ml (SD 1.87). The CCC for the ellipsoid, Growcut, and *k*-means clustering methods were: **0.92** (95% CI 0.83 – 0.99), **0.12** (95% CI -0.12 – 0.44), and **0.95** (95% CI 0.90 – 0.99), respectively.

DISCUSSION/CONCLUSIONS:
In comparing the three segmentation techniques, *k*-means clustering performed the best, next Ellipsoid, followed by GrowCut in determining orbital cavernous hemangioma tumor volumes. This proof of concept study demonstrates that simple segmentation software can be utilized to monitor three-dimensional tumor volumes in a reproducible manner. Such measurements may aid clinicians in more closely monitoring tumor progression and response to therapeutic intervention over time.

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Name of Author(s): **Poonam Misra, MD**, Amanda Lu, BS, Marina Krygin, BS, Jennifer Alcantara-Castillo, Vipul Patel, Dan Gong, MD, Benjamin Whigham, MD, Stephen Walters, MD, Kai Chu MD, Golnaz Moazami, MD, Dana Blumberg, MD, MPH, Lama A. Al-Aswad, MD, MPH

Abstract Title: Cost Analysis of a Tele-Ophthalmology Mobile Screening Unit

PURPOSE: The Tele-Ophthalmology Mobile Screening Program provides exams to communities and individuals at risk for developing sight-threatening disease. In this study we analyze the expenses of this operation, and identify strategies for cost-effectiveness.

METHODS: Program costs were analyzed using a micro-costing approach, including staff and non-staff costs. We analyzed the total cost per participant, for comparison to office-based expenditure.

RESULTS: In 2017, 340 patients were screened, while 640 were screened in 2018. The total cost per participant was $372.83 in 2017, $291.99 in 2018. The cost per new sight-threatening diagnosis after follow-up was found to be $6,671.66 in 2017 and $3,603.10 in 2018. The average office visit cost was estimated to be $589.96, more than double the per-patient cost of mobile screening in 2018.

DISCUSSION/CONCLUSIONS: Analyzing cost-effectiveness in the mobile unit will help maximize efficiency, to serve a greater number of patients with limited access to traditional office-based ophthalmologic care.

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Name of Author(s): **Tavish Nanda**, Patrick Tierney, Dana Blumberg

Abstract Title: Eye-Drop Abstinence in Glaucoma Patients Admitted to the Hospital Service

PURPOSE:
Anecdotally, many patients admitted to an inpatient general medicine service do not have their glaucoma eye drops started. The purpose of this study was to determine the extent of eye-drop abstinence after inpatient admission.

METHODS:
A retrospective, cross-sectional, hospital-based study of four hundred seventy-five patients admitted to the general medicine regional hospital service from January 2016 through February 2018 with a known past medical diagnosis of or active outpatient medications for glaucoma. A combination of an administrative database and cross-referenced patient charts were reviewed for demographic data, past medical problems, inpatient orders, intake history and physical, length of stay, and admitting diagnosis. Main outcome measures included, 1) the effect of outpatient glaucoma drops reconciliation and (2) recognition of glaucoma as a pertinent past medical problem in a patient's intake history and physical on inpatient eye-drop administration. The overall rate of eye-drop abstinence also was recorded.

RESULTS:
Of 475 patients, 46.3% were women, with an average age of 80.2 years (standard deviation, 11.1 years). Average length of stay was 4.61 days (standard deviation, 3.7 days). In total, 63.8% achieved successful administration of medication on the hospital floor, resulting in a 36.2% eye-drop abstinence rate during the hospital stay. Three hundred eighty-six of 475 patients (81.3%) achieved successful glaucoma medication reconciliation. Patients with successful reconciliation had a significantly different rate of eye-drop administration (73.3% vs. 21.0%; P 0.001). Recognition of glaucoma in the history and physical occurred in only 42.5% of patients. There was a significant difference in eye-drop administration when glaucoma was included in the history and physical (75.7% vs. 55.0%; P 0.001).

DISCUSSION/CONCLUSIONS:
Glaucoma treatment incurs a high rate of medication noncompliance, especially in the elderly. The present study demonstrates that more than one third of patients admitted to an academic medical center do not receive their glaucoma medications. Patients discharged to nursing homes, subacute rehabilitation, and assisted living facilities rely on appropriate discharge medication reconciliation, resulting in forced abstinence during transition of care. An emphasis on appropriate medical reconciliation and recognition of glaucoma as a pertinent past medical problem will improve rates of eye-drop discontinuation on inpatient admission significantly.

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Name of Author(s): Sanjai Jalaj

Abstract Title: Refractive outcomes after cataract surgery combined with DMEK versus Ultrathin-DSAEK

PURPOSE:
DMEK is replacing DSAEK as the endothelial keratoplasty procedure of choice because of proven better post-op BCVA and UCVA. However, ultra-thin DSAEK (UT-DSAEK), defined as a donor graft < 100 microns thick, may be comparable to DMEK. The purpose of this study was to describe BCVA and refractive outcomes of DMEK and UT-DSAEK.

METHODS:
A retrospective chart analysis was performed for endothelial keratoplasty procedures from 1/1/2010 through 6/6/2018 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 2 groups.

RESULTS:
A total of 38 patients who underwent cataract surgery combined with DMEK (n=24) or UT-DSAEK (n=14) were included in the analysis. Pre-op logMAR BCVA was the same between DMEK and UT-DSAEK (0.33 vs 0.36 respectively, P=0.57). At post-op month 6, no significant differences were found in logMAR BCVA (0.095 vs 0.068, P=0.28), spherical equivalent (-0.59 vs -0.27, P=0.32), or hyperopic shift (+0.29 vs +0.62, P=0.24). 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 less hyperopic shift than expected after DMEK or UT-DSAEK.

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 less hyperopic shift after DMEK or UT-DSAEK. This suggests utilizing a target spherical equivalent closer to the desired spherical equivalent when performing DMEK or DSAEK with cataract surgery.

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Name of Author(s): **Benjamin Whigham MD,** Vipul Patel, Jennifer Alcantara-Castillo, Rahul Kapoor, Kalashree Gopal, Deborah Popplewell, Emery Jamerson, Dan Gong, Maya Ramachandran, Poonam Misra, Lama Al-Aswad

Abstract Title: Detecting Narrow-Angles and Angle-Closure Glaucoma using Mobile Tele-Ophthalmology in At-Risk Populations

PURPOSE: Glaucoma is a blinding condition that may progress with no symptoms until vision has been permanently damaged. Here we screen for a major risk factor for glaucoma, anatomically narrow angles, using a mobile screening unit equipped with anterior segmented optical coherence tomography (OCT).

METHODS: A tele-ophthalmology mobile unit was used to screen for narrow angles in underserved communities in New York City between June 2017 and October 2018. The only inclusion criterion for the study was age 20 years or older. The participants underwent visual acuity, non-contact tonometry, frequency doubling technology visual field, anterior and posterior segment OCT, corneal thickness, and fundus photos. Data was transmitted in real time to be analyzed by an ophthalmologist or optometrist and follow up was recommended. For each eye the anterior segment OCT was performed at both the 3 and 9 o'clock positions; of the two positions, the more open angle was used to grade the eye as open (normal), narrow (threatened closure), or closed. An eye was deemed to have angle closure if it had closed angles or narrow angles with evidence of glaucoma. Glaucoma suspicion was based on glaucomatous nerve appearance, elevated intraocular pressure, or retinal nerve fiber layer (RNFL) abnormalities.

RESULTS: A total of 890 subjects were screened. Genders were 56% female and 44% male. Narrow angles were identified in 98 patients (11%) and concern for angle-closure glaucoma was found in 32 patients (3.6%). Demographic risk factors for narrow angles included gender and age. Female gender was associated with a 1.679 increased odds-ratio of narrow angles ($p = 0.0305$). Older age was also a risk factor for narrow angles, with patients aged 45-56 years having 6.387 times the risk of patients aged 20-44 years ($p = 0.0002$); this risk remained similar in older age brackets.

DISCUSSION/CONCLUSIONS: Our data suggest that our tele-ophthalmology screening project was an effective method for identifying patients with narrow angles. A significant number of patients were identified and directed towards in-office testing and possible treatment. Additional data on patient follow-up and management will help to confirm the utility of this screening.

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Name of Author(s): **James Winebrake**, Anca Askanase, Lisa Park

Abstract Title: Multidisciplinary perspectives on risks of HCQ toxicity: reconciling the great divide over HCQ guidelines.

PURPOSE:
Hydroxychloroquine (HCQ) retinal toxicity is an ongoing concern for rheumatologists taking care of lupus patients. The revised 2016 American Academy of Ophthalmology (AAO) guidelines created controversy in the rheumatology community regarding the correct dosing and evaluation of HCQ toxicity. The current study was initiated by an ophthalmology/rheumatology team to further understand rheumatologists' practice and to bridge the alleged divide on guidelines.

METHODS:
A questionnaire-based survey was distributed electronically to an international cohort of rheumatologists. Participants provided information on HCQ dosing and clinical decision-making processes, as well as their familiarity with and perceived shortcomings of the AAO 2016 guidelines.

RESULTS:
74 Rheumatologists completed the survey (51% from North America, 18% from Europe, others from SE Asia, Australia and Brazil; 90% from academic practices; 82% self-identified as lupus experts). The mean cohort size was 659±914 (range 50-6,571) and a total cohort of 48,797 patients. HCQ is prescribed to over 85% of lupus patients in these cohorts; all rheumatologists report routine counseling about ophthalmic risks. The typical dose of HCQ used is 200-400 mg/day. When required for SLE activity, 15% of the rheumatologists use doses up to 600 mg/day, while 5 use up to 6.5 mg/kg/day. Dose adjustments for patient weight are "routinely" and "sometimes" performed by 53 (72%) and 17 (23%) of responders, respectively; 63 (85%) and 8 (11%) responders adjust using actual and ideal body weight, respectively. All the replies stated that HCQ adherence is routinely assessed through questioning during the clinical encounter, formal questionnaire, or serum HCQ levels. 482 cases of HCQ retina toxicity (1.0%) and 9 cases of HCQ associated blindness (1.8/10,000 patients) were reported. 82.6% of respondents proved familiarity with the AAO guidelines and recognized the various patient factors associated with the increased risk of retinal toxicity: responders associated cumulative HCQ and excessive HCQ dose as greatest risk, followed by pre-existing renal or retinal disease and concomitant tamoxifen use as risk factors for the development of HCQ retinal toxicity. 6 clinical vignettes and 4 multiple choice questions were used to assess knowledge of and compliance with the current dosing guidelines. Interestingly, for the case of a 55-year-old woman with over 25 years of HCQ exposure in clinical remission 88.4% of respondents suggested tapering or discontinuation of HCQ. Those aware of the guidelines cited limited dosing options (41), lack of supporting evidence (41), and low patient adherence (31) as obstacles to greater implementation of the guidelines.

DISCUSSION/CONCLUSIONS:
These data suggest that HCQ toxicity and blindness are rare in patients with SLE. Rheumatologists treating SLE patients are generally aware of the guidelines and appreciate the importance of partnering with ophthalmologists in preventing retinal toxicity. The vast majority of surveyed rheumatologists cited extrinsic obstacles to the adoption of AAO guidelines, and indicated a need for additional multidisciplinary dialogue and collaboration.

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Name of Author(s): **Cameron Yang** and Lisa Park, MD

Abstract Title: The Impact of School Eye Screenings in Ethiopia – A Retrospective Record Review

PURPOSE:
Vision loss has been thoroughly studied in developed countries; however, the prevalence and etiologies of vision loss have not been as thoroughly investigated in Africa, particularly in the pediatric population. This retrospective record review aims to elucidate the causes of visual impairment in school-aged children from Ethiopia and evaluate the efficacy of Vision Care's school screenings.

METHODS:
A retrospective chart review was conducted using records from Vision Care's school screenings (2015-2018) as well as records obtained from Ras Desta Damtew Memorial Hospital (2015-2017). The children were enrolled at elementary schools throughout Addis Ababa. Descriptive statistics were performed on Excel and Stata. Two-sample t-tests were used to evaluate the difference between visual acuity measurements acquired by school teachers and optometrists.

RESULTS:
Of the 16,872 students screened by vision care, 4,261 were seen by an optometrist for a second screening. 60 of these children were then evaluated by an ophthalmologist. Regarding visual acuity measurements, teacher-measured visual acuity tended to underestimate visual acuity measured by an optometrist by 0.18 (OD) and 0.16 (OS) ($p < 0.01$). The prevalence of refractive error among this population was 4.8%, with 72% having hyperopia and 18% having myopia. Astigmatism was present in 47% of children with refractive error.

DISCUSSION/CONCLUSIONS:
Refractive error was found to be the most common etiology of vision impairment in this population, and a majority of the children with refractive error were hyperopic. Additionally, teacher-measured visual acuity tended to underpredict visual acuity compared to measurements made by an optometrist. This difference in measurement may be affecting Vision Care's school screenings; however, in order to ascertain the magnitude and direction of this effect, further investigation is required.