
**Department of Ophthalmology and Vision Sciences
University of Toronto**

64th Annual Research Day
and
41st Clement McCulloch Lecture

Virtual Session I - April 26th 2022
Virtual Session II - May 3rd 2022
Virtual Session III - May 10th 2022

(7:00 – 9:00 PM)

Meeting Chairperson

Matthew Schlenker, MD, MSc, FRCSC
Assistant Professor
Department of Ophthalmology and Vision Sciences
University of Toronto

**64th Annual Ophthalmology Research Day
and
41st Clement McCulloch Lecture
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Virtual Session I

**April 26/ May 3/ May 10
(7:00 – 9:00 PM)**

PROGRAM

7:00-7:03 PM Department Chair’s Welcome
Dr. Sherif El-Defrawy

7:03-7:05 PM Annual Ophthalmology Research Day Chair Welcome
Dr. Matthew Schlenker

F= Fellow, R=Resident, M=Medical Student, G=Graduate Student, VS=VSRP (Vision Science Research Program) Student, RF= Research Fellow, U=Undergraduate Student

7:05 - 9:00 PM Session Panelist: Valerie Wallace, Rajeev Muni, Matthew Schlenker, Brian Ballios and Stephan Ong Tone
Format: 9 min. Presentation + 3 min. Discussion

7:05 – 7:14 PM	Evaluation of Subretinal Fluid Drainage Techniques in Pars Plana Vitrectomy for Primary Rhegmatogenous Retinal Detachment Repair (ELLIPSOID Study)	Bryon R. McKay (F)
7:17– 7:26 PM	Developing a model of photoreceptor somal translocation during murine retinal development	Akshay Gurdita (VS)
7:29 – 7:38 PM	Assessment of Zonular Integrity in Phakic Eyes post Vitrectomy Using Ultrasound Biomicroscopy (UBM) ; A Paired Eye Comparative Study	Mohammed Alfalah (F)
7:41 – 7:50 PM	Proof-of-concept analysis of a deep learning model to conduct automated segmentation of optical coherence tomography images for macular hole volume	Austin Pereira (R)
7:53 – 8:01 PM	A Mouse Model of Spaceflight-Associated Neuro-ocular Syndrome	Arya Zarrinbakhsh (VS)
8:05 – 8:15 PM	Discovering new molecular and cellular therapies for inherited retinal disease	Faculty Speaker Dr. Brian Ballios
8:18 – 8:28 PM	Investigating Fuchs Endothelial Corneal Dystrophy and Corneal Regeneration for Corneal Blindness	Faculty Speaker Dr. Stephan Ong Tone
8:31 – 8:55 PM	Q & A and Discussion	
8:55 – 9:00 PM	Closing Session I	

**64th Annual Ophthalmology Research Day
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Virtual Session II

**April 26/ May 3/ May 10
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PROGRAM

7:00-7:03 PM Department Chair’s Welcome
Dr. Sherif El-Defrawy

7:03-7:05 PM Annual Ophthalmology Research Day Chair Welcome
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7:05 - 9:00 PM Session Panelist: TBD
Format: 9 min. Presentation + 3 min. Discussion

7:05 – 7:14 PM	A Matched Longitudinal Cohort Study of Serious Adverse Reactions from Oral or Topical Carbonic Anhydrase Inhibitors	Marko Popovic (R)
7:17– 7:26 PM	Initial Pars Plana Vitrectomy Compared to Tap-and-Inject for the Management of Endophthalmitis Secondary to Intravitreal Injections of Anti-Vascular Endothelial Growth Factor Agents: A Systematic Review and Meta-Analysis	Yuliya Lytvyn (F)
7:29 – 7:38 PM	Novel Home Monitoring of Visual Fields with the Toronto Portable Perimeter	Bill Shi (VS)
7:41 – 7:50 PM	Choroidal hypoperfusion defects as a new fluoresceine angiographic finding in patients with retinopathy of prematurity	Tianwei Zhou (R)
7:53 – 8:01 PM	Sustained Release of RdCVF-Sh3 to Rescue Cone Photoreceptor Death	Lai Huo (VS)
8:05 – 8:25 PM	<i>41st Clement McCulloch Lecturer</i> What should I know about Ocular Gene Therapy?	Guest Speaker Dr. Ian Macdonald
8:25 – 8:55 PM	Q & A and Discussion	
8:55 – 9:00 PM	Closing Session II	

**64th Annual Ophthalmology Research Day
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Virtual Session III

**April 26/ May 3/ May 10
(7:00 – 9:00 PM)**

PROGRAM

7:00-7:03 PM Department Chair’s Welcome
Dr. Sherif El-Defrawy

7:03-7:05 PM Annual Ophthalmology Research Day Chair Welcome
Dr. Matthew Schlenker

F= Fellow, R=Resident, M=Medical Student, G=Graduate Student, VS=VSRP (Vision Science Research Program) Student, RF= Research Fellow, U=Undergraduate Student

7:05 - 9:00 PM Session Panelist: TBD
Format: 9 min. Presentation + 3 min. Discussion

7:05 – 7:14 PM	Early results of the novel 63µm ab interno gelatin microstent versus conventional 45µm microstent	Jessica Cao (RF)
7:17– 7:26 PM	The Cataract Surgery Learning Curve: Quantitatively Tracking a Resident’s Operative Actions Throughout Their Training	Michael Balas (M)
7:29 – 7:38 PM	Corneal Hysteresis and Central Corneal Thickness: A Significant Association with SIBS Microshunt Surgical Outcomes	James Armstrong (RF)
7:41 – 7:50 PM	TBD	Poster Winner 1
7:53 – 8:01 PM	TBD	Poster Winner 2
8:05 – 8:25 PM	<i>Dr. Martin J. Steinbach Lecturer</i> Diabetes and the Corneal Endothelium (Yes It Happens There Too)	Guest Speaker Dr. Mark A. Greiner
8:25 – 8:55 PM	Q & A and Discussion	
8:55 – 9:00 PM	Closing Session III	

ABSTRACTS FOR ORAL PRESENTATIONS

Virtual Session I

April 26th, 2022

Evaluation of Subretinal Fluid Drainage Techniques in Pars Plana Vitrectomy for Primary Rhegmatogenous Retinal Detachment Repair (ELLIPSOID Study)

Bryson R. McKay¹, Adytia Bansal¹, Michael Kryshchalskyj¹, David T Wong^{1,2}, Alan Berger^{1,2}, Rajeev H. Muni^{1,2,3}

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²Department of Ophthalmology, St. Michael's Hospital, Unity Health Toronto, CANADA

³Kensington Vision and Research Centre, University of Toronto, CANADA.

Purpose: To compare visual acuity and photoreceptor integrity following pars plana vitrectomy (PPV) with subretinal fluid (SRF) drainage from the original retinal breaks (RB) vs. posterior retinotomy (PR) vs. perfluorocarbon liquid (PFCL) for rhegmatogenous retinal detachment (RRD).

Methods: Retrospective analysis of 300 eyes (300 patients) with primary uncomplicated RRD that underwent PPV (100 consecutive patients included in each group). Exclusion criteria included giant retinal tears, grade B or worse proliferative vitreoretinopathy, ocular trauma, retinopexy or other vitreoretinal diseases. Primary outcomes were visual acuity and discontinuity of the external limiting membrane (ELM), ellipsoid zone (EZ) and interdigitation zone (IDZ) on spectral-domain optical coherence tomography (SD-OCT) at 1 year assessed independently by 2 masked graders with adjudication by a third senior masked grader.

Results: Proportion of patients with visual acuity assessment and gradable SD-OCT at 1 year was similar between group (RB 90%, PR 87%, PFCL 90%). There were no significant differences in age, sex, baseline visual acuity, lens status, extent of RRD and time from macula-off to presentation. Single-operation reattachment rate at 12 months was similar between groups (RB 86%; PR 85%; PFCL 83%, $p=0.9$). Mean(\pm SD) logMAR visual acuity at 12 months was significantly better in the RB and PR groups compared to PFCL (RB 0.6 ± 0.5 ; PR 0.7 ± 0.6 ; PFCL 0.9 ± 0.6 , $p=0.002$). There was an association between drainage technique and discontinuity of the ELM (PFCL 44%, PR 24%, RB 26%, $p=0.001$), EZ (PFCL 49%, PR 31%, RB 29%, $p<0.001$) and IDZ (PFCL 56%, PR 39%, RB 43%, $p=0.004$) on the 3-mm foveal scans. There was also an association of drainage technique with the risk of cystoid macular edema (CME) (PFCL 46%, PR 39%, RB 28%; $p=0.003$) and ERM formation (PFCL 61%, PR 90%, RB 64%, $P<0.001$).

Conclusions: Visual acuity at 1 year was inferior in eyes with PFCL compared with drainage from the original breaks or posterior retinotomy for primary uncomplicated RRD. There was a corresponding greater risk of discontinuity of the EZ, ELM and IDZ in PFCL cases, and a greater risk of CME with PFCL and ERM with PR. Drainage technique may impact long-term visual acuity results and photoreceptor integrity.

Developing a model of photoreceptor somal translocation during murine retinal development

Akshay Gurdita, Victor Q.B. Pham Truong, Parnian Dolati, Nobuhiko Tachibana, Arturo Ortin-Martinez, Zhongda C. Liu, Mostafa Ibrahim, Nenad T. Pokrajac, Lacrimioara Comanita, Valerie A. Wallace

Donald K Johnson Eye Institute, Krembil Research Institute, University Health Network; Department of Laboratory of Medicine and Pathobiology, University of Toronto

Background: Regenerating photoreceptors with the capability to migrate into and develop within the retina is essential if we hope to manipulate these processes for the treatment of retinal diseases; however, the molecular regulation of these processes is poorly understood. We hypothesize that rod photoreceptor somal migration, during murine retinal development, is mediated by passive displacement of neighbouring progenitors.

Methods: Subretinal injections of lentivirus, encoding a fluorescent reporter and Cre recombinase, was used to label rod photoreceptors in post-natal *ROSA^{mTmG}* pups. EdU was injected subcutaneously, immediately following subretinal injections, to label retinal progenitor cells. Rod photoreceptor and progenitor cell soma positions in post-natal day (P)0-injected mice eyes were analyzed by immunohistochemistry (IHC) 5, 7, 10 and 14 days post-injection. P3 and P5 mice were also transduced and analyzed at P14 by immunohistochemistry. P0 *Smo^{Cre}* mice were simultaneously electroporated with an empty-vector or Cre expressing plasmid and a fluorescent reporter encoding lentivirus. Rod somal positions were analyzed using whole-mount retinas at P14. Rod somal positions in P0-injected *Rd1*, *Rd10*, *Prph2^{-/-}*, *Nrl^{-/-}* and *Crx^{-/-}* mice eyes were also analyzed at P14.

Results: Post-mitotic rod somas migrate basally from P0 to P10. In contrast, Edu-labelled progenitor cell somas exhibit a rapid apical migration, followed by slow basal translocation. However, by P14, these Edu-labelled somas remain apically opposed to post-mitotic rod somas irrespective of the post-natal injection day suggesting that rod somal positioning is correlated with birth order. Cre-dependent knockout of smoothelin in retinal progenitors alters the final somal position of post-mitotic rods. This suggests that rod somal translocation is mediated by non-cell autonomous mechanisms. Rod somal position, within the ONL, appear disorganized in *Nrl^{-/-}* and *Crx^{-/-}* retinas.

Conclusions: We propose a passive displacement model of rod photoreceptor somal translocation. Aberrant somal translocation may be implicated in models of photoreceptor degeneration. Understanding how photoreceptors migrate during development may reveal mechanisms implicated in disease and insights towards controlling these processes for the treatment of vision loss.

Assessment of Zonular Integrity in Phakic Eyes post Vitrectomy Using Ultrasound Biomicroscopy (UBM) ; A Paired Eye Comparative Study.

Mohammed Alfalah^{1,2}, Catherine Birt^{1,3}, Kenneth T. Eng^{1,3}, Peter Kertes^{1,3}

¹ Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, Canada

² Vitreoretinal surgery Fellow, University Health Network and Sunnybrook Health Sciences

³ The John and Liz Tory Eye Centre, Sunnybrook Health Sciences Centre

Purpose: To assess zonular integrity in phakic patients post vitrectomy using ultrasound biomicroscopy (UBM).

Study Design: Cross sectional, comparative, double masked, paired eye study.

Methods: We used UBM to evaluate phakic patients with history of unilateral pars-plana vitrectomy (PPV). Recruitment included patients presenting to the John and Liz Tory Eye Centre, Sunnybrook Health Sciences Centre in the period between January 1st – December 31st 2021.

Inclusion criteria: 1. Phakic patients with history of PPV in one eye as the only procedure. 2. Normal unoperated fellow eye. 3. Complete SF6/C3F8/air resolution for patients who had gas/air tamponade. 4. Patients with silicone oil tamponade were included if they are still phakic.

Exclusion criteria: 1. Monocular patients. 2. History of intraoperative lenticular trauma. 3. History of trauma, pseudo-exfoliation or ectopia lentis in either eye. 4. Eyes with extreme myopia/long axial length. 6. History of intravitreal injection in either eye.

Technique: High frequency (50 MHz) UBM device was used by a masked technician to obtain radial section images from zonular bundles at eight clock positions. An experienced masked observer (CB) has then assessed the quality of images and graded the zonular findings. Only patients with adequate studies have been included. Each clock hour was graded according to a unique grading system that has been specifically devised for this study and the total score was then calculated for each eye. Two main groups were analyzed; the vitrectomized and non-vitrectomized eyes. The mean total UBM score (TUS) from each group was compared and analyzed.

Results: Twenty five patients have been recruited into this study. Eleven patients were males and fourteen were females. The mean age was 66.24 (Range: 46-75). Twenty-one patients had PPV for vitreomacular interface disorders (either macular hole or epiretinal membrane), one patient had vitreous hemorrhage and three patients had rhegmatogenous retinal detachment. SF6 was used as vitreous substitute in 12 patients, air in 9 patients, C3F8 in 3 patients and silicon oil in one patient. The mean TUS in the vitrectomized eyes was 4.68 versus 4.56 in the non vitrectomized eyes (p=0.829). Further analysis was also done to compare the mean TUS among two vitrectomized subgroups (air and SF6) and there was no significant difference (p=0.323).

Conclusions: This study concluded that there was no difference in the mean TUS in eyes post vitrectomy when compared to their contralateral healthy and non-vitrectomized eyes. This likely indicates that PPV does not affect the integrity of zonules in phakic patients.

Proof-of-concept analysis of a deep learning model to conduct automated segmentation of optical coherence tomography images for macular hole volume

Austin Pereira¹, Jonathan D. Oakley², Simrat K. Sodhi³, Daniel B. Russakoff², Netan Choudhry^{1,4,5}

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² Voxeleron LLC, San Francisco, USA

³ University of Cambridge, Cambridge, United Kingdom

⁴ Vitreous Retina Macula Specialists of Toronto, Toronto, Ontario, Canada

⁵ Cleveland Clinic Canada, Toronto, Ontario, Canada

Purpose: Macular hole (MH) volume offers less inter-user variability and offers improved prognostic considerations for postoperative visual outcomes following pars plana vitrectomy (PPV) surgery compared to conventional minimum linear diameter. The purpose of this study was to determine if an automated artificial intelligence (AI) model could assess MH volume on swept-source optical coherence tomography (OCT) images.

Methods: In this proof-of-concept case series, consecutive patients with an idiopathic full-thickness MH undergoing PPV between 2017 - 2019 were considered for inclusion. Swept-source OCT images were required at the preoperative, postoperative 1-month and postoperative 1-year time-points. MHs were manually graded by a vitreoretinal surgeon from preoperative OCT images to delineate MH volume and closure success. This information was used to train a fully 3-dimensional convolutional neural network (CNN) for automatic segmentation. Cross-validation was used to assess

Results: Twenty-four eyes were included in analysis. The correlation between manual and automated MH volume was $R^2=0.94$. The average dice coefficient between manual and automated metrics was 0.73 [0.65 - 0.86]. Automated MH volume demonstrated higher correlation to change in visual acuity from preoperative to the postoperative 1-year time-point compared to MLD (volume: $R^2=0.53$, MLD: $R^2=0.39$).

Conclusions: Automated volume segmentation of MHs on swept-source OCT imaging demonstrated high correlation to manual MH volume measurements, offering an improved preoperative biomarker for MH surgical planning.

A Mouse Model of Spaceflight-Associated Neuro-ocular Syndrome

Arya Zarrinbakhsh^{1,2}, Neeru Gupta^{1,3}, Xun Zhou^{1,3}, Hyacinth Irving¹, Yeni Yücel^{1,4}

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² Department of Laboratory Medicine & Pathobiology, Temerty Faculty of Medicine, University of Toronto

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⁴ Institute of Biomedical Engineering, Science and Technology (iBEST), St. Michael's Hospital, Ryerson University

Introduction: Astronaut health and well-being are at the forefront of biomedical research with plans for more long-duration spaceflight missions well underway. A major eye health barrier and potential cause of vision impairment affecting almost half of astronauts within a month of spaceflight is called Spaceflight-Associated Neuro-ocular Syndrome (SANS). Swelling in the optic nerve and retina are hallmarks of the disease, although the etiology is unknown. Our lab has previously described a glial-cell-dependent lymphatic circulation that allows entry of CSF fluid into the optic nerve, and we hypothesize that fluid shifts involving this pathway may play a role in retinal changes seen in astronauts. Since there is no animal model of SANS, our lab has been developing the first mouse model for SANS and here report eye changes observed.

Methods: We developed a Hindlimb Unloading (HU) protocol in which we suspended mice from the tail at approximately 30° for 21 days, before releasing them (“landing”) for 14 days. We categorized 8-month-old male ($n = 10$) and female ($n = 10$) B6(Cg)-Tyr^{c-2l}/J albino mice into control ($n = 4$ males, 4 females) and HU groups ($n = 6$ males, 6 females). We used *in vivo* spectral domain optical coherence tomography (SD-OCT via infrared laser (870 nm); Spectralis, Heidelberg Engineering) in both eyes before suspension (day 0), during suspension (days 7, 14 and 21) and after landing (days 22, 28 and 35) to evaluate retinal thickness in 9 ocular sectors (central, nasal-inner, nasal-outer, temporal-inner, temporal-outer, inferior-inner, inferior-outer, superior-inner, and superior-outer). Control mice were not suspended and were imaged according to the same protocol. We analyzed retinal thickness in all sectors of both eyes in both groups using mixed linear models.

Results: Mixed model cubic regression identified significant interactions in the central ($p = 0.0411$), nasal-inner ($p = 0.0029$) and nasal-outer sectors ($p = 0.0016$) of the right eye of HU mice compared to controls. At 7 day of HU, retinal thinning was observed, and between days 7 and 21 of HU, thickening in all 3 sectors was observed. Retinal thinning was again observed after landing at days 28 and 35. Remaining sectors of the right eyes showed no changes and significant changes were not observed in the left eye ($p > 0.05$).

Discussion: Significant changes in retinal thickness were observed in our mouse model of microgravity. This model may be highly relevant to understanding vision impairment in astronauts due to SANS.

Acknowledgements: We acknowledge the support of the Canadian Space Agency [19HLSRM02], the Henry Farrugia Research Fund and the Vision Science Research Program.

Discovering new molecular and cellular therapies for inherited retinal disease

Dr. Brian Ballios, MD, PhD, FRCSC, DABO



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Clinician-Scientist, Retinal Disease and Ocular Genomics, Donald K. Johnson Eye Institute, University Health Network,
Kensington Vision and Research Centre
Staff Ophthalmologist, Retina Specialist, John and Liz Tory Eye Clinic, Sunnybrook Health Sciences Centre
Associate Member, Institute of Medical Science
Associate Member, Laboratory Medicine and Pathobiology, School of Graduate Studies University of Toronto
Scientist, Krembil Research Institute, University Health Network

Abstract:

Inherited retinal disorders (IRDs) affect an estimated 90,000 Canadians, with a total cost of disease – including healthcare costs, productivity and well-being – at upwards of \$6.7 billion. More than 270 genes have been identified for inherited monogenic retinal disease. With rare exception, treatments do not exist for inherited conditions. New therapies for retinal degeneration are focused on the next generation of regenerative medicines. These include gene and cell-based therapeutics, including stem cells. While gene therapy has the potential to correct the underlying mechanism of disease in monogenic disorders, it depends on the presence of viable light-sensitive cells. Stem cell therapy has the potential to replace the light-sensitive photoreceptors lost in later-stage disease, when patients have suffered significant vision loss. Our research program seeks to determine more efficient ways of making rods and cones from new sources of stem cells, and to design novel approaches to facilitate stem cells survival and integration in the damaged eye. We will discuss the challenges facing therapeutic development for rare genetic retinal disorders. We will also give an overview of how we are using *in vitro* stem cell models of human retinal development to understand the pathobiology of rare retinal disease, and to study specific concerns in the field. This includes deriving optimized populations of cells for transplantation, and deconvoluting the competing effects of cell integration and survival that limit cell transplantation efficacy in specific IRDs. Finally, we will review the establishment of a new clinical research centre for the study of rare retinal disorders in adults, and a platform to establish first-in-human trials.

Investigating Fuchs Endothelial Corneal Dystrophy and Corneal Regeneration for Corneal Blindness

Dr. Stephan Ong Tone, MDCM, PhD, FRCSC



Clinician-Scientist in Cornea and External Eye Disease, Sunnybrook Health Sciences Centre and Sunnybrook Research Institute

Assistant Professor, Department of Ophthalmology and Vision Sciences, University of Toronto

Abstract:

Fuchs endothelial corneal dystrophy (FECD) is the most common primary corneal endothelial dystrophy and the leading indication for corneal transplantation worldwide. FECD is characterized by the progressive decline of corneal endothelial cells that leads to apoptosis, decreased endothelial cell density, and the formation of abnormal extracellular matrix excrescences called guttae. FECD is a complex and heterogeneous genetic disease, with a strong genetic association to a trinucleotide CTG repeat expansion within the third intron of the transcription factor 4 (*TCF4*) gene. There are no pharmacological treatments for FECD, and corneal transplantation, typically endothelial keratoplasty, is the only treatment. More recently, a surgical technique termed Descemet's stripping only (DSO), also referred to as Descemetorhexis without endothelial keratoplasty (DWEK), has been developed where the central corneal endothelium is removed without replacement with a corneal transplant. DSO relies on the ability of the peripheral corneal endothelium to regenerate the central endothelium through cellular migration. However, how this process is regulated is not well understood. We have previously demonstrated that corneal endothelial cells from FECD patients demonstrate increased cellular migration speeds compared to normal controls as detected through a novel live imaging human corneal culture model using *ex vivo* FECD and normal specimens, and immortalized FECD and normal corneal endothelial cell lines. FECD corneal endothelial cells also displayed altered morphology and increased endothelial-to-mesenchymal transition (EMT) markers.

We now aim to further investigate FECD pathogenesis, and possible predictors of corneal transplant and DSO success, by analyzing aqueous humor cytokine profiles from FECD patients undergoing surgery. We also are further exploring the relationship between the trinucleotide CTG repeat expansion in *TCF4* and EMT. Finally, we are testing the potential of adeno-associated viruses as a delivery vector to human corneal endothelial cells for gene therapy aimed at targeting causal genetic mutations in FECD.

ABSTRACTS FOR ORAL PRESENTATIONS

Virtual Session II

May 3rd, 2022

A Matched Longitudinal Cohort Study of Serious Adverse Reactions from Oral or Topical Carbonic Anhydrase Inhibitors

Marko M. Popovic¹, Matthew B. Schlenker^{1,2,3,4}, Deva Thiruchelvam^{5,6}, Donald A. Redelmeier^{5,6,7}

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Introduction: Some ophthalmologists may be reluctant to prescribe oral carbonic anhydrase inhibitors due to the potential for life-threatening systemic adverse events. The objective of this study was to evaluate the safety of oral or topical carbonic anhydrase inhibitors in clinical care.

Methods: In this matched, population-based, longitudinal cohort study, we identified consecutive patients over the age of 65 years who were prescribed an oral or topical carbonic anhydrase inhibitor in Ontario, Canada between January 1st 1995 and January 1st 2020. Patients were matched one-to-one based on age, gender, and diabetes status. Time-zero was defined as the date of the first identified prescription for the medication, and the primary analysis focused on the first 120 days of follow-up. The primary endpoint was a severe complicated adverse reaction (SCAR) of either Stevens-Johnson syndrome, toxic epidermal necrolysis, or aplastic anemia. The primary analysis examined the risk of SCAR events in the 120 days following initial treatment using a conditional logistic regression to compare patients initiating oral CAI (cases) to those initiating topical CAI (controls) while accounting for pair matching. In addition, univariable and multivariable logistic regression analyses were performed for baseline covariates as other potential risk factors.

Results: Overall, 128,942 patients initiated an oral or topical carbonic anhydrase inhibitor during the 25-year study period. The oral and topical carbonic anhydrase inhibitor groups had similar baseline demographics. Patients prescribed an oral carbonic anhydrase inhibitor had an absolute risk of a SCAR event of 2.90 per 1,000 patients, whereas patients prescribed a topical carbonic anhydrase inhibitor had an absolute risk of 2.08 per 1,000 patients. This difference was equivalent to a risk ratio of 1.40, with a number needed to harm of 1 in 1220 patients (95% confidence interval: 1.12-1.74, $p=0.003$). This generally low risk was replicated in multivariable regression controlling for confounding factors. Additional risk factors for a SCAR event included patients with more comorbidities and those with more frequent clinic contact.

Conclusions: The risk of a serious adverse reaction following prescription of a carbonic anhydrase inhibitor was low for both oral and topical formulations. Given the low risk of severe adverse events, this population-level analysis supports reconsidering the reluctance towards prescribing an oral carbonic anhydrase inhibitor.

Funding/Support: This work was supported by a grant from the Glaucoma Research Society of Canada and a Canada Research Chair in Medical Decision Sciences.

Conflicts of Interest: M.M.P.: PSI Foundation (R). M.B.S.: Alcon (C,S); Allergan (C,S); Bausch Health (S); Johnson & Johnson Vision (S); Light Matter Interaction (C); Théa-Labtcian (S); Santen (C). D.T.: no conflicts of interest to disclose. D.A.R.: no conflicts of interest to disclose. *Legend:* C – consultant/consulting fees; S – speaker honoraria; R – research grant/support

Initial Pars Plana Vitrectomy Compared to Tap-and-Inject for the Management of Endophthalmitis Secondary to Intravitreal Injections of Anti-Vascular Endothelial Growth Factor Agents: A Systematic Review and Meta-Analysis

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⁴Department of Ophthalmology, St. Michael's Hospital/Unity Health Toronto, Toronto, Canada.

Introduction: In this meta-analysis, we aim to compare the efficacy and safety of pars plana vitrectomy (PPV) versus tap-and-inject (TAI) of intravitreal antibiotics for the management of endophthalmitis secondary to intravitreal injections of anti-vascular endothelial growth factor (VEGF) agents.

Methods: A systematic literature search was conducted on Ovid MEDLINE, EMBASE, and Cochrane Central (2005 - March 29th, 2021) to identify articles comparing PPV to TAI for infectious endophthalmitis secondary to intravitreal anti-VEGF agents. The primary analysis considered initial PPV versus TAI, and the secondary analysis examined the efficacy and safety of TAI alone compared to TAI followed by PPV. The quality of non-randomized observational studies was assessed using the Newcastle-Ottawa Scale. The quality of the evidence for each prespecified outcome was also assessed. A random effects meta-analysis was performed. For all analyses, weighted mean differences (WMDs) with 95% confidence intervals were reported.

Results: Of 5,868 articles that were identified in the database search, 111 proceeded to full-text screening. Ten studies reporting on 165 eyes were included in the final analysis, with 104 eyes with post anti-VEGF injection endophthalmitis that were treated with initial TAI and 61 eyes with initial PPV. The mean cohort age was 72.1±8.7 years, with 29.1% (n=48/165) comprised of male patients. The difference between mean best corrected visual acuity (BCVA) at presentation of endophthalmitis and at last post-treatment follow-up did not significantly differ between the initial TAI versus PPV groups (WMD=0.01 units; 95% CI -0.27 to 0.30; P=0.92; heterogeneity P=0.13). The proportion of patients requiring repeat injections, PPV, enucleation or those with retinal detachment was not significantly different between the 2 treatment groups (p=0.225, 0.999, 0.999, 0.329 respectively). The difference in pre- to post-treatment mean BCVA did not significantly differ between eyes that received versus did not receive PPV post-TAI (WMD=-0.13 units; 95% CI -0.45 to 0.18; P=0.40; heterogeneity P=0.46).

Conclusions: There was no significant difference between PPV and TAI to treat endophthalmitis secondary to anti-VEGF agents. The quality of evidence was low with potential for confounding and selection bias. Certain subgroup analyses of interest were not feasible given a paucity of data, such as comparing the effect of initial treatment based on visual acuity at initial presentation. Furthermore, most studies did not report adverse events comprehensively and had a relatively short duration of follow-up. Considering such inherent limitations, our findings should be regarded as hypothesis generating. Further well-designed studies in this setting are needed.

Conflicts of Interest: MMP: Financial support (to institution) – PSI Foundation. PJK: Advisory board – Novartis, Alcon, Bayer, Roche, Novartis; Financial support (to institution) – Bayer, Roche, Novartis; Financial support – Novartis, Bayer; Equity owner – ArcticDx. RHM: Advisory board- Bayer, Novartis, Allergan, Roche; Financial Support (to institution)- Bayer, Novartis.

Novel Home Monitoring of Visual Fields with the Toronto Portable Perimeter

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⁴University of Toronto The Edward S Rogers Sr Department of Electrical and Computer Engineering, Toronto, Ontario, Canada

⁵University of Toronto Institute of Biomaterials and Biomedical Engineering, Toronto, Ontario, Canada

Purpose: To investigate home visual field monitoring with the Toronto Portable Perimeter (TPP) by glaucoma patients in a prospective cohort study.

Methods: Patients with recent visual fields on the Humphrey Field Analyzer (HFA) were recruited from the Glaucoma Clinic at Toronto Western Hospital. Each participant participated in a 20-min instruction session on how to use the TPP by themselves and each performed a bilateral TPP-Standard 24-2 protocol. Then, participants were instructed to perform bilateral tests twice monthly at home with a personal TPP. Mean deviation (MD), pattern standard deviation (PSD), visual field index (VFI) and test duration of reliable visual fields on the TPP were compared with the most recent reliable HFA SITA-Standard results. A reliable test was defined as: false positive < 20%, false negative < 20%, and fixation loss < 33%. Inter-test variability was measured by calculating the root mean square deviation of visual field indices in consecutive visual field tests of the same eye.

Results: To date 777 reliable home TPP visual field tests were performed by 16 patients (mean age: 69 years; range: 52 to 81) on 32 eyes (mean HFA MD: -5.76 dB; -11.91 to +1.33). Patients completed home TPP visual field tests at an average rate of 2.2 tests per 30 days (0.6 to 4.3). Across all eyes, the TPP MD was slightly lower but not statistically different from the HFA's MD (mean±std: -1.4±1.0 dB, p=0.17); PSD (-0.2±1.1 dB, p=0.88), VFI (-2%±3%, p=0.52), and test durations (-17±11 seconds, p=0.13) were similar between the two devices. The inter-test variability was lower in TPP compared to HFA for MD (1.14 vs. 1.44 dB, p<0.001), PSD (1.00 vs. 1.13 dB, p<0.001), and VFI (3.7% vs. 4.1%, p<0.04). In 27 eyes after 12 reliable home tests, the standard error of the mean MD, PSD, VFI in each eye was reduced to 0.47 dB, 0.28 dB, and 1.1%, respectively.

Conclusions: Our preliminary results indicated that glaucoma patients can perform TPP visual fields reliably at home. Results from the TPP were similar to the HFA. Consecutive tests at home exhibited less variability than consecutive tests on the clinic HFA. Patients found TPP more convenient, relaxing, and easier to perform at home. Frequent testing over short periods of time may improve precision of estimates of visual field indices and thus may possibly enable earlier detection of change, but this potential still needs verification.

Conflict of interest: Runjie Bill Shi and Moshe Eizenman are the inventors of Toronto Portable Perimeter. All other authors have no conflict of interests.

Choroidal hypoperfusion defects as a new fluorescein angiographic finding in patients with retinopathy of prematurity

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Introduction: Retinopathy of prematurity (ROP) remains the major ocular disorder of the neonate and the dominant cause of severe visual impairment in childhood in North America and Europe. The retinal pathology has been thoroughly studied in ROP. In recent years, numerous clinical and animal studies have reported choroidal involution as a key feature in ROP development. Of note, choroid is the exclusive energy source to the photoreceptors and retinal pigment epithelium. Therefore, choroidal involution could predispose visual loss, as it can lead to substantial sub-retinal hypoxia.

Intravenous fluorescein angiography (IVFA) is the key modality for in-depth choroidal evaluation. In premature children, it is not commonly available and usually requires examination under anesthesia. Therefore, imaging studies based on choroidal IVFA remain scarce in the literature. In this project, we systematically assessed IVFA data in ROP patients who needed treatment, and described key imaging features in this population.

Methods: In this retrospective study, ROP patients who received treatment with intravitreal bevacizumab [IVB] and/or laser photocoagulation from 2015–2020 were identified at the Hospital for Sick Children (SickKids). Clinical information, including birth weight (BW), gestational age (GA) and ROP staging were collected. All images were first screened for the presence of abnormal choroidal IVFA patterns. Three abnormal choroidal patterns – delayed choroidal entry, linear choroidal pattern and choroidal hypoperfusion defects - were found based on thorough literature review and screening.

Results: Sixty-five (65) ROP patients were identified for review. Among them, 35 patients had IVFA; and 28 had high quality that enabled further analyses. For these 28 patients, they had an average BW of 602.6 grams, and an average GA of 24.0 weeks. The majority (68.0%) had zone I, stage 3+ ROP. 67.8% received IVB; 7.2% had lasers; and the remaining 25% had IVB followed by prophylaxis lasers. The average age at which the IVFA was performed was 9.8 months (range: 2.5 to 24 months). In terms of choroidal IVFA patterns, 75.0% demonstrated hypoperfusion defects; 71.4% showed delayed choroidal entry, and 60.7% had linear choroidal patterns.

Conclusion: To our knowledge, this study represented the largest series that systematically described choroidal vascular abnormalities in children with ROP. It highlights the notion that ROP affects both the retina and the choroid. Our findings raise the possibility that choroidal involution may precipitate outer retinal dysfunction, thereby impacting long-term visual outcomes. Long-term ophthalmic follow-up with angiography are needed to further study ROP patients.

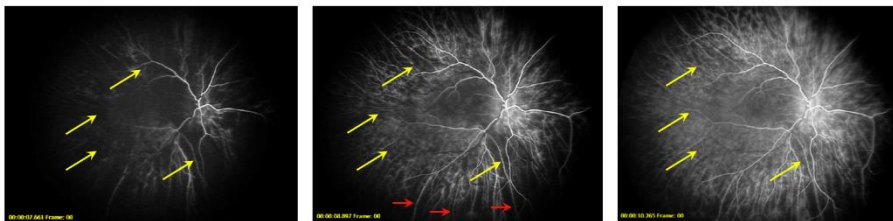


Figure 1. This series of IVFA is from a girl who was born at 23 weeks with a BW of 600g. She had bilateral zone III, stage 3+ ROP and received IVB. Her IVFA series at 1 year-old showed substantial choroidal hypoperfusion defects that are most visible at the arterial phase (yellow arrows). She also demonstrated delayed choroidal entry in the earliest phase, as well as linear choroidal patterns (red arrows).

Sustained Release of RdCVF-Sh3 to Rescue Cone Photoreceptor Death

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Purpose: Retinitis Pigmentosa (RP) is an inherited retinal degenerative disease that can lead to blindness. In RP, an initial loss of night vision caused by the death of rod photoreceptors eventually progresses to the loss of high acuity vision due to the apoptosis of cone photoreceptors. This two-phase degeneration is caused by the loss of rod-secreted protein factors that are necessary for cone survival. One recently discovered protein – rod-derived cone viability factor (RdCVF) – has been shown to increase cone viability in both *in vitro* and *in vivo* studies. Though RdCVF is a promising therapeutic that could rescue dying cones, it cannot be translated to the clinic because of its rapid clearance, limited bioavailability, and the need for repeated invasive injections. Therefore, there is a need to develop a drug delivery system that can sustain the release of therapeutics to the eye. To address this need, we expressed RdCVF with a Src homology 3 (Sh3) domain and modified an oxime-crosslinked hyaluronan (HA) hydrogel with Sh3 binding peptides to slow protein release through Sh3 and Sh3-binding peptide interactions. Here, we investigated the release profile and bioactivity of RdCVF-Sh3 *in vitro*.

Methodology: The delivery system was synthesized by incorporating RdCVF-Sh3 in an injectable hyaluronan-based hydrogel crosslinked via oxime ligation, whereby Sh3-binding peptides were covalently bound to the polymer backbone through an inverse electron demand Diels-Alder ligation. To investigate tunability of release, the hydrogel was made with increasing molar excesses of Sh3-binding peptide to RdCVF-Sh3, and released protein was quantified using an ELISA at different time points for 14 days. Bioactivity of the protein was tested on E6 chick retinal dissociates stained with the cone-specific marker visinin to assess if the Sh3 domain would affect the function of RdCVF.

Results: Our results show sustained release of RdCVF-Sh3 from our delivery system with tunability dependent on peptide to protein ratio: as the molar excess of Sh3 binding peptide increases with respect to the RdCVF-Sh3 protein, the slower the protein release. Furthermore, the RdCVF-Sh3 was bioactive as shown by an increase in cone viability in chick retinal dissociates.

Conclusion: In conclusion, the release of RdCVF is controllable with our affinity-based release system and the additional Sh3 domain does not disrupt protein function. Beyond RP, this versatile injectable hydrogel could be explored in many other retinal degenerative diseases and circumvent repeated repeated invasive intravitreal or subretinal drug injections.

Guest Lecture

8:05 – 8:25 PM

41st Clement McCulloch Lecturer

What should I know about Ocular Gene Therapy?

Dr. Ian MacDonald MSc, MD CM



An ophthalmologist and clinical geneticist. He began his academic career at the University of Ottawa, as an Ontario Ministry of Health Career Scientist before moving to Alberta in 1992. He served 4 terms as Department Chair of Ophthalmology and Visual Sciences at the University of Alberta and is currently Acting-Chair and Acting Edmonton Zone Chief of Ophthalmology for Alberta Health Services. He served as Branch Chief, Ophthalmic Genetics and Visual Function, at the National Eye Institute of NIH for 2 years, returning to Edmonton in 2009. His clinical and research interest are the investigation and management of inherited retinal disorders. In 2015, with funding from CFI, CIHR, Alberta Innovates, Foundation Fighting Blindness Canada, and the Choroideremia Research Foundation, Canada Inc., he led the first trial of ocular gene therapy in Canada. In 2018, he received the Canadian National Institute for the Blind: Century of Change Award (serving on its Board for Alberta/NWT) and the Foundation Fighting Blindness, Canada Founder's Award. For mentoring many trainees in medical genetics and genetic counselling, he received the 2020 Lifetime Achievement Award of the Canadian College of Medical Geneticists. In 2021, he presented the Franceschetti Lecture (with medal) at the biannual meeting of the International Society of Genetic Eye Disease and Retinoblastoma.

Abstract: Patients and their families frequently ask you questions about Ocular Gene Therapy. I intend to provide you with some talking points for your conversation with them and relate some lessons learned from our team's experience. There is only one Health Canada approved treatment for an inherited ocular disorder, Luxturna™ for the *RPE65* form of Leber congenital amaurosis. Yet, to date, the provinces have not agreed on a funding formula to address its significant price. The remaining therapies are in different stages of clinical trials to define safety and efficacy. Viral and non-viral mediated gene replacement approaches are being studied with either subretinal or intravitreal approaches. This approach is different from gene editing with for example CRISPR-Cas9. Inflammation is commonly present after delivery of a vector into the eye and can significantly limit its safety and efficacy. RNA interference with anti-sense oligonucleotides is another approach in trials for the several inherited disorders and have in general a better safety profile. The care pathway to treatment or clinical trial usually begins with genetic confirmation of the patient's underlying ocular condition.

ABSTRACTS FOR ORAL PRESENTATIONS

Virtual Session III

May 10th, 2022

Early results of the novel 63µm ab interno gelatin microstent versus conventional 45µm microstent

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Purpose: The 63µm ab interno gelatin microstent (Xen63) is a novel device with a larger lumen than the currently available 45µm microstent (Xen45). This study is amongst the first compare the impact of the Xen63 device on IOP and glaucoma medication use versus Xen45.

Study Design: Retrospective comparative cohort study.

Methods: Consecutive patients who underwent Xen63 implantation from February 2020 to June 2021 were compared with randomly selected patients who underwent Xen45 implantation. Standalone and combined cases with phacoemulsification were included. Success was defined as IOP ranges of 6-14 mmHg, 6-17 mmHg, or 6-21 mmHg plus 20% IOP reduction from baseline, starting at 1 month after surgery, without reoperations. Success without glaucoma medications (complete) and with medications (qualified) were tabulated. Data up to 6 months after surgery were analyzed.

Results: 42 eyes underwent Xen63 implantation, and 42 eyes underwent Xen45 implantation. The groups had similar baseline characteristics. Overall, mean age was 66.7 ± 14.0 years, 47 (55.9%) patients were female, and 38 (45.2%) patients had advanced disease. 12 Xen63 (28.6%) and 13 Xen45 (31.0%) cases were combined with phacoemulsification.

Preoperative IOP was similar between the two groups (Xen63: 25.9 ± 9.2 mmHg, Xen45: 26.0 ± 8.4 mmHg, $p=0.88$). At 6 months, mean IOP was significantly lower in Xen63 eyes (12.1 ± 4.2 mmHg vs. 15.6 ± 4.7 mmHg, $p<0.001$). Similarly, Xen63 eyes used significantly fewer medication classes at 6 months (0.4 ± 1.1 classes vs. 1.3 ± 1.4 classes, $p<0.001$), despite similar use at baseline (Xen63: 3.9 ± 1.1 classes, Xen45: 3.6 ± 1.0 classes, $p=0.26$).

6-month complete success was higher in the Xen63 group with IOP criteria of 6-14 mmHg (75.1% vs. 47.6%, $p=0.01$) as well as criteria 6-17 mmHg (75.6% vs. 50.0%, $p=0.043$). The crude hazard ratio of failure of Xen63 relative to Xen45 was 0.42 (0.21-0.83) and 0.50 (0.25-0.99) for criteria of 6-14 mmHg and 6-17 mmHg, respectively.

Needling occurred in 7 (16.7%) Xen63 eyes and 8 (19.0%) Xen45 eyes. Xen63 eyes had 5 (11.9%) reoperations, consisting of 3 Xen revisions and 2 Ahmed valve implantations. In the same period, the Xen45 group had 2 (4.8%) Xen revisions.

Conclusions: The novel Xen63 microstent resulted in significantly greater IOP lowering and medication reduction compared to Xen45 in the early postoperative course with good safety profile.

The Cataract Surgery Learning Curve: Quantitatively Tracking a Resident's Operative Actions Throughout Their Training

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The degeneration of photoreceptors (PRs) leads to irreversible and untreatable vision loss. A widely investigated therapeutic strategy has been cell replacement to restore photoreceptor function. While early studies of PR precursor transplantation reported the presence of host cells expressing the donor cell tracker (e.g. cytosolic GFP), more recent studies provide evidence that donor cells rarely, if ever, integrate into the host retina; instead, positive results of transplantation could be due to material exchange (ME) of proteins from donor to host photoreceptors. However, the mechanism of ME remains largely unknown. To investigate the mechanism of ME, our lab has established *in vivo* and *in vitro* co-culture models of ME that suggest mitochondria is exchanged through a contact dependent mechanism. CRISPR screening using an explant-based transfer assay will identify novel modulators of photoreceptor material exchange. We hypothesize that these genes are involved in adhesion of protrusions. To identify genetic regulators of ME, we will use CRISPR-mediated gene inactivation in PRs from Cre-inducible Cas9 mice infected with lentivirus carrying a sgRNA library, cre-recombinase, and RFP reporter regulated by the rod-specific *Nrl* promoter, to generate a pool of gene-targeted acceptor cells. These guide-targeted acceptor cells are then co-cultured with a donor pool of PRs labeled with MitoTracker Red (MTR) to track transfer of mitochondria. After two days, the single positive (RFP+) and double positive (RFP+MTR+) acceptor cells are enriched by flow cytometry, genomic DNA is isolated and subjected to next generation sequencing and analyzed by changes in the frequency of guide RNAs between the two pools of cells. Because dissociated primary retinal cells have poor viability after extended culture *in vitro*, we developed an explant based assay that enhances the feasibility of this screen. Explants from P0 Rosa-YFP mice were cultured for 9 days, the time necessary for CRISPR-mediated gene inactivation, then dissociated to provide a pool of recipient cells. To determine their ability to partake in ME, explant-derived cells were co-cultured for 2 days with retinal dissociates labeled with MTR. Flow cytometry analysis demonstrated 44% of the YFP+ acceptor PRs accepted MTR. We have demonstrated the feasibility of using explant derived PRs as an acceptor pool of mitochondria as a platform for screening.

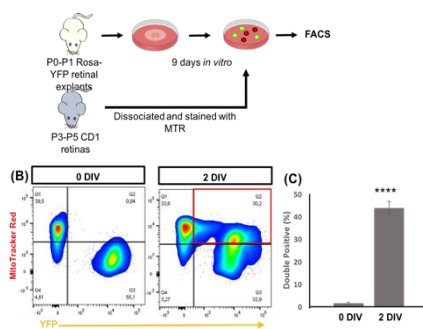


Figure 1. *In vitro* cultured explant-derived photoreceptors can serve as acceptors of mitochondria. (A) Postnatal day 1 Rosa-YFP retinal explants ($n=4$) are maintained in explant culture for 9 days *in vitro* (DIV), then dissociated, using a papain-based kit (Worthington Biochemical, UK), and co-cultured with postnatal day 3 MTR-labeled CD1 retinal dissociates (MTR+CD1) ($n=3$). Flow cytometry analysis was performed after 2-day co-culture using a BD LSR Fortessa and analyzed using FlowJo software. (B) Flow cytometry analysis of Rosa-YFP explant-derived and MTR+CD1 photoreceptor co-culture showing transfer of MTR after 2 DIV compared to 0 DIV. Events collected were gated for eFluor (live) and CD73+ photoreceptors. Q1: MTR+; Q2: MTR+ and YFP+; Q3: YFP+; MTR- and YFP-. (C) Proportion of Rosa-YFP explant-derived photoreceptors accepting MTR out of entire YFP+ photoreceptor population. All data are presented as well replicate \pm SEM; one-way ANOVA; n.s. no statistical significance, **** $p \leq 0.0001$, *** $p \leq 0.001$, ** $p \leq 0.01$, * $p \leq 0.05$

Corneal Hysteresis and Central Corneal Thickness: A Significant Association with SIBS Microshunt Surgical Outcomes

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Purpose: Recent work has associated low corneal hysteresis (CH) with higher trabecular bypass surgery reoperation rates.(1) Post-operative wound healing impacts all glaucoma surgeries, and in particular bleb forming surgeries. Matrix and cell biology studies demonstrate that increased extracellular matrix stiffness is a major factor promoting scarring through direct myofibroblast activation.(2,3) CH may be considered a surrogate marker of ocular extracellular matrix biomechanical properties, as it can predict the compliance of posterior ocular tissues such as the optic nerve surface(4) and lamina cribrosa.(5,6) We hypothesize that lower CH is associated with stiffer ocular tissues and can identify patients with a propensity for dysregulated ocular wound healing, and by extension, increased failure rates of bleb-forming surgeries.

Study Design: Retrospective, interventional case series.

Methods: Consecutive patients with recent CH and central corneal thickness (CCT) measurements undergoing SIBS microshunt implantation between July 2015 and July 2020 were included. For comparisons, the cohort was divided into lower and upper 50th percentiles based on CH and/or CCT. Main outcome was proportion of eyes at 1-year with (1) no 2 consecutive IOPs >14 mmHg or clinical hypotony, without (complete) or with (qualified) glaucoma medications; and (2) ≥20% reduction from baseline IOP. Secondary outcomes included median IOP, medications, risk factors, post-operative interventions, complications, and reoperations.

Results: Fifty-one eyes of 50 patients were included. Low (<9mmHg) and high (≥9mmHg) CH cohorts only differed significantly in median [IQR] baseline medication use (4 [3-4] vs. 3 [1-4], respectively). After 12-months, patients with low CH achieved a 53.8% success rate and the high CH cohort achieved 76.0%. Patients with both low CH and low CCT (<533µm) achieved success in 43.8% of cases, whereas the remaining patients achieved an 85.7% success rate. The low CH cohort experienced a significantly higher risk of failure (HR 9.3; 95%CI 2-43). Further, for each 1 mmHg lower a patient's CH, a significantly increased risk of failure was observed (HR 1.6; 95%CI 1.1-2.2). Patients in the low CH cohort required significantly more post-operative medications (2.9 vs. 0.6; p<0.0001) and experienced significantly shorter medication-free survival time (5.8 v. 7.3 months; p<0.001). Needling rates were significantly higher in the low CH cohort (OR 4.3; 95%CI 1.1-16.2), as were reoperations (OR 4.1; 95%CI 2.1-8.1).

Conclusions: Our findings, while limited by sample size and their retrospective nature, strongly suggest that CH impacts subconjunctival glaucoma surgery outcomes. More work encompassing basic science and prospective clinical studies is required to fully explore this novel and potentially robust risk factor.

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Guest Lecture

8:05 – 8:25 PM

Dr. Martin J. Steinbach Lecturer

**Diabetes and the Corneal Endothelium
(Yes It Happens There Too)**

Dr. Mark Greiner MD



Associate Professor of Ophthalmology and Visual Sciences
Medical Director, Iowa Lions Eye Bank
Fellowship Director, Cornea, External Diseases and Refractive Surgery
Robert and Joell Brightfelt Professor of Cornea Research