Department of Ophthalmology and Vision Sciences University of Toronto

67th Annual Research Day

And

44th Clement McCulloch Lecture

Friday, May 23, 2025

7:15 AM – 4:00 PM

St. Michael's Hospital

Li Ka Shing Knowledge Institute

209 Victoria Street

Toronto, Ontario M5B 1T8

Ophthalmology & Vision Sciences
UNIVERSITY OF TORONTO

Chair's Message

It is my great pleasure to welcome you to the 67th Annual Research Day of the University of Toronto Department of Ophthalmology and Vision Sciences.

Research Day is a highlight in our academic calendar—an opportunity to celebrate the remarkable breadth and depth of scientific inquiry across our department. Vision science is at the heart of what we do, and it is through our continued pursuit of knowledge, innovation, and collaboration that we remain global leaders in the field. The work showcased today reflects the strength of our research community and our shared commitment to improving patient care through discovery.

Our department's mission includes nurturing the next generation of clinicians, clinician-scientists, and vision researchers. Whether our trainees pursue academic, clinical, community, or industry careers, we aim to instill a lifelong curiosity and a rigorous approach to scientific thinking. It is this foundation that drives forward better diagnostics, novel therapies, and a deeper understanding of ophthalmic disease.

This year's program, once again under the thoughtful leadership of Dr. Matthew Schlenker, is rich in content and diverse in scope. Featuring outstanding oral and poster presentations from our trainees, along with talks from our esteemed faculty and guest speaker, the day promises to be engaging, educational, and inspiring.

We are honoured to welcome our keynote speaker, Dr. Pradeep Ramulu, as well as our faculty speakers, Dr. Rajeev Muni and Dr. Brian Ballios, who will be sharing exciting updates from their research.

I would like to extend my heartfelt thanks to Dr. Schlenker for his dedication to organizing this event, and to our outstanding administrative team—Sandra Gauci and Helena Medeiros—for their invaluable support behind the scenes.

We are also deeply grateful to our sponsors—AbbVie, Bayer, and Roche—for their generous educational grants, which help make this day possible.

I hope you enjoy today's sessions, feel inspired by the discoveries being made across our department, and leave with new insights, new questions, and renewed enthusiasm for the future of vision science.

Thank you for being part of this important day.

Peter J. Kertes, MD CM, FRCSC
Chair, Department of Ophthalmology and Vision Sciences
University of Toronto

Research Day Chairperson's Remarks

Research Day for the Department of Ophthalmology and Vision Sciences at the University of Toronto is our sentinel event showcasing research from our pre-clinical, clinical, and research trainees. For many trainees, this experience represents their first foray into sharing their research, including myself when I was a medical student. The day represents an opportunity to feast at the smorgasbord of clinical and basic science initiatives across our institution, in addition to many cross institution and discipline collaborations that have been forged through the presentations and subsequent interactions.

The quality and volume of content for this Research Day Program shows that our Department continues to be a fertile ground for rigorous research. This year, we celebrate the 67th Ophthalmology Departmental Research Day and the 44th Clement McCulloch Lecture. We would like to welcome Dr. Pradeep Ramulu, a renowned clinician-scientist and Glaucoma Surgeon. Dr. Ramulu is the Sheila K. West Professor and Chief of Glaucoma at the Wilmer Eye Institute, Jon Hopkins Medicine. He conducts award-winning research into the functional impact of glaucoma on patients, including how it impacts their physical activity, fall risk, and cognition.

This scientific gathering would not be possible without the generous support from our sponsors Abbvie, Bayer, and Roche. I would like to thank our abstract reviewers, abstract judges, moderators, faculty speakers, organizing committee, and ancillary staff who are responsible for the success of Research Day. A special thanks to Helena Medeiros, Sandra Gauci, and Mano Chandrakumar who spent countless hours assisting with the organization of this year's Research Day. None of this research would be possible without all our supervisors and mentors of our trainees. And finally, thank you to all of you who attended in person, and listen to the presentations and mingled with our trainees.

This event entitles eligible participants to obtain CME credits. Please complete the evaluation form to get your CME credits. Your evaluation is vital for us to improve this event in the future and is greatly appreciated.

Matt Schlenker, MD, MSc (Clin Epi), FRCSC

Chair, Annual Ophthalmology Research Day Director of Resident Research
Glaucoma, Cataract, & Anterior Segment Surgeon Assistant Professor
Department of Ophthalmology and Vision Sciences University of Toronto

Evaluation of Presentations

Each judge completes an evaluation form for every presentation. To avoid potential conflicts of interest, any judge listed as a co-author on a paper will not evaluate that paper. Presentations are assessed based on presentation skills, quality of work, and clinical or scientific relevance.

Particular emphasis is placed on the overall quality of the work, including the clarity of the published abstract.

Each candidate receives a numerical score, and the average score determines the winner of each award. While the value of competition on Research Day may be debated, the department believes it is important to formally recognize excellence and outstanding effort in research.

The Alumni Award for the Best Resident Paper, the John Gaby Prize for the Best Clinical Fellow Paper, and the Best Poster Award will be presented at the Ophthalmology graduation dinner.

Research Day Organizing Committee

- Waleed Alsarhani
- Sandra Gauci
- Joseph Hanna
- Peter Kertes
- Helena Medeiros
- Rajeev Muni
- Matt Schlenker
- Tina Tang
- Valerie Wallace

Dr. Clement McCulloch, Professor and Chair Department of Ophthalmology 1961 – 1982

Dr. Clement McCulloch graduated from the University of Toronto Faculty of Medicine in 1939. He then pursued further ophthalmological training at Columbia Presbyterian Hospital in New York City, where he spent three years working alongside Dr. Phillip Thygeson on the pathophysiology of external eye diseases, including trachoma.

He later enlisted in the Royal Canadian Air Force, serving on the Central Medical Board. During this time, he worked with a research unit, where he further demonstrated his passion for investigation, focusing on the retinal effects of high-altitude flying and the optics of night vision.

At the conclusion of the Second World War, Dr. McCulloch returned to Toronto as Chief of the Ophthalmology Service at Toronto Western Hospital. There, he established an ophthalmology training program that was eventually integrated into the University of Toronto's teaching system under the direction of Dr. A.J. Elliott. In 1961, Dr. McCulloch was appointed Chair of the Department of Ophthalmology. His goal was to raise the standard of practice in Toronto to match that of other leading centers around the world.

A staunch advocate for research, Dr. McCulloch devoted considerable effort to supporting staff members interested in advancing scientific knowledge. He was known for the collegial and friendly atmosphere he cultivated within the department. Monthly hospital chiefs' meetings were often hosted in members' homes, fostering lively debate and a personal approach to policy development.

During his 21-year tenure as Chair, the University of Toronto became recognized for its strong commitment to ophthalmological research. Dr. McCulloch promoted excellence across all subspecialty fields. He published more than 80 articles in international journals on topics ranging from the ultrastructure of zonules to crystalline corneal dystrophy. His scientific contributions have been compiled and published by University of Toronto Press.

Dr. McCulloch's extensive experience and broad knowledge continue to be valued by the department. In 1980, a group of his friends established a fund to support an annual lectureship in ophthalmological research. This initiative has helped fund the University of Toronto's annual Research Day and the Clement McCulloch Lecture.

Dr. McCulloch passed away in early 2007. Through this lectureship, his legacy in education and research continues to thrive.

44th Clement McCulloch Lecture - Dr. Pradeep Ramulu

Dr. Pradeep Ramulu is a glaucoma specialist and Director of the Glaucoma Division at the Wilmer Eye Institute, Johns Hopkins University. He holds the Sheila K. West Professorship in Ophthalmology and is internationally recognized for his contributions to both clinical care and vision science.

Dr. Ramulu graduated with honors from Stanford University before entering the MD/PhD program at Johns Hopkins University. He completed his doctoral research in retinal biology under the mentorship of Dr. Jeremy Nathans, followed by residency training at the Wilmer Eye Institute and a glaucoma fellowship at the Bascom Palmer Eye Institute.

After completing his fellowship, Dr. Ramulu returned to Wilmer to establish a research program focused on the functional consequences of visual impairment. His current work explores the protective role of physical activity in eye disease, strategies to prevent falls in older adults with vision loss, and the use of ocular imaging to identify individuals at risk for cognitive decline.

Dr. Ramulu has published over 180 peer-reviewed articles, contributed to 10 book chapters, and authored two books. He holds leadership positions in several national and international organizations, serving as Program Chair for the American Glaucoma Society and Director of the Education Committee for the World Glaucoma Association.

A committed educator and mentor, Dr. Ramulu has guided numerous students, residents, and fellows in medicine and public health. He is a two-time recipient of Wilmer's resident teaching award and has led a transformation in glaucoma education through the introduction of online lectures and the implementation of interactive, game-based, and case-based classroom learning.

Since joining the Wilmer faculty in 2006, Dr. Ramulu has led a division comprising more than 30 clinical, research, and administrative team members. His research has been continuously funded by the National Institutes of Health since 2007. He has received numerous honors for his work, including the Secretariat, Achievement, and Senior Awards from the American Academy of Ophthalmology, and the prestigious Pisart Award for Vision Science. In 2021, he was named one of *Newsweek's* "America's Best Eye Doctors."

7:15 AM - 7:45 AM	**Continental Breakfast and Registration**	
7:45 AM - 7:50 AM	Department Chair Welcome	Peter Kertes, MD CM, FRCSC
7:50 AM – 8:00 AM	Research Day Chair Welcome	Matthew B. Schlenker, MD, MSc, FRCSC

8:10 AM - 9:30 AM **Session moderator: Dr. Efrem Mandelcorn**
Location: **Auditorium**

8:10 AM - 8:25 AM	Novel Insights in Rhegmatogenous Retinal Detachment	Rajeev H. Muni, MD, MSc, FRCSC
8:25 AM - 8:33 AM	Impact of GLP-1 Receptor Agonists and SGLT-2 Inhibitors on the Treatment Burden of Retinopathies in Patients with Diabetes: A Population-Based, Retrospective Cohort Study.	Moiz Lakhani, BHSc Medical Student Supervisor: Radha Kohly, MD, PhD
8:33 AM - 8:41 AM	Assessing the EyeArt Artificial Intelligence-Based System for Diabetic Retinopathy Screening in the Toronto Tele-Retinal Screening Program	Elizabeth Wei, BMSc MD(C) Medical Student Supervisor: Amrit S. Rai, MD FRCSC
8:41 AM - 8:49 AM	Quantitative Analysis of Hyper-Reflective Dot Distribution and Texture in Regulated Versus Dysregulated Rhegmatogenous Retinal Detachment	Shiva Sabour, MD, Research Fellow Supervisor: Rajeev H. Muni, MD, MSc, FRCSC
8:49 AM - 8:57 AM	Long-term Outcomes of Eyes Lost to Follow-up with Proliferative Diabetic Retinopathy and Diabetic Macular Edema Receiving Intravitreal Anti-Vascular Endothelial Growth Factor or Panretinal Photocoagulation	Ryan Huang, MSc Medical Student Supervisor: Radha, Kohly, MD
8:57 AM - 9:05 AM	Impact of Baseline Morphologic Stage of Full-Thickness Macular Hole on Postoperative Visual Acuity	Aurora Pecaku, MD Fellow Supervisor: Rajeev H. Muni, MD, MSc, FRCSC
9:05 AM - 9:13 AM	Deep phenotyping of PRPF31-associated Autosomal Dominant Retinitis Pigmentosa	Kirk Stephenson MD, FRCSI, DRCPSC -AFC DOVS Clinical Fellow Supervisor: Ajoy Vincent MB, BS, MS, FRCSC
9:13 AM - 9:30 AM	Question Period	

9:30 AM - 10:30 AM	**COFFEE BREAK + POSTER SESSION**	**Even numbered posters are judged**
10:30 AM - 12:00 PM	**BREAK ROOM SESSIONS**	

Variety of Topics

Moderator: **Dr. David Yan**
Location: **Auditorium**

10:30 AM - 10:40 AM	Prevalence and Clinical Significance of Incidental Findings in Neuro-Ophthalmology Imaging: A Retrospective Analysis of 5000 Cases	Samira Jafari, MD Research Fellow Supervisor: Jonathan A. Micieli, MD, CM, FRCSC
10:40 AM - 10:50 AM	Adverse Events Associated with Teprotumumab Use: A Population-Based Pharmacovigilance Study	Victoria Leung, MD(C) Medical Student Supervisor: Georges Nassrallah, MD, FRCSC
10:50 AM - 11:00 AM	Comparing One Year Outcomes of Open and Closed Conjunctival Surgical Approaches in the 63-µm Gelatin Microstent	Minoo Tohidi Kaloorazi, MD Supervisor: Iqbal Ike K. Ahmed, MD, FRCSC
11:00 AM - 11:10 AM	Impact of Anesthesia on Oscillatory Potentials in Electroretinographic Responses: A Comparative Study in a Pediatric Population	Patrick Xiang Ji, MD(C), MSc, Medical Student Supervisor: Ajoy Vincent, MBBS, MD
11:10 AM - 11:20 AM	Outcomes of SIBS microshunt implantation in eyes with previously failed gelatin microstent surgery.	Mohammad Javad Ghanbarnia, MD Research Fellow Supervisor: Iqbal Ike K. Ahmed, MD, FRCSC
11:20 AM - 11:30 AM	Identifying allo-HLA antibodies and cross match incompatibility in children after penetrating keratoplasty	Ashley Porter, MD, MMed Clinical Fellow Supervisor: Asim, Ali, BA.Sc., MD, FRCSC
11:30 AM - 12:00 PM	Question Period	

Retina

Moderator: **Dr. Valerie Wallace and Dr. Peter Kertes**
Location: **Room 211**

10:30 AM - 10:40 AM	CRB1-mutation Increases Differentiation Into Early-Born Retinal Cell Types in Human Induced Pluripotent Stem Cell-Derived Retinal Organoids	Jessica Wang, BHSc/MSc Graduate Student Supervisor: Brian, Ballios, MD, PhD, FRCSC, DABO
10:40 AM - 10:50 AM	Molecular Recognition and Selectivity in Phototransduction and Visual Disease	Jing Liu, BSc VSRP Supervisor: Belinda S.W., Chang, PhD
10:50 AM - 11:00 AM	Risk of Retinal Detachment with GLP-1 Receptor Agonists and SGLT2 Inhibitors: A Population-Based Study	Andrew Mihalache MD(C) Medical Student Supervisor: Rajeev H. Muni MD, MSc, FRCSC
11:00 AM - 11:10 AM	Ocular Adverse Events Associated with Pegcetacoplan and Avacincaptad Pegol for Geographic Atrophy: A Population-Based Pharmacovigilance Study	Zeena Kailani, MD(C) Medical Student Supervisor: Rajeev H. Muni MD, MSc, FRCSC
11:10 AM - 11:20 AM	Assessment of Re-detachment Based on Proliferative Vitreoretinopathy Findings on SS-OCT	Isabela Martins Melo, MD Clinical Fellow Supervisor: Rajeev H. Muni MD, MSc, FRCSC
11:20 AM - 11:30 AM	The epidemiological burden and characteristics of uveitis cases identified in health administrative data: An Ontario population-based study over two decades.	Tina Felfeli, MD, PhD Resident Supervisor: Efrem D Mandelcorn, MD, FRCSC
11:30 AM - 12:00 PM	Question Period	

12:00 PM - 1:00 PM	**LUNCH + POSTER SESSION**	**Odd numbered posters are judged**

The 44th Clement McCulloch Lecturer

1:00 PM - 1:10 PM	Introduction to Dr. Pradeep Ramulu	Dr. Matthew Schlenker
1:10 PM - 2:10 PM	Uncertainty in Glaucoma Testing and Measurement: Implications for Clinical Care	Dr. Pradeep Ramulu, MD, PhD
2:10 PM - 3:00 PM	**COFFEE BREAK + POSTER SESSION**	**All remaining posters are judged**

3:00 PM - 4:00 PM **Session moderator: Dr. Rahul Sharma**
Location: **Auditorium**

3:00 PM - 3:15 PM	New molecular and cellular therapies for inherited retinal disease	Brian Ballios, MD, PhD, FRCSC, DABO
3:15 PM - 3:23 PM	Artificial Intelligence Diagnosis of Extraocular Movement Disorders from Clinical Videos	David Mikhail, MD(C), MSc(C) Medical Student Supervisor: Jonathan A. Micieli, MD, CM, FRCSC
3:23 PM - 3:31 PM	Glucagon-Like Peptide-1 Receptor Agonists and Neovascular Age-Related Macular Degeneration: A Population-Based Study	Reut Shor, MD Research Fellow Supervisor: Radha P. Kohly, MD, PhD
3:31 PM - 3:39 PM	Canadian Provincial Cataract Surgery Wait Times 2008-2023: A Retrospective Study of Canadian Institute for Health Information Data	Brendan Tao, BHSc Medical Student Supervisor: Matthew B. Schlenker, MD, MSc, FRCSC
3:39 PM - 3:47 PM	A Real-World, Population-Based Pharmacovigilance Analysis of Drugs Attributed to Blepharitis, Meibomian Gland Dysfunction, and Chalazion	Dana Taghaddos MD(C) Medical Student Supervisor: Clara Chan MD FRCSC FASC
3:47 PM - 4:00 PM	Question Period	

4:00 PM	**Closing Remarks**	**Dr. Matthew Schlenker**

PROGRAM SPONSORED BY

Oral Presentations

Moiz Lakhani **Medical student**

Impact of GLP-1 Receptor Agonists and SGLT-2 Inhibitors on the Treatment Burden of Retinopathies in Patients with Diabetes: A Population-Based, Retrospective Cohort Study

Co-authors: Moiz Lakhani, BHSc, Faculty of Medicine, University of Ottawa, Angela T.H. Kwan, MD(C), MSc, Faculty of Medicine, University of Ottawa, Reut Shor, MD, Department of Ophthalmology and Visual Sciences, University of Toronto, Marko M. Popovic, MD, MPH, Department of Ophthalmology and Visual Sciences, University of Toronto, Radha Kohly, MD, PhD, Department of Ophthalmology and Visual Sciences, University of Toronto.

Introduction: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and sodium-glucose cotransporter-2 (SGLT2) inhibitors have transformed diabetes mellitus (DM) and obesity management by improving glycemic control, promoting weight loss, and providing cardiovascular protection. However, concerns about a potential link between GLP-1 RAs and diabetic retinopathy (DR) progression have raised questions about their ocular safety. This study examines whether long-term use of GLP-1 RAs or SGLT-2 inhibitors impacts the treatment burden of retinopathies in DM patients, measured by the frequency of intravitreal anti-VEGF injections in real-world settings.

Methods: We conducted a population-based, retrospective matched-cohort study using Ontario's health administrative data from 2011 to 2021. Adults (≥18 years) with DM who received at least two anti-VEGF injections before and during follow-up were included. A total of 1,074 patients were propensity score-matched (1:1:1) using the Mahalanobis distance method into three cohorts (n=358 each): GLP-1 RA users, SGLT2 inhibitor users, and a control group of unexposed patients to either agent. Treatment burden was assessed by the total number of anti-VEGF injections and the interval from the first retinal injection to the index date ("treatment year"), with the primary outcome being the mean annual frequency of intravitreal injections during follow-up.

Results: Baseline demographics were well-matched across groups, with mean ages of 67.04 (±2.5), 67.03 (±2.2), and 68.10 (±3.0) years for the GLP-1 RA, SGLT-2 inhibitor, and control groups, respectively, and similar female distributions (37-38%). Average follow-up durations were 4.45, 4.06, and 3.85 years, and the annual anti-VEGF injection rates were 3.6, 3.5, and 3.7, respectively. One-way ANOVA showed no statistically significant differences in annual injection frequency among groups ($p>0.05$), suggesting that neither GLP-1 RAs nor SGLT-2 inhibitors impact injection rates.

Conclusion: While GLP-1 RAs and SGLT-2 inhibitors provide systemic benefits for DM management, our findings indicate that their long-term use does not reduce the frequency of intravitreal injections required for DM-associated retinopathies. This analysis confirms these agents do not worsen ocular complications, addressing previous safety concerns. Although additional retinal surveillance beyond standard care may not be warranted, potential adverse effects in specific patient subtypes not captured in this study cannot be ruled out. Prospective trials, such as the FOCUS study, will provide greater insight into semaglutide's role in DR progression by leveraging standardized detection protocols (e.g., dilation status, fundus imaging) and criteria for disease evaluation. In the interim, ophthalmologists should remain vigilant when managing patients with pre-existing retinopathy or those undergoing rapid HbA1C reductions, given the serious consequences of DR progression.

Elizabeth Wei **Medical student**

Assessing the EyeArt Artificial Intelligence-Based System for Diabetic Retinopathy Screening in the Toronto Tele-Retinal Screening Program

Co-authors: Elizabeth Wei, BMSc MD(C), Temerty Faculty of Medicine, University of Toronto, Tina Felfeli, MD PhD, Department of Ophthalmology & Vision Sciences, University of Toronto, Charbel Wahab, BSc MD, Department of Ophthalmology & Vision Sciences, University of Toronto, Hamid Moghimi, MA, South Riverdale Community Health Centre, Michael H. Brent, MD FRCSC, Department of Ophthalmology & Vision Sciences, University of Toronto.

Introduction: Diabetic retinopathy (DR) is a leading cause of preventable vision loss, affecting 22% of people living with diabetes in Canada. However, 33% of people living with diabetes in Ontario were unscreened in 2017-2019. Tele-retinal screening programs can help meet this gap with the help of Artificial Intelligence (AI) and hand-held fundus cameras. AI can provide point-of-care diagnoses and referral decisions, and hand-held cameras are portable and have lower upfront costs compared to traditional imaging modalities. This study aimed to determine the performance of the Health Canada approved EyeArt AI system for diabetic retinopathy detection in a tele-retinal screening program in Toronto, and to compare the performance of the AI using two fundus imaging modalities; a hand-held camera, and a table-top camera.

Methods: Adults ≥ 18 years of age diagnosed with type 1 or type 2 diabetes mellitus were enrolled in the Toronto Tele-Retinal Screening Program from July 2022 to September 2024. Two-field colour fundus photographs were captured (macula centered, optic disc centered) using a table-top camera (TopCon Maestro2), and in a subset of patients, hand-held camera (Optomed Aurora IQ) fundus photographs were also captured. Images were assessed by a retina specialist (reference standard) and the AI for detection of vision-threatening DR (vtDR; defined as the presence of at least one eye with severe non-proliferative DR, proliferative diabetic retinopathy, or diabetic macular edema [DME]), DR grade, and DME. Ungradable cases were included as vtDR positive cases. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. Statistical significance was defined as $p<0.05$, and 95% confidence intervals (CIs) were reported.

Results: A total of 656 patients (1,312 eyes) were screened with the table-top camera, and of these, 255 patients (510 eyes) were additionally screened with a hand-held camera. The overall prevalence of DR was 27.1%, DME prevalence was 4.5%, and vtDR prevalence was 8.5%. The AI was unable to grade 7.5% of eyes. With the table-top camera, the AI had a sensitivity, specificity, PPV, and NPV of 89.3% [86.9-91.7%], 87.0% [84.4-89.6%], 39.1% [35.3-42.8%], and 98.9% [98.1-99.7%], respectively. With the hand-held camera, the AI sensitivity, specificity, PPV, and NPV were 89.5% [85.7-93.2%], 82.2% [77.5-86.9%], 28.8% [23.3-34.4%], and 99.0% [97.7-100%], respectively.

Conclusion: The EyeArt AI system has high overall model quality for detecting patients with vtDR with both the hand-held and table-top cameras, with high sensitivity and specificity. EyeArt AI holds promise for improving triaging of patients for ophthalmology referral.

Shiva Sabour **Research Fellow**

Quantitative Analysis of Hyper-Reflective Dot Distribution and Texture in Regulated Versus Dysregulated Rhegmatogenous Retinal Detachment

Co-authors: Shiva Sabour , MD,Department of Ophthalmology and Vision Science , University of Toronto, Aurora Pecaku , MD ,Department of Ophthalmology and Vision Science , University of Toronto, Isabella Martins Melo , MD ,Department of Ophthalmology and Vision Science , University of Toronto, Rashita Kalra , PHD , Department of Ophthalmology, St. Michael's Hospital, Unity Health Toronto, Rajeev H.Muni , MD , MSc , Department of Ophthalmology, St. Michael's Hospital, Unity Health Toronto.

Introduction: Two distinct clinical patterns of rhegmatogenous retinal detachment (RRD) exist. Acute, progressive, and extensive cases are defined as those with RPE-photoreceptor/subretinal space dysregulation whereas localized, slow or non-progressive RRDs where the RPE is in relative control of the subretinal space are classified as regulated.
The purpose of this study was to quantitatively compare the characteristics of subretinal fluid (SRF) in patients with regulated versus dysregulated (RRD).

Methods: This retrospective study included patients diagnosed with RRD who presented to St. Michael's Hospital, Toronto, Canada from November 2012 to August 2024.Sixty patients were retrospectively reviewed, including 25 with regulated RRD and 35 dysregulated cases, all of whom had high-quality baseline swept-source or spectral domain OCT images. Custom-developed MATLAB codes were employed to select the region of interest (ROI) in each OCT image and to count hyper reflective dots within the SRF. The software further categorized these dots into four groups based on size and intensity: large + high intensity, large + low intensity, small + high intensity, and small + low intensity. Additionally, texture analysis was performed by plotting the ROI histogram and calculating its standard deviation (SD) and full width at half maximum (FWHM), with higher values indicating a more heterogeneous texture.

Results: The regulated group exhibited a significantly higher total average count of hyper reflective dots (22 vs. 5; p = 0.002) and a greater average density per square millimeter (4.755 vs. 1.427; p = 0.01) compared to the dysregulated group. In regulated RRD, the predominant dot type was large + high intensity (32.5% 186/572), whereas in dysregulated RRD, small + low intensity dots were most prevalent (44% ,82/186). While the distribution across the four dot categories in the regulated group did not reach statistical significance, the dysregulated group demonstrated a significant predominance of the small + low intensity dots (p = 0.02). Moreover, the SD and FWHM of the ROI histogram were significantly higher in the regulated group (SD p = 0.0003; FWHM p = 0.007), suggesting a more heterogeneous SRF texture.

Conclusion: Our findings indicate that regulated RRD, is associated with a denser SRF containing a higher number of hyper reflective particles and a more heterogeneous texture compared to dysregulated RRD. The increased particle density in regulated RRD may reflect prolonged absorption processes by the retinal pigment epithelium, leading to a hyperosmolar SRF. In contrast, dysregulated RRD appears to have a more hypo osmolar more homogeneous SRF. This study not only elucidates the distinct SRF characteristics between regulated and dysregulated RRD but also demonstrates the utility of quantitative OCT image analysis as an objective tool in retinal research.

Ryan Huang **Medical student**

Long-term Outcomes of Eyes Lost to Follow-up with Proliferative Diabetic Retinopathy and Diabetic Macular Edema Receiving Intravitreal Anti-Vascular Endothelial Growth Factor or Panretinal Photocoagulation

Co-authors: Ryan, Huang, MSc, Temerty Faculty of Medicine, University of Toronto, Marko, Popovic, MD, MPH, Department of Ophthalmology and Vision Sciences, University of Toronto, Peter, Kertes, MD, CM, Department of Ophthalmology and Vision Sciences, University of Toronto, Rajeev, Muni, MD, MSc, Department of Ophthalmology and Vision Sciences, University of Toronto, Radha, Kohly, MD, PhD, Department of Ophthalmology and Vision Sciences, University of Toronto.

Introduction: Anti-vascular endothelial growth factor (VEGF) intravitreal injections (IVIs) have demonstrated comparable efficacy to panretinal photocoagulation (PRP) in managing proliferative diabetic retinopathy (PDR). However, these findings are largely dependent on strict adherence to follow-up. This study aims to evaluate the long-term functional and anatomic outcomes in patients with PDR or diabetic macular edema (DME) that were lost to follow-up (LTFU) for over one year after treatment.

Methods: In this multicenter, retrospective cohort study, we analyzed patients with PDR or DME treated with either anti-VEGF IVIs or PRP between January 2012 and December 2021 in Toronto, Canada. Temporary LTFU was defined as the absence of an ophthalmic visit for at least one year followed by subsequent return to care. Eyes with prior PRP were excluded from the anti-VEGF group and those receiving anti-VEGF IVIs within the past 3 months were excluded from the PRP group. We compared best-corrected visual acuity (BCVA) and anatomic outcomes between treatment groups at four timepoints: pre-LTFU baseline visit, first return visit after being LTFU, one-year post-return from LTFU, and final recorded visit using t-tests and chi-square tests.

Results: A total of 338 eyes from 276 patients who were temporarily LTFU were included. Of these, 137 (41%) eyes received anti-VEGF IVIs and 201 (59%) eyes underwent PRP. Prior to being LTFU, the mean number of treatments was 7±5 IVIs in the anti-VEGF group and 3±2 sessions in the PRP group. The anti-VEGF group demonstrated a significant worsening in BCVA from pre-LTFU (0.39±0.36 logMAR) to both the first return visit (1.03±0.67 logMAR; $p<0.001$) and final recorded visit (0.90±0.62 logMAR; $p<0.001$). The PRP group showed an initial reduction in BCVA from pre-LTFU (0.40±0.29 logMAR) to the first return visit (0.72±0.58 logMAR; $p=0.04$), but no significant difference at final visit (0.42±0.51 logMAR; $p=0.46$). At return from LTFU, a significantly higher proportion of eyes in the anti-VEGF group had diabetic macular edema (88% [121/137] vs 35% [71/201]; $p<0.001$), neovascularization of the disc (40% [55/137] vs 22% [44/137]; $p<0.001$), neovascularization elsewhere (37% [50/137] vs 27% [51/137]; $p=0.03$), and tractional retinal detachment (7% [10/137] vs 2% [3/201]; $p=0.01$) compared to the PRP group.

Conclusion: Patients with PDR or DME who were LTFU for over one year experienced a greater worsening in BCVA and worse anatomic outcomes if treated with intravitreal anti-VEGF therapy compared to PRP. These findings highlight the importance of treatment selection and measures to improve follow-up adherence in this patient population.

Aurora Pecaku **Clinical Fellow**

Impact of Baseline Morphologic Stage of Full-Thickness Macular Hole on Postoperative Visual Acuity

Co-authors: Aurora Pecaku, MD, St. Michael's Hospital, Department of Ophthalmology, University of Toronto, Shiva Sabour, MD ,St. Michael's Hospital, Department of Ophthalmology, University of Toronto, Fahad Butt MD(c), University of Toronto, Charles Wykoff MD, PhD, Retina Consultants of Texas, Texas, Houston, US, Rajeev H. Muni, MD ,MSc, FRCSC St. Michael's Hospital, Department of Ophthalmology, University of Toronto.

Introduction: The morphologic stage of full-thickness macular hole (FTMH) may be a reliable preoperative predictor for postoperative anatomical and functional outcomes

Methods: Multicenter retrospective cohort study. Consecutive primary FTMH referred to St. Michael's Hospital, Toronto, Canada, and Retina Consultants of Texas, Texas, Houston, US from 2012 to 2021. Patients with primary FTMH, no history of vitrectomy, and no prior macular pathology, were assessed. Best-corrected VA (BCVA) was assessed at the presentation and 1,3, 6, and 12 months postoperatively. OCT scans were graded for the morphologic stage of FTMH. The purpose of this study evaluate the association of baseline morphologic stage of full-thickness macular hole using optical coherence tomography (OCT) with postoperative visual acuity (VA) outcomes.

Results: Two hundred fourteen patients were included. 65.9%(141/214) were female. The mean(SD) age of the cohort was 67.5(7.04) years, and 70.5%(151/214) of them were phakic. Seven percent (15/214) presented in Stage A, 50.5%(108/214) in Stage B, 30.4%(65/214) in Stage C, and 12.1%(26/214) in Stage D. Increasing morphologic stage (from A to B, C, D) was associated with worse baseline VA ($P<0.01$) and longer duration of central vision loss ($P<0.001$). The mean(SD) 12-month BCVA by stage was 0.60 (± 0.28) for Stage A; 0.61(0.49) for Stage B, 0.84(± 0.65) for Stage C, and 1.2(± 1.0) for Stage D. There was no statistically significant difference when comparing postoperative VA at 1 year between stages A and B ($P=0.9$). However, increasing morphologic stage from Stage B to Stage C ($P = 0.03$), Stage B to Stage D ($P < 0.001$), and Stage C to Stage D ($P = 0.008$) were significantly associated with reduced postoperative BCVA at the 12-month follow-up, after adjusting for covariates such as sex, age, lens status, and time to surgery.

Conclusion: This study validates the clinical relevance of a recently proposed OCT-based staging system for outer retinal morphologic changes over time in FTMH. Postoperative BCVA was consistently lower in patients with more advanced presenting stages. At 12 months, BCVA was significantly better in Stages A and B compared to Stages C and D. These findings suggest that earlier stages of FTMH may be associated with better outer retinal recovery than Stage C or Stage D.

Kirk Stephenson **Clinical Fellow**

Deep phenotyping of PRPF31-associated Autosomal Dominant Retinitis Pigmentosa

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Introduction: Deleterious variants in the PRPF31 gene may cause autosomal dominant (AD) retinitis pigmentosa (RP) which has characteristic incomplete penetrance. We prospectively assessed subjects with PRPF31-RP to characterize the structural and functional ophthalmic features of retinal degeneration.

Methods: This prospective observational study was approved by the Research Ethics Board of The Hospital for Sick Children and international guidelines. Subjects with a heterozygous pathogenic or likely pathogenic PRPF31 variant with clinical features of RP were included after providing informed consent. All participants had detailed examination with multimodal retinal imaging (MMI), axial length measurement and flood illumination adaptive optics [AO (rtx1, Imagine Eyes, France)] imaging. AO images underwent semi-automated analysis assessing the cone mosaic at 2o temporal to the fovea. Cone mosaic data (cone density [CD], cone spacing [CS]) was contrasted with best corrected visual acuity (BCVA), Goldmann visual fields (GVF) III4e isopter horizontal diameter and other MMI features (including optical coherence tomography [OCT] horizontal ellipsoid zone [EZ] width and central retinal thickness [CRT]). Findings were contrasted between children, parents and controls.

Results: Eight participants met the inclusion criteria (age 12 – 59 years, 63% female) including 3 parent-child pairs (2/3 parents were 'asymptomatic' but had features of RP). Mean BCVA was 0.20 ±0.30 LogMAR, with 88% of eyes having ≤0.3 LogMAR BCVA. Mean GVF III4e horizontal diameter (84.4±46.7o) was less than normal (130o, p<0.001). CD and CS at 2o temporal to the fovea were not associated with any GVF abnormalities. EZ width was significantly less than controls (4484 ±2952 vs 7870 ±262, p=0.014). Mean spherical equivalent (SE) refraction was +0.41 ±1.73D. Cone mosaic showed significant differences from normative values for CD (16656 ±4890 vs 28884 cones/mm2, p<0.001) and CS (8.95 ±2.07 vs 6.49µm, p<0.001). Neither CD (r2=0.006, p=0.772) nor CS (r2=0.097, p=0.087) were linearly associated with age. Although parents and children had differing peripheral measures, including CRT3-6mm (265 ±13 vs 232 ±25µm, p=0.009), parents were indistinguishable from their affected children for CRT1mm (p=0.168), CD (19284 ±2491 vs 18021 ±2325 cones/mm2, p=0.556) and CS (8.00 ±0.55 vs 8.30 ±0.56, p=0.502).

Conclusion: PRPF31-RP shows highly variable expressivity though all subjects in this study showed signs of RP. Abnormalities in the central cone mosaic were identified even in pre-symptomatic subjects where standard measures such as BCVA were normal. Cone mosaic assessment by AO may be useful as an anatomical outcome measure (with functional extrapolations) for future therapies targeting PRPF31-RP.

Samira Jafari **Research Fellow**

Prevalence and Clinical Significance of Incidental Findings in Neuro-Ophthalmology Imaging: A Retrospective Analysis of 5000 Cases

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Introduction: Patients referred to ophthalmology and neuro-ophthalmology clinics often present with complex neurological and visual symptoms, such as headaches, double vision, and vision loss, requiring thorough history, comprehensive examinations, and advanced imaging to identify the underlying cause. While advances in neuroimaging have improved diagnostic accuracy, they have also introduced challenges with incidental findings and unexpected abnormalities discovered during unrelated imaging. This study aims to determine the prevalence, spectrum, and clinical relevance of incidental findings in neuro-ophthalmology patients at an academic center.

Methods: A retrospective, observational cohort study of 5,000 patients (59% female, 41% male; mean age 53.7 years) who underwent neuroimaging (MRI and CT) for neuro-ophthalmic symptoms at an academic neuro-ophthalmology clinic between July 2008 and June 2024. Details of imaging type, region scanned, and reason for imaging were recorded from electronic medical records. Incidental findings were defined as abnormalities unrelated to the original reason for imaging and categorized into four follow-up categories (none, routine, urgent, and emergency). Imaging reports were independently reviewed and categorized by an ophthalmologist and a neuro-ophthalmologist. Descriptive statistics were used to assess the prevalence of incidental findings and their clinical significance. Chi-square tests and analysis of variance were applied to assess associations between imaging modalities, age, and the presence of incidental findings.

Results: Incidental findings were present in 31% (n=1,532) of patients; 20.6% required no follow-up, 9.6% required routine follow-up, 0.34% required urgent follow-up, and 0.1% required emergency follow-up. The most common incidental findings were microangiopathic changes (14.2%), sinus changes (6.96%), and brain atrophy (3.26%). MRI showed a higher prevalence of incidental findings than CT (31.8% vs 25.1%, $p<0.05$). There was no difference in incidental findings between 1.5T vs. 3T MRI. Age was significantly associated with certain findings, such as microangiopathy and brain atrophy. The most common findings by follow-up category were microangiopathic changes (no follow-up), meningiomas (routine follow-up), suspected neoplasms (urgent), and suspected metastasis (emergency).

Conclusion: Incidental findings are common in neuro-ophthalmology imaging, with the majority requiring no or routine follow-up. However, a small percentage (0.44%) of cases required urgent or emergency attention, underscoring the need for careful evaluation and management protocols. These findings emphasize the importance of developing guidelines to manage incidentalomas in neuro-ophthalmology, particularly for older patients and those undergoing MRI.

Victoria Leung **Medical student**

Adverse Events Associated with Teprotumumab Use: A Population-Based Pharmacovigilance Study

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Introduction: Teprotumumab is the first FDA-approved medication for the treatment of thyroid eye disease (TED). While clinical trials have demonstrated its efficacy in reducing proptosis and inflammation, numerous reports have raised safety concerns. Given the novelty of teprotumumab and its relatively short period of widespread clinical use, real-world data are essential to comprehensively assess its systemic safety profile. We aimed to conduct a population-based, real-world pharmacovigilance analysis to investigate associations between teprotumumab and adverse event reports using data from the Food and Drug Administration Adverse Event Reporting System (FAERS).

Methods: A pharmacovigilance analysis of adverse events attributed to teprotumumab reported to the FAERS database from October 2003 through October 2024 was conducted using Open Vigil 2.1 (Kiel, Germany) data-mining software. Drug-specific adverse events attributed to teprotumumab were compared to background rates for other drugs in the FAERS database. Disproportionality analyses were performed using reporting odds ratios (RORs) and Bayesian confidence propagation neural network algorithms to identify significant safety signals.

Results: A total of 3,486 adverse events were attributed to teprotumumab over the study period. Teprotumumab was disproportionately overreported for 48 adverse events (≥10 events with an ROR≥10). Notable associations included permanent deafness (3.1%, n=109/3,486; ROR=10306.5, 95%CI=[7185.7, 14782.7], IC025=8.0), autophony (0.4%, n=13/3,486; ROR=1972.7, 95%CI=[950.4, 4094.7], IC025=5.0), auditory disorder (0.7%, n=23/3,486; ROR=107.3, 95%CI=[70.8, 162.6], IC025=4.4), gingival recession (0.7%, n=23/3,486; ROR=92.7, 95%CI=[61.2, 140.3], IC025=4.3), and onychoclasis (2.3%, n=81/3,486; ROR=89.5, 95%CI=[71.5, 112.0], IC025=5.1). Several other safety signals including but not limited to hyperglycemia, muscle spasms, menstrual disorder, tinnitus, and taste disorder were also identified.

Conclusion: There is a pressing need for increased clinical vigilance in monitoring for early adverse events in patients administered teprotumumab. Proactive monitoring and early intervention may mitigate the impact of these adverse events, improving patient safety and outcomes in the setting of TED. Clinicians must engage in shared decision-making with patients, ensuring that the benefits of therapy are carefully weighed against the potential risks. Future research should also explore potential strategies to minimize or manage these adverse events while preserving the drug's efficacy.

Minoo Tohidi Kaloorazi **Associate**

Comparing One Year Outcomes of Open and Closed Conjunctival Surgical Approaches in the 63-µm Gelatin Microstent

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Introduction: The 63-µm Gelatin Microstent can be placed in the sub-Tenon or subconjunctival space via an open (open) or closed with primary needling (closed) conjunctival approach respectively. We aim to determine the IOP-lowering and adverse event profile of the open and closed 63-µm Gelatin Microstent implants after 1 year follow-up.

Methods: In this retrospective cohort study, eighty-nine glaucomatous eyes that received standalone 63-µm Gelatin Microstent Implants at 6 surgical centres across 4 countries (Canada, Italy, Austria, Belgium) were included. The primary outcome was complete success (ie. no two consecutive IOP>17mmHg, <6mmHg, or < 20% reduction from baseline on no medications and no reoperations). Secondary outcomes included upper IOP thresholds of 14mmHg and 21mmHg, qualified success (with medications), change in IOP, medications, complications, interventions, and re-operations. A Cox proportional hazards model was used to assess risk factors for failure.

Results: Baseline median IOP were 24.0 (19.0-26.5) and 24.0 (19.0-29.8) mmHg, and baseline medications were 3.0 (3.0-4.0) and 4.0 (3.0-4.0) for open and closed eyes, respectively. Final IOP were 10.0 (8.0-11.3) and 12 (8.5-16.5), and final medication was 0 (0-0) and 0 (0-1) for open and closed eyes respectively. Complete success was achieved in 57.1% of 35 open eyes and 64.2% of 54 closed eyes (HR, 1.33; 95% CI, 0.67-2.65). Qualified success was achieved in 79.3% and 91.8% (HR, 2.82; 95% CI, 0.83-9.64). Cox regression did not identify risk factors for failures, including open approach (HR, 1.33; 95% CI, 0.67-2.65; p=0.411), high preop IOP, poor preop vision, and disease severity. Complications occurred in 28 open and 49 closed eyes, most of which were transient. Open and closed had similar IOP and medication reduction at 12 months (p>0.05). Five (14.2%) open and 11 closed (20.3%) eyes underwent reoperations, and 1 (2.9%) and 6 (11.1%) eyes underwent needling (p=ns).

Conclusion: Our results are in line with previous studies reporting an overall success of 59.5% for 63-µM Gelatin Microstent. However, whereas previous work showed open eyes achieved higher success than closed eyes in 45-µM Gelatin Microstents (56% versus 31%, p=0.01), we found that both techniques were comparable in the larger 63-µM device. Conclusion: The standalone open conjunctiva approach demonstrated similar success rates as the closed approach in 63-µm Gelatin Microstent implantation. Both showed comparable IOP reduction from baseline at 1-year follow-up.

Patrick Xiang Ji **Medical student**

Impact of Anesthesia on Oscillatory Potentials in Electroretinographic Responses: A Comparative Study in a Pediatric Population

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Introduction: Oscillatory potentials (OPs) in an electroretinogram (ERG) provide insights into the function of the inner retina, specifically amacrine cells. The effects of general anesthesia (GA) or sedation on OPs in this population are not well understood. This study aims to evaluate the effects of GA or sedation on OPs in pediatric patients with otherwise normal ERGs.

Methods: This retrospective study, conducted between 2019 and 2024, analyzed normal ERGs from three groups: i. children under GA (intravenous propofol and inhalational agent), ii. children under sedation (oral chloralhydrate), and iii. control cohort (no anesthesia). Light-adapted (LA) and dark-adapted (DA) 3.0 ERGs were evaluated, focusing on corresponding OP peaks (OP1-OP4) timing and amplitudes.

Results: A total of 75 patients were evaluated: 25 GA, 25 sedations, and 25 controls. For DA ERGs, there were significant differences in OP1-OP4 amplitudes across the three groups ($p<0.05$, effect sizes: 0.40–1.02). The DA-GA patients showed the lowest amplitude, followed by sedation patients, and both groups showed significantly lower amplitudes compared to controls for all OPs. LA ERGs showed significant differences in OP1 and OP2 amplitudes across the three groups ($p<0.05$, effect sizes: 0.38–0.59). While we observed significantly reduced OP amplitudes in both anesthesia groups compared to controls, there was no clear trend in amplitude decrease across the three groups in LA conditions. OP implicit times also showed significant differences across all three groups for DA ERGs ($p<0.05$, effect sizes: 0.34–1.26). Both anesthesia groups showed significantly delayed implicit times compared to controls, with the DA-GA group exhibiting the longest timing. However, no clear trends were observed for LA ERGs.

Conclusion: The present work suggests a potential dose-response relationship between anesthesia depth and OP characteristics, with GA showing the most pronounced effects. The more significant effects on DA ERGs may indicate higher sensitivity of the dark-adapted retinal circuits to the slowing-down effects of anesthetics, or the preferential effects on rod-dominant pathways. Age-related confounding factors and the low sample size of the study warrant further investigation. The findings of this study highlight the importance of considering the effects anesthesia on OPs when interpreting ERG clinically. Future work should explore the complex interplay between anesthetics, retinal pathophysiology, and ERG parameters, to enhance the care for pediatric patients requiring ERG under GA or sedation.

Mohammad Javad Ghanbarnia **Research Fellow**

Outcomes of SIBS microshunt implantation in eyes with previously failed gelatin microstent surgery.

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Introduction: Glaucomatous eyes with previously failed glaucoma surgery are at increased risk of surgical failure and complications in subsequent glaucoma surgeries. The purpose of this study was to evaluate the efficacy and safety of SIBS microshunt implantation in glaucomatous eyes with previously failed gelatin microstent surgery.

Methods: Consecutive patients with previously failed 45µm gelatin microstent surgery who underwent SIBS microshunt implantation between August 2015 and August 2019 were included. Primary outcome measure was the cumulative proportion of complete success at 1 year defined as 1) no 2 consecutive intraocular pressure (IOP) >17 mm Hg or clinical hypotony, without glaucoma medications; and (2) ≥20% reduction from decision IOP. Surgical reoperations and no light perception were also counted towards failure. Secondary outcome measures included complete success with IOP thresholds of 14 and 21 mmHg, IOP and medication decrease after 12 months, risk factors for failure based on 17mmHg IOP threshold, post-surgery adverse events and interventions.

Results: Overall 28 eyes with mean age of 59.2 (±16.3) years were included. Median (IQR) decision IOP and medication classes were 23.0 (19.0-28.0) mmHg and 3 (3-4), respectively. Median (IQR) preoperative best corrected visual acuity (BCVA) was 0.4 (0.2-0.7). After 12 months of follow up cumulative probability of complete success based on 14, 17, and 21 mmHg IOP thresholds was 37.3%, 58.5% and 62.3%, respectively. Compared to baseline, IOP (11.5, 8.0-18.5 mmHg) and medication classes (0, 0-2) at the last follow up decreased significantly ($P<0.001$). In a multivariate adjusted model, factors such as low preoperative BCVA, older age, female gender and glaucoma severity weren't significantly associated with increased risk of failure based on complete success definition with 17mmHg IOP threshold. There were 22 (78.6%) post-surgery adverse events and 13 (46.4%) interventions including 5 (17.8%) needlings.

Conclusion: In this cohort of high risk eyes with previously failed 45µm gelatin microstent surgery, SIBS microshunt implantation resulted in significant reduction in IOP and medication use and reasonable surgical success, adverse event and intervention rates after 12 months.

Ashley Porter **Clinical Fellow**

Identifying allo-HLA antibodies and cross match incompatibility in children after penetrating keratoplasty

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Introduction: The rate of allo-human leucocyte antigen (HLA) antibody formation in paediatric post penetrating keratoplasty (PK) patients who have a clear graft or previous rejection, and the effect on cross match incompatibility has not been previously investigated.

Methods: A prospective cohort study of paediatric post-PK patients with and without graft rejection, had serum testing for the presence of HLA antibodies, and were compared with 34 non-keratoplasty patients as a control cohort.
Outcome measures were the prevalence and number of alleles of class I and II allo-HLA antibodies, and calculated panel reactive antibodies rate (cPRA) as a measure of cross match incompatibility.

Results: A total number of 22 eyes in 22 patients (M:F, 11:11) were recruited; 13 patients had apparent rejection and 9 did not. Of the patients in the rejection cohort, 8 (61.1%) had either class I or II antibodies compared to 2 (22.2%) patients with clear grafts and 6 (17.6%) in the control cohorts. In the rejection cohort there was a statistically significant difference in the prevalence of class I ($p < 0.001$), class II ($p<0.01$) and total ($p<0.01$) when compared with clear grafts and control cohorts. The mean number of class I alleles in the rejection cohort was 6.69 and was significantly higher than the clear graft (1.55, $p <0.05$) and control (0.26, $p <0.05$) cohorts. The mean number of class II alleles was not found to be statistically significant. The mean of the total number of all alleles in the rejection (7.38), clear graft (2.1), and control (0.38) cohorts demonstrated statistical significance ($p<0.05$). The mean cPRA among the patients with positive antibodies was calculated. The class I cPRA difference in the rejection (30%), clear graft (10%) and control (0.82%) cohorts, was statistically significant ($p<0.05$). Class II cPRA in the rejection (8.07%), clear graft (6.33%) and control (1.79%) cohorts were not significantly different. The total of both class I and II rates in the rejection (38.07%), clear graft (16.33%) and control (2.61%) cohorts, demonstrated a statistically significant difference between the rejection and clear graft ($p<0.05$); and control ($p<0.01$) cohorts.

Conclusion: Paediatric patients with corneal rejection demonstrated a significantly higher rate of allo-HLA antibodies both in terms of prevalence and number of class I and total alleles, and class I and total cPRA. This represents an elevated risk of rejection for both subsequent corneal and solid organ transplants.

Jessica Wang **Graduate student**

CRB1-mutation Increases Differentiation Into Early-Born Retinal Cell Types in Human Induced Pluripotent Stem Cell-Derived Retinal Organoids

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Introduction: CRB1-associated disease is an inherited retinal disease causing progressive vision loss in youths. However, the mechanisms are difficult to study due to a lack of models that accurately replicate human disease. Human retina organoids (ROs) show great promise as an in vitro model to recapitulate human disease development. This study hypothesizes that CRB1-mutated ROs would have increased differentiation into early-born retinal cell types at the expense of late-born cell types.

Methods: ROs were generated from two induced pluripotent stem cell lines: a healthy donor line and a CRB1-associated Leber congenital amaurosis patient line (p.Q120X; p.Q120X). Immunofluorescent staining for cell-type specific markers was performed. Proliferation was measured at early timepoints, weeks 8 and 12, by incubating the ROs in EdU for 1h and either fixing immediately (single pulse) or fixing after a 24h incubation in EdU-free media (pulse-chase). The presumptive neuroblastic layer was divided into four equal areas from apical to basal, and the EdU+ cells were quantified per area. RNA was extracted from whole ROs, and qRT-PCR was used to quantify gene expression.

Results: Observing the proportion of early-born cell types between weeks 8-16, the percentage of BRN3a+ retinal ganglion cells in the ganglion cell layer and ARR3+ cones in the outer nuclear layer were significantly higher in CRB1-mutated ROs compared to healthy ROs. However, the percentage of later-born OTX2+ bipolar cells in the inner nuclear layer was significantly lower in CRB1-mutated ROs compared to healthy ROs at weeks 20 and 28. Relative to healthy ROs following a pulse-chase, the percentage of total EdU+ cells located basally was higher and the percentage located apically were lower in CRB1-mutated ROs at week 12. Quantifying the mRNA expression, the expression of NOTCH effector HEY1 was significantly decreased in CRB1-mutated ROs compared to age-matched controls at week 8 and 40.

Conclusion: The change in cell population in CRB1-mutated ROs suggests that the retinal progenitor pool is depleted by early-born cells, resulting in a decreased number of late-born cells vital to retinal structure and function. As one of the first studies to examine the localization of proliferating cells in a human model, the basal localization suggests a defect in interkinetic nuclear migration, which may underlie the unique laminar disorganization characteristic of CRB1-associated disease. These results indicate that CRB1-associated disease causes developmental anomalies, potentially mediated by the NOTCH pathway, prior to degeneration in patients.

Jing Liu **VSRP Student**

Molecular Recognition and Selectivity in Phototransduction and Visual Disease

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Introduction: Visual perception mediated by precise phototransduction of visual information requires tightly regulated protein-protein interactions. In photoreceptor cells, the visual pigments rhodopsin (responsible for dim-light vision) and cone opsins (responsible for color vision) interact with different G protein subtypes to initiate distinct signaling cascades. However, because many G protein subtypes are expressed in the retina, molecular recognition between visual pigments and G proteins must be tightly regulated and fine-tuned to ensure precise activation of the appropriate visual response. Genetic perturbations that disrupt visual pigment-G protein interactions are strongly implicated in visual diseases, including congenital stationary night blindness and retinitis pigmentosa. Protein structures of visual pigments in complex with G proteins have shown that amino acids at the extreme C-terminus of the G□□G protein interacts extensively with visual pigments. Although many studies point towards genetic perturbations of the G□ C-terminus as a major source of visual disease, the pathogenic mechanisms that give rise to clinical phenotypes remain poorly understood.

Methods: To investigate this, I have engineered a novel cell-based system capable of measuring the selectivity between visual pigments and Ga subtypes via a fluorescent reporter. To validate our engineered system, I co-expressed the visual pigment rhodopsin against a panel of Ga proteins with each member containing distinct selectivity-determining residues from all known human Ga subtypes. Panel analysis using flow cytometry confirmed that rhodopsin couples selectively to its cognate Ga subtype in our system.

Results: To investigate how mutations perturb the coupling interactions between the Ga C-terminus and rhodopsin, I synthesized a variant library that encodes all possible combinations of amino acids (160,000 variants) at four selectivity-determining sites within the Ga C-terminus. I then expressed this library in our engineered system, revealing that ~2.4% of the library can couple to and be activated by rhodopsin. This finding suggests that although coupling selectivity is highly conserved, functionally permissive alternatives exist. To discriminate variants in the library that can couple to rhodopsin from those that cannot, I am now upscaling my assay to screen this library using fluorescence-activated cell sorting and next generation sequencing.

Conclusion: While most variants will undoubtedly be incapable of being activated by rhodopsin, the functionally permissive alternatives may represent asymptomatic variants that persist transiently or at low frequencies within human populations. The results from this work will yield deep insights into the molecular mechanisms underpinning coupling selectivity in the visual system. Ultimately, this will advance our understanding of retinal disease etiology, offering new avenues to address disease phenotypes caused by defective G protein coupling.

Andrew Mihalache **Medical student**

Risk of Retinal Detachment with GLP-1 Receptor Agonists and SGLT2 Inhibitors: A Population-Based Study

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Introduction: Given the widespread use of glucagon-like peptide-1 receptor agonists (GLP-1RAs) and sodium-glucose cotransporter-2 (SGLT2) inhibitors in the management of diabetes mellitus (DM), a more nuanced understanding of their long-term ocular safety is crucial for clinicians. This population-based, matched cohort study aimed to investigate the association between systemic exposure to GLP-1RAs and SGLT2 inhibitors with the risk of retinal detachment (RD).

Methods: This study utilized administrative health and demographic data from Ontario, Canada, as collected by the ICES. Adults aged >65 years with ≥12 months of follow-up between 2011 and 2022 were recruited. Two comparative analyses were conducted: one assessing the risk of new-onset RD in GLP-1RA users (>6 months) versus non-users and another assessing the risk in SGLT2 inhibitor users (>6 months) versus non-users. To balance patient sociodemographic characteristics and comorbidities between groups, 1:1 propensity score matching was applied. The risk of RD was evaluated using an adjusted Cox proportional hazards model, with hazard ratios (HRs) and 95% confidence intervals (CIs) reported. Subgroup analyses were conducted based on DM status, and sensitivity analyses stratified participants by medication exposure duration (≤1 year, 1-2 years, >2 years). Statistical analyses were performed using R.

Results: Data from 77,325 GLP-1RA users, 223,457 SGLT2 inhibitor users, and 300,782 non-user controls were analyzed. GLP-1RA exposure did not significantly impact the risk of RD in patients with DM (n=32/68,192, 0.05% vs. n=25/68,192, 0.04%; HR=1.43, 95%CI=0.85-2.41, p=0.18). However, in the sensitivity analysis, a significantly increased risk of RD was observed during the first year of exposure (HR=3.50, 95%CI=1.50-8.12, p<0.01). No elevated risk was identified in individuals without DM. Similarly, SGLT-2 inhibitor exposure did not significantly affect RD risk in patients with DM (n=119/191,272, 0.06% vs. n=103/191,272, 0.05%; HR=1.02, 95%CI=0.77-1.33, p=0.91). However, in individuals without DM, SGLT2 inhibitor use was associated with a significantly reduced risk of RD (n=6/32,185, 0.02% vs. n=21/32,185, 0.06%; HR=0.39, 95%CI=0.16-0.98, p=0.04). Sensitivity analyses indicated this protective effect was unrelated to the exposure duration.

Conclusion: The use of GLP-1RAs in patients with DM was associated with a significantly increased risk of RD within the first year of exposure. As the utilization of GLP-1RAs, particularly semaglutide, continues to rise, this finding underscores the need for heightened clinical vigilance. In contrast, SGLT2 inhibitor use did not significantly impact RD risk in patients with DM, but was associated with a reduced risk in individuals without DM. These findings offer reassurance regarding the ocular safety of SGLT2 inhibitors.

Zeena Kailani **Medical student**

Ocular Adverse Events Associated with Pegcetacoplan and Avacincaptad Pegol for Geographic Atrophy: A Population-Based Pharmacovigilance Study

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Introduction: Geographic atrophy (GA), an advanced form of age-related macular degeneration (AMD), is a leading cause of irreversible central vision loss in older adults. Pegcetacoplan and avacincaptad pegol, the first and only treatments for GA to be approved by the FDA, have demonstrated efficacy in slowing GA progression in early clinical trials and have represented a significant breakthrough in the management of this historically untreatable condition. However, their post-marketing ocular adverse event (AE) profiles remain poorly defined. This study evaluates real-world ocular AEs associated with these agents using data from the FDA Adverse Event Reporting System (FAERS).

Methods: Using OpenVigil 2.1 data mining software, we conducted a retrospective pharmacovigilance study of FAERS data from inception to September 2024. Reports in which pegcetacoplan or avacincaptad pegol were identified as primary suspect drugs were analyzed. Disproportionality analysis was performed using reporting odds ratios (RORs) to assess the association of these drugs with specific ocular AEs compared to all other drugs in the database.

Results: Our analysis identified that various ocular AEs were overreported for both pegcetacoplan and avacincaptad pegol, but a significantly broader spectrum of ocular AEs was associated with pegcetacoplan. A total of 652 and 63 patients with AEs secondary to pegcetacoplan and avacincaptad pegol, respectively, were identified. Ocular AEs disproportionately overreported for pegcetacoplan included anterior segment hemorrhage (ROR=1993.2), iris neovascularization (ROR=1470.1), hemorrhagic occlusive retinal vasculitis (ROR=5399.5), retinal occlusive vasculitis (ROR=2342.9), and bacterial endophthalmitis (ROR=1324.4). Avacincaptad pegol was associated with a more limited set of ocular AEs, including vitritis (ROR=621.2), vitreous floaters (ROR=265.1), optic ischemic neuropathy (ROR=410.5), and eye inflammation (ROR=130.0).

Conclusion: The findings of this study highlight important safety considerations for pegcetacoplan and avacincaptad pegol in the treatment of GA. The broader range of ocular AEs linked to pegcetacoplan may be partly attributable to its longer market presence, broader mechanism of action, and increased utilization. In contrast, avacincaptad pegol was associated with fewer reported AEs, though its shorter market presence may contribute to underreporting. These results underscore the need for careful monitoring and risk assessment when initiating treatment with either agent. Further post-marketing studies and long-term observational data are necessary to better define the comparative safety profiles of these therapies and optimize GA management strategies.

Isabela Martins Melo **Clinical Fellow**

Assessment of Re-detachment Based on Proliferative Vitreoretinopathy Findings on SS-OCT

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Introduction: Swept-source optical coherence tomography (SS-OCT) findings of proliferative vitreoretinopathy (PVR) may serve as valuable predictors of re-detachment in rhegmatogenous retinal detachment (RRD). This study aims to assess re-detachment rates in primary RRDs based on PVR features identified on SS-OCT.

Methods: This was a retrospective cohort study including consecutive primary RRDs presenting to St. Michael's Hospital from 2021-2023. Ultra-wide field fundus imaging was staged per the Retina Society 1991 PVR Classification, and corresponding SS-OCT scans were assessed for microstructural retinal changes. Patients were also categorized into: no OCT PVR, intra-retinal (IR) OCT PVR, and subretinal (SR) OCT PVR. To be included in the IR group, patients had to have thick high-amplitude outer retinal corrugations (ORCs) with photoreceptor-photoreceptor apposition and/or fused ORCs. To be included in the SR group, patients had to have subretinal material in the OCT. Re-detachments that did not have membrane peeling and/or retinectomy during the second surgery were not considered to be caused by postoperative PVR.

Results: 100 patients were included, of which 49% (49/100) had no signs of PVR or PVR A, 24% (24/100) had PVR B, and 27% (27/100) had PVR C, as per the Retina Society Classification. Overall, 64% (64/100) were male, with a mean age of 54.2 (±15.9) years old, and 72% (72/100) were phakic. The mean baseline logMAR visual acuity was 1.28 (±0.63), with a mean RRD extent of 6.1 (±2.1) clock hours. Regarding the primary surgical procedure, 75% (75/100) of patients underwent pneumatic retinopexy with a 68% (51/75) success rate, 8% (8/10) had pars plana vitrectomy (PPV) with 75% (6/8) success rate, 9% (9/100) had scleral buckle (SB) with 89% (8/9) success rate, 5% (5/100) had combined PPV/SB with 80% (4/5) success rate, and finally 3% (3/100) had laser retinopexy barricade, of which all remained stable. The primary reattachment rate (PARR) was 70% (70/100). From patients who failed to reattach after the first procedure (30/100), 37% (11/30) re-detached, with 63% (7/11) of the re-detachments due to post-operative PVR formation. Among those with PAR (70/100), 4% (3/70) re-detached, being only 25% (1/4) from post-operative PVR. Among patients who had outer retinal corrugations (ORCs) at baseline [63% (63/100)], those presenting with fused ORCs or photoreceptor-photoreceptor apposition [75% (27/63)] were significantly associated with re-detachment due to postoperative PVR (p=0.0006). The presence of baseline ORCs alone was not associated with PVR re-detachments (p=0.0917). Using a logistic regression model to predict re-detachment rates, fused ORCs remained significant (p=0.0461) when controlling for other covariates, such as primary reattachment, extent of detachment and baseline Retina Society PVR grade. When considering the OCT PVR categories, 54% (54/100) of patients had no OCT PVR changes, 17% (17/100) had SR OCT PVR, and 29% (29/100) had IR/PR OCT PVR. The presence of IR OCT PVR was associated with postoperative PVR re-detachment (p=0.00972). OCT PVR (IR or SR) was also associated with a lower overall primary reattachment rate [58% (27/46)] when compared to patients with no OCT PVR changes [83% (45/54)], p=0.00624. When creating a model to predict re-detachments with baseline RRD characteristics, including age, extent of detachment, baseline OCT PVR and Retina Society PVR grade, the model achieved an overall predictive accuracy for postoperative PVR re-detachments of 91% (AUC 0.91). A classification threshold of 0.86 yielded the best combination of sensitivity (0.91) and specificity (0.89).

Conclusion: Primary PVR can be assessed into different groups based on SS-OCT findings: no OCT PVR, IR OCT PVR, and SR OCT PVR. Thick, high-frequency, high-amplitude ORCs with photoreceptor-photoreceptor apposition within and between individual corrugations (fused ORCs) are the most characteristic component of the IR PVR OCT. Fused ORCs were shown to be associated with re-detachment due to post-operative PVR after adjusting for covariates. A PVR re-detachment prediction model using age, extent of detachment, baseline OCT PVR and Retina Society PVR grade achieved a predictive accuracy of 91%. We hypothesize that outer retinal photoreceptor apposition is an important stimulus for retinal gliosis and postoperative PVR formation. A refined staging system that includes baseline microstructural changes on OCT may be critical for the proper assessment of novel therapeutic agents for PVR.

Tina Felfeli **Resident**

The epidemiological burden and characteristics of uveitis cases identified in health administrative data: An Ontario population-based study over two decades.

Co-authors: Tina Felfeli, MD, PhD, Sherif El-Defrawy, MD, PhD, FRCSC, Liisa Jaakkimainen, MD, Jessica Widdifield, PhD, Efrem D Mandelcorn, MD, FRCSC.

Introduction: To identify individuals with uveitis using health administrative data in Ontario and support surveillance to analyze evolving trends in epidemiology and care.

Methods: This is a retrospective, population-based study using Ontario health administrative data from 2000 to 2021. A cohort of 200,386 eligible patients was drawn from Ontario's primary care electronic medical records, from which 1,020 individuals were selected for detailed chart review. Multiple case definitions were employed to assess the performance of administrative data for identifying uveitis cases. Annual age- and sex-standardized incidence and prevalence rates with 95% confidence intervals (CI) were determined using annual population denominators. Patient demographics, comorbidities, resource utilization, and temporal trends in incidence were analyzed. Furthermore, cases were classified as limited (≤3 months) or persistent (>3 months) uveitis.

Results: The age- and sex-standardized prevalence ranged from 1,998.3 per 100,000 (95% CI: 1,989.1-2,007.5) in 2000 to 2,761.2 per 100,000 (95% CI: 2,752.7-2,769.7) in 2021, representing a significant rise in the burden of uveitis over the past two decades. From 2000 to 2021, incidence rates declined, dropping from 184.4 per 100,000 (95% CI: 181.5-187.2) in 2000 to 109.2 per 100,000 (95% CI: 107.4-110.9) in 2021. The median age of identified uveitis was 55 years, with a higher prevalence of females (59.9%) and anterior uveitis (64%). Amongst the total of 289,031 limited and 41,482 persistent uveitis cases identified, 89-91% resided in urban areas. The incidence of uveitis in the 1-12 years old age group showed an upward trajectory in the limited cases, with 25.4 per 100,000 (95% CI: 23.2-27.8) in 2021. The comorbidity burden was moderate-high in 86% of persistent versus 16% of limited uveitis cases. Notably, persistent uveitis cases had substantially higher resource utilization, with 97% falling in the moderate-high resource utilization bands (RUB, ranging from 0 for no utilization to 5 for very high expected utilization), compared to limited uveitis cases where 39% were in the moderate-high RUB.

Conclusion: Administrative data case definitions offer a valid method for identifying uveitis cases for population-based epidemiology studies. Over the study period, incidence rates declined while prevalence rose, indicating an increasing burden of chronic uveitis. Persistent uveitis cases were associated with higher comorbidities and resource utilization. These findings emphasize the importance of ongoing efforts in uveitis diagnosis, and public health awareness to mitigate the impact of this eye condition on the population.

David Mikhail **Medical student**

Artificial Intelligence Diagnosis of Extraocular Movement Disorders from Clinical Videos

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Introduction: Recent advancements in multimodal artificial intelligence (AI) have included video analysis. In ophthalmology, one early application of this technology is to detect extraocular movement (EOM) disorders. This study is the first to evaluate the diagnostic performance of Gemini 2.0 in analyzing publicly available clinical videos of EOM disorders.

Methods: We retrospectively collected 107 YouTube videos of EOM disorders—including cranial nerve (CN) palsies, internuclear ophthalmoplegia (INO), supranuclear disorders, nystagmus, and ocular myasthenia gravis (MG), alongside 8 control videos demonstrating normal EOMs. Videos were trimmed to include only the relevant clinical examinations, and audio was removed to avoid diagnostic cues. Using a standardized zero-shot prompt, Gemini 2.0 analyzed each video via the Google AI Studio platform. The AI was evaluated based on its ability to provide the correct diagnosis, identify the affected eye, and recognize the specific movement limitation (if any). Descriptive statistics, Pearson correlations, and comparative analyses were used to assess performance.

Results: The AI correctly identified the primary diagnosis in 33 of 107 videos, yielding an overall diagnostic accuracy of 30.8%. Diagnostic performance varied by condition, with the highest accuracies observed in CN III palsy (72.7%), CN VI palsy (66.7%), INO (50%), ocular MG (20%), while normal EOMs were correctly classified in 87.5% of cases. In misclassified cases, the correct diagnosis appeared in the differential diagnosis in 14.9% of instances. Laterality was correctly identified in 27.3% of eligible cases overall—73.1% among correctly diagnosed cases versus 9.6% in misclassified ones. Similarly, movement limitations were accurately identified in 30.3% of eligible cases overall, with a marked increase to 88.5% accuracy in correctly diagnosed cases compared to 9.6% in misclassified cases. The mean processing time was 11.1 seconds per video, with similar durations for both correctly and incorrectly diagnosed cases. Significant correlations were observed between diagnostic accuracy and laterality identification ($R=0.63$, $p<0.001$), and between diagnostic accuracy and movement limitation identification ($R=0.75$, $p<0.001$).

Conclusion: Gemini 2.0 demonstrated variable performance in diagnosing EOM disorders from clinical videos, with higher accuracy in more common, easily discernible conditions. Notably, when the model accurately identified the affected eye and movement limitation, it was much more likely to yield the correct primary diagnosis. The observed correlations underscore the potential of AI-driven video analysis for clinical assessment of EOM disorders, though overall diagnostic accuracy remains low. Further refinement and standardization of AI protocols are needed to enhance the reliability of such objective diagnostic tools.

Reut Shor **Research Fellow**

Glucagon-Like Peptide-1 Receptor Agonists and Neovascular Age-Related Macular Degeneration: A Population-Based Study

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Introduction: Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are extensively used in treating type 2 diabetes mellitus (T2DM) and obesity, yet little is known about the long-term ocular effects of systemic prolonged exposure. This study aims to assess the risk of developing neovascular age-related macular degeneration (nAMD) associated with the use of GLP-1RA in patients with type 2 diabetes mellitus (T2DM).

Methods: This population-based, retrospective cohort study was conducted from January 2020 to November 2023, with a follow up period of 3 years. We utilized comprehensive administrative health and demographic data in Ontario, Canada collected by the ICES in the context of a universal public health care system. Inclusion criteria were patients aged 66 years or older with a diagnosis of T2DM and a minimum follow-up period of 12 months post-initial T2DM diagnosis. We excluded patients with incomplete OHIP or Ontario Drug Benefit data or patients exposed to a GLP-1RA for less than 6 months. Of 1,119,517 eligible patients, a 1:2 matched cohort of 139,002 patients was created, including 46,334 patients who were exposed to a GLP-1RA and 92,668 unexposed matched patients.

Results: Among 139,002 matched patients, the mean (SD) age was 66 (7) and 64,775 were females. There was a significantly higher incidence of nAMD among the exposed group compared to non-exposed (0.2% vs 0.1%, $p<0.001$). In crude and adjusted Cox proportional hazards models, there were greater hazard ratios of developing nAMD in those exposed to GLP-1RA (HR=2.11, 95% CI=1.58, 2.82 and HR=2.21, 95% CI=1.65, 2.96 respectively). A sensitivity analysis for duration of exposure to GLP-1RA revealed that longer durations of exposure were associated with higher risks.

Conclusion: The use of GLP-1RA among T2DM patients was associated with a significant higher risk for developing nAMD.

Brendan Tao **Medical student**

Canadian Provincial Cataract Surgery Wait Times 2008-2023: A Retrospective Study of Canadian Institute for Health Information Data

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Introduction: Surgical wait times in Canada are segmented into “wait time 1” (WT1; duration between primary care referral to initial surgical consultation, reflecting accessing to specialist care) and “wait time 2” (WT2; duration between surgery booking date and day of surgery, reflecting the capacity of hospital surgical resources). Herein, we compare provincial WT2 metrics for cataract surgery using the Canadian Institute for Health Information (CIHI) priority procedure database.

Methods: Province-stratified WT2 data (surgical volume; median wait time in days; 90th percentile wait time in days; and proportion of patients undergoing surgery within the pan-Canadian benchmark of 16 weeks) between 2008 and 2023 were acquired from the CIHI. Simple linear regression was used to determine the average year-over-year change in each WT2 metric. Interprovincial comparisons were conducted via the Kruskal-Wallis test, and where applicable, with post-hoc pairwise comparisons controlling for multiple comparisons.

Results: The cohort consisted of 2,322,451 cataract procedures in Canada from 2008 to 2023. Over this period, there was a best-fit increase in the national median and 90th percentile cataract surgery WT2 by 3.04 days/year ($p=0.03$; 57 days in 2010; max of 133.32 days in 2020; 66 days in 2023) and 11.26 days/year ($p<0.01$; 147 in 2010; max 309.52 days in 2020; 241 days in 2023), respectively. In the primary analysis between 2008-2023, six provinces (Manitoba, New Brunswick, Newfoundland and Labrador, Ontario, Prince Edward Island, and Quebec) experienced significant average annual increases to their 50th and 90th percentile WT2, alongside reductions in the proportion of patients meeting the benchmark period. In the inter-provincial analysis, Prince Edward Island and Manitoba had the greatest increase in median WT2 and fewer patients meeting the benchmark period compared to other provinces. Quebec had the lowest WT2 and a higher proportion of cataract surgeries within the benchmark period.

Conclusion: From a health systems perspective, between 2008 to 2023, there was a pattern of longer WT2 and higher proportion of missed patient benchmarks across Canada. In each province, these findings should be reconciled with local data to inform future strategies that optimize the regional delivery of cataract surgery services.

Dana Taghaddos **Medical student**

A Real-World, Population-Based Pharmacovigilance Analysis of Drugs Attributed to Blepharitis, Meibomian Gland Dysfunction, and Chalazion

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Introduction: Blepharitis, meibomian gland dysfunction (MGD), and chalazia are common disorders impacting quality of life. This population-based, pharmacovigilance study aims to identify systemic drugs disproportionately linked to these disorders.

Methods: The Food and Drug Administration Adverse Event Reporting System (FAERS) database (Q4 2003 to Q2 2024) was analyzed. Drugs with at least 10 primary suspect reports for blepharitis, MGD, or chalazion were included. Disproportionality analyses assessed drug-specific adverse event (AE) reporting against all other drugs in FAERS, using reporting odds ratios (RORs) and Bayesian neural networks for signal detection.

Results: 1,923 blepharitis reports, 202 MGD, and 290 chalazia reports were identified. Finasteride was associated with MGD (ROR=71.6, 95%CI=37.9-135.3), while bortezomib was associated with chalazion development (ROR=73.9, 95%CI=51.4-106.2). Dupilumab was associated with all three conditions (blepharitis: ROR=35.7, 95%CI=22.8-55.9; MGD: ROR=15.4, 95%CI=7.3-32.5; chalazion: ROR=12.6, 95%CI=5.6-28.5). Safety signals, predominantly associated with blepharitis, were also identified for isotretinoin, docetaxel, panitumumab, cetuximab, tretinoin, alendronate, erlotinib, zoledronate, daxibotulinumtoxinA, and infliximab.

Conclusion: This pharmacovigilance study identified significant associations between several systemic medications with reports of blepharitis, MGD, and chalazion. Systemic drugs, such as finasteride and bortezomib, were disproportionately reported for MGD and chalazion, respectively, while dupilumab was overreported for all three conditions. We hope clinicians consider these medication-related associations with cases of blepharitis, MGD, and chalazion. Additionally, the continued reporting of adverse events to the FAERS database by ophthalmologists is essential for expanding pharmacovigilance efforts. Future studies are needed to validate these findings.

Posters

Amir Afsharpour **Graduate Student** **Poster # 1**

Ferrochelatase Inhibition Dysregulates Multiple Metabolic Pathways in Human Retinal Endothelial Cells

Co-authors: Kamakshi Sishtla (BSc), Leslie Dan Faculty of Pharmacy, University of Toronto, Timothy W. Corson (PhD), Leslie Dan Faculty of Pharmacy, University of Toronto.

Introduction: Neovascular retinopathies are blinding eye diseases caused by aberrant blood vessel growth in the retina. Ferrochelatase (FECH) is the enzyme catalyzing the final step of heme synthesis. Our previous work identified FECH as interacting with an antiangiogenic compound and FECH knockdown blocked angiogenesis, indicating that FECH could be a potential target for neovascularization therapy. Additionally, prior studies demonstrated that glycolysis decreases with FECH inhibition, but the connection between heme synthesis and glycolysis remains poorly understood. Further investigation of these mechanisms will enhance our understanding of cellular pathways and aid in the development of new therapeutic targets for eye diseases associated with neovascularization.

Methods: Human Retinal Endothelial Cells (HRECs) were treated with FECH inhibitors (FECHi), including a novel drug-like inhibitor developed by our group. We screened glycolytic and de novo and salvage pyrimidine synthesis enzymes using qPCR, protein immunoblotting, and enzymatic assays. The impact of FECH inhibition on glycolysis rate and glycolytic reserve was assessed with the Seahorse XF assay (Agilent). Cellular respiration metabolites such as lactate, NAD, and NADH were analyzed with fluorescent assays. Finally, proteomic analysis was performed to identify dysregulated proteins following FECH inhibition.

Results: FECH inhibition decreased expression and activity of de novo pyrimidine synthesis enzymes, accompanied by increased expression of salvage pathway enzymes. FECH inhibition also reduced glycolysis enzyme levels and glycolytic reserve in HRECs. The NAD:NADH ratio increased with FECH inhibition, suggesting an attempt to enhance electron transport, although oxidative phosphorylation was suppressed. Further, proteomics data revealed upregulation of enzymes involved in serine synthesis, the Krebs cycle, and electron transport, indicating reduced glycolysis and a shunt to downstream cellular respiration pathways. Interestingly, lactate levels rose significantly shortly following inhibitor treatment, suggesting that lactate may play a role in the observed metabolic reprogramming.

Conclusion: FECH inhibition decreases de novo pyrimidine synthesis while increasing salvage pathway activity, ultimately leading to a reduction in overall pyrimidine synthesis due to HRECs' reliance on the de novo pathway. Additionally, FECH inhibition limits glycolysis but promotes downstream cellular respiration, including the Krebs cycle and electron transport, resembling the "reverse Warburg" effect. However, previous studies show that Complex IV is disrupted after FECH loss, ultimately inhibiting oxidative phosphorylation. Elevated lactate levels shortly following FECH inhibition suggest lactate's significance in this metabolic shift. These findings not only elucidate how FECH inhibition suppresses endothelial cell growth but also highlight metabolic targets that could be explored for treating proliferative retinopathies.

Layla Ahmed **Graduate Student** **Poster # 2**

Investigating Missing Heritability in Inherited Retinal Dystrophy

Co-authors: Rahma Osman, BSc, Department of Medicine, Queen's University, Genevieve Ah-Sen, Department of Biomedical Engineering, University of British Columbia. Erika Tavares, PhD, Genetics and Genomic Biology, The Hospital for Sick Children, Ajoy Vincent, MD, Institute of Medical Science, University of Toronto, Canada.

Introduction: Inherited Retinal Dystrophy (IRD) is a group of degenerative disorders causing vision loss. Around 300 genes are associated with IRDs, but 15-50% of cases remain "gene-elusive." This study aims to investigate missing heritability in "gene-elusive" cases.

Methods: Seven cases with presumed autosomal/X-linked recessive IRD & inconclusive/negative clinical panel tests underwent ocular exams and genome sequencing (GS). Variants were filtered using phenotype-driven panels, followed by whole genome filtering and prioritization using an in-lab pathogenicity prediction pipeline. Candidate variants were validated by segregation analysis and functional studies.

Results: Three children & four adults with IRDs were included. Diagnoses included Leber's congenital amaurosis (LCA), early onset retinal dystrophy (EORD), retinitis pigmentosa (RP), fundus albipunctatus, multifocal vitelliform dystrophy (MVD), and gyrate atrophy (GA). Candidate variants were identified in 6/7 cases. Case 2, a 14-month-old male with LCA, had 4 RPGRIP1 variants. Maternal variants included 1 pathogenic variant (c.1468-2A>G) & 2 variants of uncertain significance (VUS) (c.3100-229_3238+234dup, c.491-112G>A). One paternal VUS (c.906+26T>C) was identified. Functional validation of the paternal variant is being conducted. Case 3, an 11-year-old male with EORD had compound heterozygous variants in CRB1, 1 pathogenic (c.3415C>T/p.Q1139X) & 1 VUS (c.849-26A>G). Minigene confirmed the VUS to cause exon 4 skipping & a premature stop codon (p.[Arg284fs6*]). Case 4, a 33-year-old male with X-linked RP, had a VUS in RPGR (c.*78_*3782delins13). Functional validation is being conducted. Case 5, a 22-year-old female with MVD, had 3 VUSs in IMPG1 in trans; (c.563-174T>G, c.2045-7421C>T, c.1291+13335G>A). Functional validation is being conducted. Case 6, a 22-year-old female with RP, had compound heterozygous VUSs in HGSNAT (c.1634C>A/p.T545K, c.235-4486T>C). RT-PCR of patient fibroblast RNA confirmed the exonic variant to cause exon 18 skipping & premature stop codon (p.[Ser550Asnfs12*]). Intronic variant causes aberrant exonization & premature stop codon (p.(Cys78Aspfs16*)). Case 7, a 14-year-old female with GA, had compound heterozygous variants in OAT, 1 VUS (c.413C>T/p.P138L) and one duplication (c.1160-1284_901-82dup). RT-PCR of patient lymphoblast RNA confirmed the duplication to cause a frameshift & premature stop codon (p.(D387Gfs5*)).

Conclusion: This study underscores the value of whole-genome sequencing in resolving gene-elusive cases, as both non-coding variants and novel structural variations can contribute to IRDs. These findings highlight the importance of comprehensive genome analysis for accurate diagnosis.

Kristen Ashworth **VSRP Student** **Poster # 3**

Building the human in vitro phenotype of USH2A-associated retinitis pigmentosa: early defects and late-stage photoreceptor degeneration in human stem cell-derived retinal organoids

Co-authors: Cassandra D'Amata, MSc, Donald K. Johnson Eye Institute, Toronto Western Hospital, Jackson Zhang, BSc, Laboratory Medicine and Pathobiology, University of Toronto, Jessica Wang, BSc, Institute of Medical Science, University of Toronto, Carlos De la Cruz Herrera, PhD, Donald K. Johnson Eye Institute, Toronto Western Hospital, Brian Ballios, MD, PhD, Institute of Medical Science, University of Toronto.

Introduction: Mutations in the USH2A gene are the leading cause of autosomal recessive retinitis pigmentosa (RP), an incurable blinding eye disease. The objective of this project was to establish the early and late structural and molecular human USH2A phenotype with the use of patient-derived retinal organoids (ROs). We hypothesize that USH2A-ROs will manifest phenotypic differences upon onset of USH2A expression; and, at mature stages, have a pathogenic structural and molecular outer retinal phenotype compared to healthy ROs.

Methods: ROs were derived from USH2A-mutated, patient induced pluripotent stem cells (PSCs) and two healthy human PSC control lines. ROs were assessed at early (Wk6), mid (Wk16–20), and late (Wk30–42) stages. Changes in cellular organization and morphology (retinal cell-specific protein expression, photoreceptor outer segment (OS) formation) were evaluated throughout RO development by immunohistochemistry and electron microscopy (EM). RT-qPCR was used to analyze gene expression.

Results: USH2A expression begins between Wk16–20 of RO development; at this time, phenotypic differences between healthy and USH2A-ROs emerge. At Wk16, expression of pan-photoreceptor precursor marker RCVN is decreased in USH2A-ROs compared to healthy ROs. By Wk20, cell death gene Casp-3 is significantly upregulated in USH2A-ROs ($p=0.017$) and, structurally, outer nuclear layer thickness is significantly decreased ($p=0.002$) compared to healthy ROs. Between Wk30–42, USH2A-ROs show a distinct photoreceptor phenotype, including delayed brush border growth, limited photoreceptor OS formation (by transmission EM), and decreased photoreceptor cell surface density (by scanning EM) compared to healthy ROs. At Wk42, USH2A-ROs have significantly shorter brush border length ($p=0.004$) and decreased expression of mature photoreceptor markers Arr3 ($p=0.036$) and CRX ($p=0.035$) compared to healthy ROs.

Conclusion: USH2A-ROs show early reductions in retinal-specific protein and gene expression from Wk16–20, followed by pronounced abnormalities in photoreceptor growth, maturation, and OS formation at Wk30–42. These findings provide novel insights into the temporal progression of USH2A-RP and may help inform future therapies for this currently-incurable blinding eye disease.

Michael Balas **Resident** **Poster # 4**

Association between Intravitreal Anti-Vascular Endothelial Growth Factor Agents and Hypertension: A Meta-Analysis

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Introduction: Intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents are widely used for the treatment of retinal diseases such as age-related macular degeneration, diabetic macular edema, and retinal vein occlusion. While these agents provide significant visual benefits, concerns regarding systemic adverse events, particularly cardiovascular risks, have been raised. Hypertension is a notable systemic event that may be linked to VEGF inhibition, as VEGF plays a role in endothelial function and vascular homeostasis. However, the association between intravitreal anti-VEGF therapy and the risk of developing hypertension remains unclear. This meta-analysis aims to compare the risk of hypertension among patients receiving intravitreal anti-VEGF agents versus those receiving sham injections.

Methods: A systematic search was performed on Ovid MEDLINE, EMBASE, and the Cochrane Controlled Register of Trials from January 2005 to August 2023. Inclusion criteria included published randomized clinical trials (RCTs) reporting on cases of hypertension as an adverse event for standard dose intravitreal anti-VEGF agents. Using random-effects modelling, risk ratios (RR) and 95% confidence intervals (CI) were used to estimate the frequency of hypertension between patients who received anti-VEGF agents versus sham injections.

Results: 20 RCTs with 11,196 patients were included. There were 189/2873 (6.6%) new cases of hypertension in the ranibizumab 0.5mg group, 61/1448 (4.2%) in the bevacizumab 1.25mg group, 287/3450 (8.3%) in the aflibercept 2mg group, 32/412 (7.8%) in the brolucizumab 6mg group, 99/2063 (4.8%) in the faricimab 6mg group, and 73/950 (7.7%) new cases of hypertension in patients receiving sham injections. There was no significant difference in the risk of developing hypertension between any of the included anti-VEGF agents. Compared to sham injection, ranibizumab (RR=0.81, 95% CI [0.43 to 1.53], p=0.52) and aflibercept (RR=0.67, 95% CI [0.44 to 1.01], p=0.06) did not significantly increase the risk of developing hypertension.

Conclusion: This meta-analysis found no significant difference in the risk of hypertension between different intravitreal anti-VEGF agents or sham injections. These findings suggest that intravitreal anti-VEGF agents do not pose a significant risk of systemic hypertension, reinforcing their safety profile in patients requiring long-term treatment. These results provide reassurance to clinicians that the choice of anti-VEGF agent should be based on efficacy and patient-specific factors rather than concerns regarding hypertension risk.

Joshua Bierbrier **Medical Student** **Poster # 5**

Macular Neovascularization in Patients with Gyrate Atrophy

Co-authors: Yusuf Ahmed, MD, Department of Ophthalmology and Vision Sciences, UofT, Mario Ventresca, MD FRCSC, Niagara Health. Steve A. Arshinoff, MD FRCSC, Department of Ophthalmology and Vision Sciences, UofT, Keyvan Koushan, MD FRCSC.

Introduction: Gyrate Atrophy of the Choroid and Retina (GACR) is a rare metabolic disease caused by an autosomal recessive deficiency of ornithine aminotransferase. It is characterized by hyperornithinemia and progressive chorioretinal lesions. Macular neovascularization (MNV) is an uncommon complication of GACR, with limited reports in the literature. We present two new cases of MNV in patients with GACR.

Methods: We performed a retrospective case report detailing the presentation, examination, treatment, and outcomes of two patients managed by the same ophthalmologist with GACR that developed MNV. Relevant clinical data were extracted from their medical records. A literature review was conducted to identify other cases of MNV in patients with GACR.

Results: The first case is a 50-year-old high myope (-14D, axial length: 28.09mm) with GACR diagnosed in childhood that presented following a decrease in best-corrected visual acuity (BCVA, 20/60) in the left eye over two months (baseline:20/30; most recent serum ornithine:340µmol/L). MNV was confirmed with OCT-Angiography. Following three intravitreal anti-vascular endothelial growth factor injection (VEGF) injections, a treat and extend scheme was implemented. Two further injections were administered at 1.5- and two-month intervals. Subretinal fluid resolved, however a subretinal scar remained. Visual acuity returned to baseline. The second case is a 31-year-old moderate myope (-4.5D, no axial length measurement) with GACR, diagnosed two years prior, that presented with blurred vision (BCVA:20/400) and metamorphopsia in the left eye (baseline:20/30; most recent serum ornithine:811µmol/L). OCT-Angiography confirmed subfoveal MNV. Fluid resolved with two rounds of monthly intravitreal anti-VEGF injections. The patient then experienced four recurrences of MNV over three years. One to three monthly anti-VEGF injections were required to clear the subretinal fluid. After this period, serum ornithine levels dropped to a low of 218µmol/L. The most recent MNV recurrence, 1.5 years later, occurred as their ornithine levels rose to 450µmol/L. The subretinal fluid resolved after one anti-VEGF injection. Their resulting BCVA decreased by one line from baseline.

Conclusion: These reports build on the limited literature of this rare complication. Both patients presented with decreased vision, and OCT-Angiography features were similar to myopic MNV. The second case is the first reported instance of recurrent MNV in a GACR patient. The pathophysiology may involve a combination of pathologic myopia and progressive chorioretinal retinal atrophy due to GACR. Both patients responded well to intravitreal anti-VEGF injections and regained or approached their baseline BCVA. Prompt recognition and treatment of MNV in patients with GACR can improve visual acuity outcomes.

Suman Birdee **Graduate Student** **Poster # 6**

Ref-1 Inhibition as a Promising Strategy for Preventing Retinal Degeneration in Dry AMD

Co-authors: Yang Song, PhD, Departments of Pharmacology and Toxicology and Ophthalmology, Indiana University School of Medicine, Mark R. Kelley, PhD, Departments of Pharmacology and Toxicology and Ophthalmology, Indiana University School of Medicine. Timothy W. Corson, PhD, Leslie Dan Faculty of Pharmacy, University of Toronto.

Introduction: Age-related macular degeneration (AMD) is a major cause of vision loss in older adults, with dry AMD lacking effective treatment options. While recently approved complement-targeting therapies provide benefit for some patients, many do not respond adequately, highlighting the need for alternative approaches to address disease progression. Ref-1 is a key regulator of transcription factors involved in inflammation and angiogenesis. APX2009, a Ref-1 inhibitor, has demonstrated antiangiogenic properties and systemic delivery potential. However, its role in protecting against retinal degeneration in dry AMD remains unexplored. This study evaluates our novel inhibitor's ability to prevent retinal pigment epithelium (RPE) damage and mitigate sodium iodate-induced retinal degeneration.

Methods: iPSC-derived RPE and ARPE-19 cells were treated with 1 – 10 μM APX2009 before exposure to 1.5 – 3 mM sodium iodate, after which transepithelial electrical resistance (TEER) was assessed. In vivo, wild-type mice were given 30 mg/kg sodium iodate via i.p. injection, followed by treatment with 25 mg/kg APX2009 or vehicle i.p., b.i.d. for 3, 7, or 14 days. Retinal morphology was evaluated by fundoscopy, fluorescein angiography (FA), and optical coherence tomography (OCT), and function assessed by electroretinogram (ERG). Ex vivo analysis included immunostaining of retinal sections for markers of inflammation and oxidative stress.

Results: Ref-1 inhibition dose-dependently protected RPE barrier function from sodium iodate-induced decreases. In a 14-day sodium iodate mouse study, APX2009 treatment was associated with reduced fundus depigmentation, decreased FA hyperfluorescence, preservation of retinal thickness, and improvement of scotopic a- and b-wave responses compared to vehicle-treated controls. Preliminary immunostaining data indicated lower levels of the inflammatory marker NF-κB in APX2009 treated mice.

Conclusion: Sodium iodate-induced retinal degeneration models key pathological features of dry AMD, including RPE barrier disruption, retinal thinning, and functional decline. These phenotypes were improved through inhibiting Ref-1 via APX2009. To further understand the drivers of these phenotypic changes, molecular markers for inflammation were studied and APX2009 treatment was shown to decrease inflammation caused by oxidative stress. These findings highlight Ref-1 as a promising systemic therapeutic target for preventing retinal degeneration in dry AMD.

Laura Botler **Graduate Student** **Poster # 7**

Investigating material transfer in hPSCs and hPSC-derived neurons

Co-authors: Karun Singh, PhD, Laboratory Medicine and Pathobiology, University of Toronto, Valerie Wallace, PhD, Laboratory Medicine and Pathobiology, University of Toronto.

Introduction: Intercellular communication is an essential process by which cells exchange information regarding their environment, internal processes, and physiological needs. This communication can happen through the exchange of intracellular cargo between neighboring cells, a process called material transfer (MT). MT can happen through the release of extracellular vesicles or through tunneling nanotubes, and studies have shown that different types of intracellular cargo, including transcripts, proteins and organelles, can be transferred by MT between cells. MT has been previously reported in mouse photoreceptors, after photoreceptor transplantation into host retinas. Whether this process happens in human cells, however, is still unknown. This way, we hypothesize that MT is an important mode of interneuronal communication. Our aim is to characterize MT in cultures of hPSCs and hPSC-derived neurons.

Methods: We maintained co-cultures of hESCs and hPSC-derived neurons, after which cells were collected for analyses. The cell lines used express different cytoplasmic fluorescent proteins, and the co-localization of said proteins is indicative of MT.

Results: Preliminary IHC and flow cytometry data indicates that MT appears to happen in both ESCs and hPSC-derived neurons, though higher in the latter. Our data also shows that there is an increase in the proportion of cells that overgo MT the longer the co-cultures are maintained. Furthermore, MT was also seen in the 3D context of unguided neural organoids, but to a much smaller degree than what was seen in 2D neuronal cultures (5% in 3D vs. 20% in 2D after one-month co-cultures). Imaging of double positive cells indicate that transferred proteins aggregate inside acceptor cells, and co-localize with lysosomal markers.

Conclusion: Our study indicates that MT potentially happens in hESCs and hPSC-derived neurons, though the exact mechanism is still unknown. We will continue to examine this mechanism in 3D retinal and unguided neural cultures through flow cytometry and IHC, as well as focus on investigating the mechanism behind the MT observed in these models.

Natalie Chen **Medical Student** **Poster # 8**

Multimodal Imaging Findings of Multiple Evanescent White Dot Syndrome in COVID-19 Patients

Co-authors: Mark, Mandell, MD FRCSC, Department of Ophthalmology and Vision Sciences, University of Toronto, Parnian, Arjmand, MD MSc FRCSC, Mississauga Retina Institute.

Introduction: To describe the multimodal imaging findings of a rare case of multiple evanescent white dot syndrome (MEWDS) associated with COVID-19.

Methods: A case report was analyzed and described alongside COVID-19 associated MEWDS cases identified in the current literature.

Results: A healthy 20-year-old man was evaluated after a three-day history of blurry vision occurring two months after COVID-19 infection. Multimodal imaging revealed signs of typical MEWDS, with optical coherence tomography angiography (OCT-A) demonstrating homogenous reflectivity. Six additional cases were reported in the literature, displaying clinical symptoms and imaging consistent with typical MEWDS but demonstrating higher rates of incomplete visual recovery and treatment use.

Conclusion: COVID-19 associated MEWDS is a novel condition. This is the first known case of COVID-19 associated MEWDS with reported OCT-A findings in an otherwise healthy patient. Although posterior uveitis following COVID-19 infection is rare, clinicians should remain informed on the best practices for diagnosing and caring for patients with MEWDS.

Miguel Cruz Pimentel **Research Fellow** **Poster # 9**

In Vivo Assessment of Peripheral Vitreous with Ultra-Widefield Swept-Source Optical Coherence Tomography in Rhegmatogenous Retinal Detachment

Co-authors: Shiva Sabour, MD. Department of Ophthalmology & Vision Sciences. University of Toronto, Rajeev H. Muni, MD, MSc. Department of Ophthalmology & Vision Sciences. University of Toronto.

Introduction: To characterize the morphological features of the peripheral vitreous associated with retinal breaks in rhegmatogenous retinal detachment (RRD).

Methods: Prospective study conducted at St. Michael's Hospital in Toronto, Canada, with approval obtained from the Research Ethics Board. Patients provided informed consent for various therapeutic interventions, including pneumatic retinopexy (PnR), laser retinopexy, and in-office suprachoroidal viscopexy (SCVEXY). Patients were prospectively followed with ultra-widefield imaging and swept-source OCT (SS-OCT) (Optos Silverstone®; Optos, PLC; Dunfermline, UK). Volumetric and line SS-OCT scans were conducted using a 1050 nm wavelength, achieving an axial resolution of less than 7 microns and a transverse resolution of less than 20 microns. The volumetric scans encompassed a scan height range of 3.5 mm to 9 mm and a scan width range of 6.0 mm to 14 mm, while the line scans had widths of 6 mm, 14 mm, and 23 mm. These scans were performed at the location of the retinal break at baseline, day 1, day 2, week one, and various other time points. Assessment for posterior vitreous detachment (PVD) indicated that it was complete when a Weiss ring was observed during the fundus exam or on color photos and when a 14 and/or 23 mm line scan confirmed the separation of the posterior hyaloid from the area of Martegiani (AM). It was considered a partial PVD when only the macular region showed separation of the posterior hyaloid. The primary outcome of the study was to characterize the relationship of the vitreous with retinal breaks in rhegmatogenous retinal detachment (RRD) pre and post-therapeutic intervention. A static and dynamic assessment of the peripheral vitreous in the location of retinal tears was conducted.

Results: 42 patients were enrolled. 92.8% (39/42) presented with total PVD while 7.1% (3/42) had partial PVD. Cystoid retinal degeneration in the region of the retinal break was observed in 47.6% (20/42) of the patients. Among these, 50% (10/20) showed degeneration around the anterior edge of the tear, 10% (2/20) around the posterior edge, 25% (5/20) patients around both edges and 15% (3/20) at the flap of the tear. Recurrent detachment occurred in 9.5% (4/42) of cases. In the rest of the cohort, longitudinal assessment showed reattachment of the anterior and posterior edges of the peripheral tears and resolved cystoid degeneration after reattachment under the buoyant force of the gas bubble or the external force applied by SCVEXY. Retinopexy after laser application was observed to maintain adhesion along the posterior and anterior portions of retinal tears in 90.4% (38/42) of the cases at day 1,2, week one and other time points. Dynamic video assessment of vitreous traction and subretinal fluid in the area of the peripheral break was conducted in a subset of the patients without recurrent detachment 13.1% (5/38), highlighting vitreous adhesion at the anterior portion of the tear that was overcome by laser retinopexy treatment.

Conclusion: Vitreous traction must be overcome but tractional removal is not mandatory to achieve retinal reattachment. Overcoming vitreous traction can be achieved with laser retinopexy, pneumatic retinopexy, or SCVEXY.

Cassandra D'Amata **Research Associate** **Poster # 10**

Antisense oligonucleotide therapies induce pathogenic exon 13-skipping in a human retinal organoid model of USH2A-associated retinitis pigmentosa

Co-authors: Kristen Ashworth, Institute of Medical Science, University of Toronto, Brian G. Ballios, MD PhD, Donald K. Johnson Eye Institute, Toronto Western Hospital.

Introduction: Mutations in the USH2A gene are a common cause of retinitis pigmentosa (RP), an autosomal recessive blinding eye disease. USH2A encodes the protein Usherin, which localizes to the base of the connecting cilium in mature photoreceptor inner segments. Progressive death of rod and then cone photoreceptors in RP patients leads to irreversible vision loss. The molecular heterogeneity of USH2A pathogenic variants makes therapy development challenging, and there are no suitable animal models of this disease. Our lab has thus generated iPSC-derived retinal organoids (ROs), from an USH2A patient and a healthy donor, to create a human in vitro model of USH2A-associated RP. We hypothesize that we can use USH2A patient-derived ROs to investigate underlying mechanisms of disease and find new therapeutic targets.

Methods: Patient-derived (USH2A-ROs, compound het: c.2299delG;c.1256G>T) and healthy donor ROs were differentiated from iPSCs using an established 2D-3D organoid protocol. ROs were grown to mature (≥Week 34) timepoints and evaluated for photoreceptor markers by gene expression (RT-qPCR, RNA-seq) and protein (immunohistochemistry). Morphology and growth dynamics of the apical “brush border”, corresponding to mature photoreceptor inner and outer segments, were assessed across development by live phase contrast imaging and electron microscopy (EM). Gene rescue of USH2A-ROs was tested using QR-421a, an ASO currently in Phase 2b clinical trials. QR-421a induces in-frame exon 13-skipping in USH2A-transcripts, which is predicted to remove all exon 13 mutations (e.g., c.2299delG) while preserving protein structure.

Results: Usherin protein expression was confirmed in photoreceptors of mature (Week 34) healthy ROs, but absent in USH2A-ROs. Despite similar brush border growth, gene expression of mature photoreceptor markers (CRX, NRL, Rhodopsin) including USH2A were found to be lower in Week 34 USH2A-ROs compared to healthy controls. EM of Week 42 ROs revealed significantly reduced photoreceptor density in USH2A-ROs compared to healthy controls. Week 24 USH2A-ROs treated with QR-421a exhibited dose-dependent exon 13-skipping by RT-PCR, which was not observed in scrambled ASO and untreated controls. Gene and protein expression analysis of QR-421a ROs across development is currently underway.

Conclusion: Our patient-derived USH2A disease model exhibits photoreceptor defects in mature ROs compared to healthy controls. We also demonstrate the first use of antisense oligonucleotide (ASO) therapy directed against USH2A mutations in a human RO model of disease. USH2A-ROs are amenable to ASO treatment in vitro, and genetic analysis of treated ROs may help uncover new therapeutic strategies.

Fowad Daud **Medical Student** **Poster # 11**

Autologous Internal Limiting Membrane Transplant, Autologous Retinal Transplant, and Human Amniotic Membrane Plug for Complicated Macular Holes - A Systematic Review

Co-authors: Kashif Daud, MSc, Marko M. Popovic, MD, MPH, Department of Ophthalmology and Vision Sciences, University of Toronto. Navid Ghaderi, MD(C), Temerty Faculty of Medicine, University of Toronto, Peng Yan, MD, Department of Ophthalmology and Vision Sciences, University of Toronto.

Introduction: The standard of care for MH is vitrectomy with ILM peel, but in 5-10% of cases, this does not result in MH closure. There is no current consensus on best practices for complicated MH cases. The purpose of this study was to evaluate the efficacy and safety of autologous internal limiting membrane transplant (AILMT), autologous retinal transplant (ART), and human amniotic membrane (hAM) graft for large primary, refractory, or persistent macular hole (MH).

Methods: Ovid MEDLINE and EMBASE were searched in December 2024 for all articles comparing at least one of the three following procedures in patients with idiopathic MH; AILMT, ART, or hAM graft. The primary outcomes were final best-corrected visual acuity (BCVA), change in BCVA, and MH closure rate. Secondary outcomes included ellipsoid zone recovery and complications. Risk of bias was assessed using the Cochrane RoB 2 and ROBINS-I V2 tools. (PROSPERO registration number, CRD42023373988)

Results: Of the 8416 studies included in the search, 1 RCT and 27 non-randomized studies met all eligibility criteria. The total number of eyes for the AILMT, ART, and hAM groups were 136, 194, and 141, respectively. The mean final BCVA (logMAR) was 0.76 ± 0.29, 0.91 ± 0.20, and 0.79 ± 0.36 for AILMT, ART, and hAM respectively (Snellen equivalents 20/115, 20/163, and 20/123, respectively). The mean change in BCVA was 0.34 ± 0.31, 0.27 ± 0.19, and 0.64 ± 0.49 for AILMT, ART, and hAM respectively, resulting in a significant between-groups difference. The MH closure rates for AILMT, ART, and hAM were 94.1%, 90.2%, and 99.3%, respectively. The ART group had the highest rate of complications, with 5 cases of vitreoretinal hemorrhage, 3 cases of retinal detachment, and 9 cases of angiogenesis occurring.

Conclusion: The results suggest no significant difference between these three procedures for MH closure rate, but hAM grafts may lead to better improvement in BCVA. Severe complications were reported more often in the ART group than the other groups. Given that most studies were retrospective and non-comparative, future high-quality RCTs are warranted.

Sue Ellen Demian **Research Fellow** **Poster # 12**

Comparative Analysis of Intraocular Pressure Changes in Pneumatic Retinopexy versus Vitrectomy for the Treatment of Retinal Detachments

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Introduction: Two common methods of surgical repair for rhegmatogenous retinal detachment (RRD) include pneumatic retinopexy (PnR) and pars plana vitrectomy (PPV) each with its own advantages. However, both can significantly impact intraocular pressure (IOP), potentially influencing postoperative outcomes and long-term visual acuity. Understanding IOP changes with RRD is important for management.

Methods: This retrospective study included 1963 patients who underwent RRD repair at St. Michael's Hospital, Toronto, from January 2009 to December 2023. Patients treated with primary PnR or PPV for RRD were included. Patients who underwent PnR generally had a minimum of 0.6 cc of pure sulfur hexafluoride gas after an anterior chamber paracentesis with a repeat paracentesis if required after gas injection. IOP was assessed at day 1, week 1 and month 1 post-surgery. Visual outcomes and complications were also compared. Statistical analysis included paired t-tests and chi-square tests with significance set at $p < 0.05$.

Results: After excluding 32 patients with previous history of glaucoma, 338 patients with no IOP measurements, the final dataset with 1593 records was used for analysis. It contains 1539 patients who received one of the two procedures: PnR (n = 1057, 68.7%) or PPV (n = 482, 31.3%). Mean age of patients was 59.89 predominantely males (68.9%).The majority of eyes were phakic (57.2%), and the most common foveal status was "off" (63.1%). The average AC tap volume was 0.35 cc/ml and the average gas volume for the first bubble was 0.64 cc/mL IOP was assessed categorically with IOP≤25 considered normal and IOP>25 (IOP≥26) being high. Proportion of patients with high IOP values were compared between procedures at each time point. Patients in the PPV group had significantly higher rates of elevated IOP at each time point (day 1, week 1 and month 1). In the PnR group proportion of patients with elevated IOP was 3.7% at day 1 vs PPV 10.8% (45/416) $p<0.001$. At week 1:PnR was 3.3% (32/962) vs 6.4% (27/423) for PPV and 1.9%(18/962) vs 7.3% (32/436) for PPV at month 1

Conclusion: PPV is associated with greater risk of intraocular pressure rise at day 1, week 1 and month 1 following retinal detachment repair.

Angel Gao **Medical Student** **Poster # 13**

Patient-Reported Outcomes in Usher Syndrome: A Systematic Review

Co-authors: Tasha Miller, BSc, Temerty School of Medicine, University of Toronto, Brian G. Ballios MD, PhD, Department of Ophthalmology and Vision Sciences, University of Toronto, Donald K. Johnson Eye Institute, University Health Network.

Introduction: This study aims to systematically review patient-reported outcomes (PROs) in Usher Syndrome, a rare genetic disorder and leading cause of deaf-blindness, affecting 1 to 4 per 25,000 people globally. With no cure available, understanding PROs is crucial for improving patient care by addressing emotional well-being and functional needs to guide therapeutic interventions and support strategies.

Methods: A systematic literature search was conducted in MEDLINE, Embase, PsychInfo, CINAHL, Web of Science, and the Cochrane Library up to September 4, 2024, to identify studies on PROs in Usher Syndrome. Two independent reviewers extracted data and assessed risk of bias using ROBINS-I, Newcastle-Ottawa, and CASP tools. Quantitative data were summarized with descriptive statistics, and a narrative review was performed for qualitative data.

Results: A total of 27 studies (1,009 participants) were included, with a mean age of 47.0 years (range 6–84) and 52.4% female. Most participants had type 2 Usher Syndrome (74.1%), followed by type 1 (31.4%) and type 3 (6.8%). Of the studies, 18 were quantitative (66.7%) and 9 were qualitative (33.3%). Cochlear implants were the only intervention studied (4 studies, 14.8%). The Glasgow Benefit Inventory (GBI) was the most frequently used PRO measure (4 studies), followed by the Nijmegen Cochlear Implant Questionnaire (NCIQ), Usher Lifestyle Survey (ULS), and Short Form-12 Health Survey (SF-12) (each used in 2 studies). The weighted GBI score of 27.5 indicated moderate benefits, while a lower physical subdomain score (-7.3) highlighted ongoing physical limitations post-intervention. The NCIQ showed variability across domains, reflecting diverse experiences with cochlear implants. The ULS indicated that participants typically needed special equipment for information access and had some independence in communication tasks, but most required assistance with mobility, such as doctor visits. Notably, no studies addressed vision-related interventions like low vision therapy or assistive devices, and only one study used a vision-related PRO measure, the Michigan Retinal Degeneration Questionnaire. Qualitative studies emphasized the importance of psychological well-being, communication, mobility, social and family support, and coping strategies, with key themes including daily challenges, health-related quality of life, and the role of family dynamics in overall well-being.

Conclusion: Data on PROs in Usher Syndrome is limited, underscoring the need for standardized PRO measures. The lack of vision-related interventions highlights a significant gap in care. While cochlear implants offer moderate benefits, persistent challenges call for comprehensive, multidisciplinary approaches to improve quality of life. Future research should prioritize developing standardized PRO tools and exploring interventions targeting quality of life.

Angel Gao **Medical Student** **Poster # 14**

Techniques for the Use of Human Amniotic Membrane in Macular Hole Repair: A Scoping Review

Co-authors: Danielle Solish, BA MD, Department of Ophthalmology and Vision Sciences, University of Toronto, Nadine Cheffi, BSc, Faculty of Medicine, University of Ottawa. Tina Felfeli, MD PhD(c), Department of Ophthalmology and Vision Sciences, University of Toronto, Efrem Mandelcorn, MD FRCSC, Department of Ophthalmology and Vision Sciences, Toronto Western Hospital, University of Toronto.

Introduction: Macular holes (MHs) are full-thickness retinal defects that can lead to significant vision loss. Currently, the standard treatment involves pars plana vitrectomy (PPV), internal limiting membrane (ILM) peeling, and gas endotamponade. Human amniotic membranes (hAM) have recently been explored for MH repair due to their regenerative properties. This scoping review examines the technique and outcomes for hAM use in MH repair.

Methods: A scoping review was conducted following a literature search of three databases (MEDLINE, EMBASE, Web of Science) on August 23, 2023. Studies evaluating hAM for MH repair were included, while studies using non-human amniotic membranes or lacking outcome data were excluded. Research letters, commentaries, and review papers were also excluded.

Results: A total of 31 studies (401 eyes) on hAM use in MH repair were included. The mean participant age was 63 years (60% female). Idiopathic MHs were most common (58%), followed by myopic (29%) and retinal detachment-associated MHs (29%).
The most common source of hAM was from eye banks (7, 22.6) and private companies (5, 16.1%). Most hAMs were cut using punch biopsies to create 1-4 mm wide circles (17, 54.8%). All participants underwent PPV with ILM peeling prior to hAM placement, which was consistently positioned stroma-side down. Various insertion techniques were employed, including ILM forceps, ophthalmic viscosurgical devices, and manipulation under fluid or perfluorocarbon liquid. Macular hydrodissection (MHH) was performed in five studies to aid graft placement. Primary endotamponade agents included SF6 (67.7%), C3F8 (35.5%), and silicone oil (32.3%). The overall MH closure rate was 89%, with 29/31 studies reporting >50% closure. BCVA improved in 59% of eyes, with 23/31 studies showing >50% of patients experiencing visual gains. Fresh hAM had the highest closure rate (100%), while cryopreserved hAM achieved 92% closure. Trauma-related cases had a perfect closure rate (100%), followed by myopic MHs (98%) and idiopathic cases (84%). Retinal detachment-associated MHs had the highest visual improvement rate (84%), while idiopathic MHs showed the lowest (44%). MHH had better postoperative BCVA (0.60 vs 0.90 LogMAR), though the impact on closure rate was modest (98% vs 94%). The most common complication was graft dislocation (2.2%), with 4 cases requiring re-operation. No systemic or uveitic complications were reported.

Conclusion: hAM shows promise in MH repair, achieving high closure rates and BCVA improvement with minimal complications. Future studies should aim to standardize surgical techniques, compare different hAM preparation methods, and evaluate long-term efficacy.

Joseph Hanna **Resident** **Poster # 15**

Glycolytic flux controls retinal progenitor cell differentiation via regulating Wnt signaling

Co-authors: Yacine Touahri, PhD, Sunnybrook Research Institute, Biological Sciences, Toronto, ON, Canada, Luke David, Sunnybrook Research Institute, Biological Sciences, Toronto, ON, Canada, Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada, Edwin van Oosten, Sunnybrook Research Institute, Biological Sciences, Toronto, ON, Canada, Isabelle Aubert, PhD, Sunnybrook Research Institute, Biological Sciences, Toronto, ON, Canada, Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada.

Introduction/Methods: Metabolic pathways are remodeled in response to energy and other homeostatic demands and are dynamically regulated during embryonic development, suggestive of a role in guiding cellular differentiation. Here, we show that glycolytic flux is required and sufficient to bias multipotent retinal progenitor cells (RPCs) to acquire a rod photoreceptor fate in the murine retina. In an RPC-specific conditional knock-out of Phosphatase and tensin homolog (Pten-cKO) and in an RPC-specific conditional gain-of-function of dominant active PFKB3 (cytoPFKB3), glycolytic gene expression and activity are elevated, correlating with precocious rod photoreceptor differentiation and outer segment maturation. Conversely, glycolytic inhibition in retinal explants, achieved either with 2-deoxy-d-glucose, a competitive inhibitor of glucose metabolism, by lowering media pH, which disables PKM2, a rate-limiting enzyme, or by inhibiting lactate/H+ symporters, which lowers intracellular pH, suppresses RPC proliferation and photoreceptor differentiation. Mechanistically, we show that Wnt signaling, the top-upregulated pathway in Pten-cKO retinas, is a glycolysis-dependent pathway. Pharmacological and genetic perturbation of Wnt signaling using a Ctnnb1-cKO phenocopies glycolytic inhibition, suppressing RPC proliferation, photoreceptor differentiation and outer segment maturation. Thus, developmental rewiring of glycolytic flux modulates Wnt signaling to drive rod photoreceptor differentiation and maturation, an instructive role that may be exploited therapeutically for cell replacement strategies.

Results: Metabolic pathways are remodeled in response to energy and other homeostatic demands and are dynamically regulated during embryonic development, suggestive of a role in guiding cellular differentiation. Here, we show that glycolytic flux is required and sufficient to bias multipotent retinal progenitor cells (RPCs) to acquire a rod photoreceptor fate in the murine retina. In an RPC-specific conditional knock-out of Phosphatase and tensin homolog (Pten-cKO) and in an RPC-specific conditional gain-of-function of dominant active PFKB3 (cytoPFKB3), glycolytic gene expression and activity are elevated, correlating with precocious rod photoreceptor differentiation and outer segment maturation. Conversely, glycolytic inhibition in retinal explants, achieved either with 2-deoxy-d-glucose, a competitive inhibitor of glucose metabolism, by lowering media pH, which disables PKM2, a rate-limiting enzyme, or by inhibiting lactate/H+ symporters, which lowers intracellular pH, suppresses RPC proliferation and photoreceptor differentiation. Mechanistically, we show that Wnt signaling, the top-upregulated pathway in Pten-cKO retinas, is a glycolysis-dependent pathway. Pharmacological and genetic perturbation of Wnt signaling using a Ctnnb1-cKO phenocopies glycolytic inhibition, suppressing RPC proliferation, photoreceptor differentiation and outer segment maturation. Thus, developmental rewiring of glycolytic flux modulates Wnt signaling to drive rod photoreceptor differentiation and maturation, an instructive role that may be exploited therapeutically for cell replacement strategies.

Conclusion: Developmental rewiring of glycolytic flux modulates Wnt signaling to drive rod photoreceptor differentiation and maturation, an instructive role that may be exploited therapeutically for cell replacement strategies.

Patrick Xiang Ji **Medical Student** **Poster # 16**

Shift Work and the Risk of Retinal Disease – A Cross-Sectional Observational Study

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Introduction: Recent preclinical studies have demonstrated that circadian disruption induces retinal disease phenotypes resembling diabetic retinopathy (DR), independent of glucose homeostasis. The present study aims to translate these findings by investigating whether shift work, a known disruptor of circadian rhythms, increases the risk of DR.

Methods: This cross-sectional observational study recruited patients who presented to two community retina clinics with retinal diseases. The participants were asked to complete a questionnaire capturing basic demographic and health information, as well as sleep and circadian disruption metrics adapted from the Canadian Health Measures Survey (CHMS), National Health and Nutrition Examination Survey (NHANES), and Munich ChronoType Questionnaire. Shift work exposure was defined as answering the question “Which of the following describes your work hours (current or past)?” with “Rotating shifts” or “Night shifts only”. Retinal diagnoses and exam findings, including optical coherence tomography results, were documented by the attending physician in a separate questionnaire.

Results: Of the 326 patients meeting inclusion criteria, 300 provided details regarding work hours. A total of 62 patients reported shift work exposure (20.7%). The age distribution was similar between those with shiftwork exposure (mean 67.8 ± SE 3 years) and without (63.3 ± 1 years, p=0.15), with an even sex distribution (54% vs. 53% female, respectively). There were no significant differences in body mass index (mean 27.7 vs. 26.7; p=0.21), smoking status (each 28.6%), recent HbA1c (each 7.1%), prevalence of hypertension (60% vs 50.7%; p=0.31), or dyslipidemia (42.9% vs 36.4%; p=0.47). The most common presenting diagnoses were wet age-related macular degeneration (AMD) (n=68), DR (n=60), and retinal vein occlusion (RVO) (n=33).
Compared to the prevalence of shiftwork exposure in the general Canadian population, estimated at 12%, the prevalence among those with clinical presentations of primarily infectious, genetic, or mechanical etiology was similar at 12.6%. Rates were similar in AMD (13.6%), whereas shiftwork exposure was more prevalent among patients with RVO (21.2%, p=0.23) or DR (20%, p=0.22), with overall exposure rates of 18% (p=0.23).

Conclusion: Preliminary evidence suggests that circadian disruption from shift work exposure may be associated with an increased risk of retinal diseases with vascular and metabolic etiology. Future work will focus on case-control analyses comparing exposure in age-, sex-, and risk factor-matched cohorts presenting with cataracts or other retinal conditions to further elucidate this relationship.

Katherine Jung **Medical Student** **Poster # 17**

In Vivo Assessment of Cystoid Macular Edema in Rhegmatogenous Retinal Detachment Using Swept-Source OCT

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Introduction: To understand the development of intraretinal cystoid macular edema (CME) in the setting of rhegmatogenous retinal detachment (RRD) using swept-source optical coherence tomography (SS-OCT).

Methods: This prospective study included 201 eyes of patients with primary rhegmatogenous retinal detachment (RRD) who presented to St. Michael's Hospital in Toronto from 2020 to 2023. Participants underwent baseline assessments using swept-source optical coherence tomography (SS-OCT) with the PLEX® Elite 9000 (Carl Zeiss, Dublin, California, USA). The protocol included high-definition horizontal and 51-line raster scans to evaluate retinal morphology. SS-OCT images were analyzed for hydration-related features, such as photoreceptor thickening, cystoid changes in the Henle's fiber layer, and the presence of cysts in the inner nuclear layer. Other evaluations included assessing outer retinal corrugations, foveal status, sub-foveal fluid height, and baseline visual acuity. Data were analyzed using JASP (Version 0.19.1, JASP Team, 2024).

Results: A total of 201 patients were included in the study. 38/201 (18.9%) showed only photoreceptor (PR) thickening, 64/201 (31.8%) displayed evidence of Henle's fiber layer (HFL) cysts and 99/201 (49.3%) presented with inner nuclear layer (INL) cysts. The presence of outer retinal corrugations (ORCs), which serve as a marker for substantial outer retinal hydration, was associated with intraretinal cystoid changes. 19/38 (50.0%) cases without any cystoid edema had ORCs, compared to 54/64 (84.4%) among those with HFL cysts and 93/99 (93.9%) among those with INL involvement ($p < 0.001$). Additionally, cases with INL cysts were significantly more likely to exhibit a detached fovea than those just HFL cysts or no intraretinal cysts, with rates of foveal detachment being 9/38 (23.7%) for cases with no intraretinal cysts, 39/64 (60.9%) for cases with HFL cysts and 79/99 (79.8%) for cases with INL cysts. This association between foveal detachment and the progression of hydration sequences was statistically significant ($p < 0.001$).

Conclusion: The morphological sequence of events leading to cystoid changes in RRD starts in the outer retina and progresses toward the inner retina. Following outer retinal hydration, eyes with RRD tend to develop HFL cystoid changes followed by INL cystoid changes. Müller cell dysfunction may play a role in fluid accumulation in the INL in RRD. Future investigations into the integrity of the inner blood-retinal barrier, particularly in retinal detachment, will yield further insight regarding the pathophysiology of HFL and INL cystoid edema.

Hargun Kaur **Medical Student** **Poster # 18**

Intraocular Inflammation, Procedural Complications and Vision Loss following Brolucizumab Compared to Aflibercept: A Decision Analysis

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Introduction: Neovascular age-related macular degeneration (nAMD) affects nearly 200 million people worldwide, with intravitreal anti-vascular endothelial growth factor (anti-VEGF) therapies serving as the primary treatment strategy. This is a post-hoc complications decision analysis based on the double-masked, multicenter, randomized HAWK and HARRIER trials that aims to evaluate the risk of vision loss associated with brolucizumab compared to aflibercept.

Methods: Participants included patients with nAMD from 408 sites in North, Central, and South America, Europe, Asia, Australia and Japan who were randomized to receive either brolucizumab or aflibercept. The main outcome measurements were the risk of mild, moderate, or severe vision loss when compared to baseline. The probabilities of vision loss after one injection and after one year were calculated for different dosing regimens of these agents.

Results: Overall, 1088 treatment-naïve eyes with untreated nAMD were randomized to brolucizumab and 729 to aflibercept. Brolucizumab was associated with higher probabilities of ocular complications, including intraocular inflammation, endophthalmitis, retinal detachment, and vitreous hemorrhage compared to aflibercept. The probabilities of mild, moderate, and severe vision loss after 1 injection were 2.42%, 1.70%, and 0.43% for brolucizumab q8w, 3.39%, 2.38%, and 0.60% for brolucizumab q12w, and 2.45%, 1.58%, and 0.36% for aflibercept q8w, respectively. After one year, brolucizumab q8w and q12w dosing regimens were associated with a higher risk of severe vision loss (3.07 – 4.07%) compared to aflibercept q8w (2.81%) and brolucizumab q16w (2.57%), while the risk of mild and moderate vision loss was similar between brolucizumab (mild: 13.7 – 21.0%, moderate: 9.8 – 15.2%) and aflibercept (mild: 18.1%, moderate: 11.9%). Consistent conclusions were found in a re-analysis at 2 years of follow-up.

Conclusion: When considering the risk of severe vision loss at either 1 or 2 years of follow-up, brolucizumab would need to be dosed at a Q16W regimen to have a lower risk of SVL compared to aflibercept Q8W treatment. These results can assist clinicians in making informed treatment decisions for patients with nAMD.

Camille Lavoie **Graduate Student** **Poster # 19**

Interphotoreceptor Mitochondrial Exchange: Mechanisms and Implications for Cellular Signaling and Metabolism

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Introduction: Intercellular mitochondrial transfer is increasingly recognized as a mediator of cell-cell communication, influencing metabolic support, signaling, and cellular adaptation. Despite the significance of mitochondrial transfer, we do not fully understand how transfer is regulated, nor the dynamics of transferred mitochondria. We aim to study the mechanism of transfer in the context of photoreceptors, the light-sensitive cells of the retina, as they are widely recognized as cells with high energy demands. We hypothesize that mitochondria use Rhot1, an adaptor protein facilitating mitochondrial transport along microtubules, to position themselves in the developing retina. Additionally, we hypothesize that mitochondria require Rhot1 for transfer between photoreceptors via tunneling nanotubes.

Methods: To investigate mitochondrial trafficking and transfer in photoreceptors, we established a transgenic mouse line with expression of GFP+ mitochondria in rod photoreceptors (MitoGFP). We used static and live-cell imaging to track mitochondrial distribution and movement in differentiating photoreceptors in vitro and in vivo. Sparse lentiviral induction of MitoGFP in photoreceptors was performed to dissect interphotoreceptor transfer events. Transplantation of MitoGFP-tagged donor photoreceptors was employed to evaluate the roles of microtubule-associated proteins in mitochondrial exchange.

Results: Rhot1 knockdown significantly disrupted mitochondrial trafficking in photoreceptor neurites in vitro, resulting in shorter travel distances compared to controls. In vivo experiments employing sparse MitoGFP induction in rods show that prior to synaptogenesis, mitochondria were apical and then also localized at the synapse by postnatal day 14. During photoreceptor differentiation, we observed shorter processes containing MitoGFP being trafficked basally. Rhot1 expression was detected before observing moving mitochondria, suggesting its role in facilitating mitochondrial transport during this developmental stage. Using an established transplantation model with MitoGFP+ cells, we demonstrated interphotoreceptor transfer of MitoGFP. Donor photoreceptors with Rhot1 knockdown exhibited reduced cell survival in the graft, implying a role for mitochondrial transport for cell health.

Conclusion: Preliminary results indicate that mitochondria are initially apical in photoreceptors and are trafficked in an apical-basal direction to supply the synapse, with translocation becoming more intermittent at late stages in photoreceptor differentiation. This could indicate that the mitochondrial pool present at the synapse maintains itself once in position. Additionally, we demonstrated that Rhot1 knockdown reduces mitochondrial transport in neurites in vitro, and reduces survival of grafted photoreceptors in vivo. With our future work, we aim to characterize the role of Rhot1 in mitochondrial transport in situ, to uncover the functional consequences of mitochondrial transfer, and to elucidate the dynamics of mitochondria in photoreceptors.

Gareth David Mercer **Clinical Fellow** **Poster # 20**

Minimally-invasive suprachoroidal buckling using a novel injector: pre-clinical evaluation in human cadaver eyes

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Introduction: To demonstrate pre-clinical proof of concept for performing suprachoroidal buckle surgery using a novel injector in human ex vivo eyes and model the relationship between injection volume, injection location, and buckle morphology. The Everads Injector (Everads Therapy Ltd., Tel Aviv, Israel), currently under clinical investigation, utilizes a non-sharp tissue separator which, via tangential blunt dissection, opens a channel to the suprachoroidal space (SCS).

Methods: Fresh whole human eyes were obtained from the Eye Bank of Canada and experiments performed within 4 days of death (standard deviation, SD: 1). 0.1, 0.2 or 0.3mL of sodium hyaluronate 2.3% was injected into the SCS using the injector with its needle tip inserted 6, 10 or 15mm posterior to the limbus. Height, longitudinal basal diameter (LBD) and transverse basal diameter (TBD) of the resulting buckles were measured using B-scan ultrasound. The relationships between these parameters were estimated using linear regression.

Results: 27 eyes were injected (63% phakic). All but one resulted in successful suprachoroidal buckle creation (Fig. 1). One eye, injected 15mm from the limbus, showed subretinal penetration of viscoelastic and was excluded. On average, a 0.1mL injection resulted in a buckle with a heigh of 2.6mm (95% confidence interval, CI: 2.3-2.9), TBD of 9.0mm (95% CI: 8.3-9.7), and LBD of 8.2mm (95% CI: 7.6-8.8). There was a linear relationship between volume of viscoelastic injected and height, TBD and LBD of the SCS buckle (R2 0.70, 0.65 and 0.75, respectively; Fig. 2). Within the range of values tested, a 0.1mL increase in volume was associated with a height increase of 0.9mm (95% CI: 0.6-1.1), TBD increase of 1.8mm (95% CI: 1.3-2.4), and LBD increase of 2.0mm (95% CI: 1.5-2.5). Needle insertion distance did not significantly influence buckle height or diameter.

Conclusion: We demonstrated successful pre-clinical proof of concept for performing suprachoroidal buckling using the Everads Injector and provide a model of expected buckle dimensions across a range of clinically relevant injection volumes. Further research is needed to determine whether injection sites near the equator of the globe have higher risk of subretinal viscoelastic injection.

Andrew Mihalache **Medical Student** **Poster # 21**

Pneumatic Retinopexy for Chronic Rhegmatogenous Retinal Detachment

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Introduction: Rhegmatogenous retinal detachment (RRD) is a vision-threatening ophthalmic emergency that can lead to permanent vision loss if left untreated. Pneumatic retinopexy (PnR), a minimally invasive procedure, can be employed in the management of RRD, particularly in cases involving superior retinal breaks. However, its effectiveness in cases of chronic rhegmatogenous RRD, where complex pathophysiological factors such as proliferative vitreoretinopathy may compromise surgical success, remains poorly defined. This study aims to comprehensively evaluate the anatomical and functional outcomes of PnR as a primary intervention in patients with chronic RRD.

Methods: This retrospective study recruited consecutive patients diagnosed with chronic RRD, defined as RRD persisting for more than two weeks, who underwent treatment at St. Michael's Hospital/Unity Health Toronto, Canada, and the National Hospital Organization Tokyo Medical Center, Japan, between 2012 and 2024. Eligibility criteria required PnR to be the initial intervention for retinal reattachment. The primary outcome measure was the primary anatomic reattachment rate at 3, 6, and 12 months post-procedure. The secondary outcome was the change in best-corrected visual acuity (BCVA) over 12 months. Descriptive statistics were employed to summarize patient demographics and clinical outcomes.

Results: A total of 59 patients were included, of whom 69% (40 of 59) were male, and 56% (33 of 59) underwent treatment in the right eye. All patients received adjunctive laser retinopexy either preoperatively or postoperatively, while 59% (35 of 59) additionally underwent cryopexy. The primary anatomic reattachment rate was 92.5% at 3 months, 84.8% at 6 months, and 69.8% at 12 months. The mean BCVA improved significantly, increasing from 0.71 logMAR (Snellen equivalent: 20/108) at baseline to 0.32 logMAR (Snellen equivalent: 20/42) at 12 months, representing a mean improvement of 0.39 logMAR (Snellen equivalent: ~4 lines).

Conclusion: PnR with adjunctive laser retinopexy exhibits robust efficacy as a primary intervention for chronic RRD, delivering significant visual acuity improvements and achieving high rates of anatomical reattachment at 12 months. Despite the inherent complexities of chronic RRD, including an increased risk of redetachment due to proliferative vitreoretinopathy, PnR remains an important minimally invasive alternative to conventional surgical approaches. These findings highlight the potential of PnR to expand treatment options for patients with chronic RRD while optimizing outcomes. Further investigation into its long-term efficacy in this context could refine treatment strategies and improve prognostic models for complex RRDs.

David Mikhail **Medical Student** **Poster # 22**

Performance of artificial intelligence-based models for macular hole diagnosis: A systematic review and meta-analysis

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Introduction: Macular holes (MH) are full-thickness defects of the neurosensory retina at the fovea. Left untreated, MH can cause progressive central vision loss, significantly impacting daily activities and quality of life. Prompt detection and surgical closure can preserve or restore visual acuity, underscoring the need for high-precision diagnostic methods. Artificial intelligence (AI) has been used to detect MH in several exploratory studies, yet the overall performance and robustness of these algorithms remains unclear across varying study designs and populations. To clarify these uncertainties, we conducted a systematic review and meta-analysis quantifying the diagnostic performance of AI-based MH detection and reporting factors that influence model accuracy and applicability.

Methods: Comprehensive searches were conducted in Medline, Embase, Cochrane Library, Web of Science, and preprint databases from inception to August 2024. Included studies were ones that applied AI to MH diagnosis. Study quality and risk of bias were evaluated with the Quality Assessment for Diagnostic Accuracy Studies 2 (QUADAS-2) tool. A random-effects model was utilized to pool diagnostic accuracy, sensitivity, specificity, and the diagnostic odds ratio (DOR) across studies. Subgroup analyses were used to explore factors affecting model performance. The study protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO - CRD42024581264).

Results: Of 1321 screened articles, 22 met the inclusion criteria, and 13 were included in the meta-analysis. Low or unclear risk of bias was found in 90.9% of studies. The pooled diagnostic accuracy was 95.4% (95% CI: 86.4-98.6), sensitivity 88.8% (95% CI: 67.6-96.8), specificity 98.7% (95% CI: 97.0-99.4), and DOR 102.6 (95% CI: 28.1-375.0). Deep learning (DL) approaches demonstrated greater specificity (98.9% vs. 91.7%) and accuracy (97.0% vs. 84.2%) compared with ML. Binary classification exhibited higher sensitivity over multi-class models (95.4% vs. 83.5%), and models using color fundus photographs outperformed those using optical coherence tomography in sensitivity (95.8% vs. 82.1%) and accuracy (97.8% vs. 92.0). External validation was performed in only 22.7% of studies, yet these models had overall higher DOR scores (454.3 vs 67.8).

Conclusion: Our meta-analysis reports a high diagnostic performance in AI-based MH detection, with externally validated and DL models showing particularly strong results. However, given the significant heterogeneity across studies, standardized methodologies and comprehensive external testing are needed to enhance reproducibility. Advancing these efforts could enable AI to streamline MH screening, expedite referrals, and ultimately improve visual outcomes.

Sung Park **Undergraduate Student** **Poster # 23**

Retinoblastoma Research in Africa: A Scoping Review

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Introduction: Creating equity in childhood cancer care and control represents a global challenge. In Africa, given higher mortality and morbidity of retinoblastoma, addressing disparities in the research capacity is crucial to develop clinical guidelines for retinoblastoma management based on local evidence to achieve optimal outcomes. This review aims to identify the scope of retinoblastoma research conducted in Africa.

Methods: A systematic search of Embase, Medline, Scopus, and Web of Science databases identified peer-reviewed English-language publications on retinoblastoma in Africa, published between January 1, 2003, and August 14, 2024. Medical Subject Headings 'retinoblastoma', 'Africa', and individual African country names and regions were the search terms while 'childhood eye cancer', 'childhood eye tumor', and 'developing countries' were the free-text terms. Articles were included if they were peer-reviewed original research articles on retinoblastoma and conducted in any African country or region. Studies were excluded if retinoblastoma was not the primary focus or if Africa was not the main study location. Data collected included journal information, author affiliations, study type, site, and summary. A narrative synthesis was used to summarize the findings. Medical Subject Headings 'retinoblastoma', 'Africa', and individual African country names and regions were the search terms while 'childhood eye cancer', 'childhood eye tumor', and 'developing countries' were the free-text terms.

Results: The database search retrieved 1413 citations, of which 98 were non-English. After de-duplication, title and abstract screening, and full text screening, 89 studies were included for data abstraction and analysis (69 from the database search and 20 from other methods). These studies represented 20 of 54 African countries (~37%). Of the 89 articles, 51 (57.3%) were authored solely by African researchers. The articles were published in 59 journals, with Journal Citation Report data available for 27. The median Journal Impact Factor (JIF) was 1.95, with an average of 2.2.

Conclusion: Published retinoblastoma research from Africa was mainly descriptive, with no secondary research and few experimental studies. Conduction of applied basic, clinical experimental and implementation research was usually associated with authors' international affiliation. The results of this study highlight the need for local capacity building and further multidisciplinary collaboration on both national and international levels to improve the detrimental outcome of retinoblastoma in Africa.

Aljeena Rahat Qureshi **Medical Student** **Poster # 24**

Realistic fundus photograph generation for improving automated disease classification

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Introduction: Deep learning methods for retinal disease detection are often limited by the scarcity and imbalance of high-quality imaging data. Denoising diffusion probabilistic models (DDPMs) have emerged as a promising alternative to traditional generative adversarial networks. This study aims to investigate whether denoising diffusion probabilistic models (DDPMs) could generate realistic retinal images, and if they could be used to improve the performance of a deep convolutional neural network (CNN) ensemble for multiple retinal disease classification, which was previously shown to outperform human experts

Methods: We trained DDPMs to generate retinal fundus images representing diabetic retinopathy, age-related macular degeneration, glaucoma or normal eyes. Eight board-certified ophthalmologists evaluated 96 test images to assess the realism of generated images and classified them based on disease labels. Subsequently, between 100 and 1000 generated images were employed to augment training of deep convolutional ensembles for classifying retinal disease. We measured the accuracy of ophthalmologists in correctly identifying real and generated images. We also measured the classification accuracy, F-score and area under the receiver operating curve of a trained CNN in classifying retinal diseases from a test set of 100 fundus images.

Results: Ophthalmologists exhibited a mean accuracy of 61.1% (range: 51.0%–68.8%) in differentiating real and generated images. Augmenting the training set with 238 generated images in the smallest class statistically significantly improved the F-score and accuracy by 5.3% and 5.8%, respectively ($p<0.01$) in a retinal disease classification task, compared with a baseline model trained only with real images

Conclusion: Latent diffusion models generated highly realistic retinal images, as validated by human experts. Adding generated images to the training set improved performance of a CNN ensemble without requiring additional real patient data.

Aishwarya Rajesh Krishnan **Medical Student** **Poster # 25**

Macronutrients and Age-Related Macular Degeneration: A Population-Based Analysis

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Introduction: Age-related macular degeneration (AMD) is the leading cause of blindness in elderly individuals, with its global prevalence steadily increasing. Age-Related Eye Disease Study 2 (AREDS2) vitamins have been well-established in preventing or delaying the onset of late AMD in mild to moderate cases, highlighting dietary modifications as an appealing and accessible intervention. Despite the associations reported between various micronutrients and AMD, the impact of macronutrient intake on AMD remains unclear. This national, population-based study investigates the association between dietary influences of macronutrients and the incidence of AMD.

Methods: The data for this study is derived from the 2007-2008 National Health and Nutrition Examination Survey (NHANES). The primary outcome assessed the association between macronutrient intake over a 24-hour and 30-day period and AMD incidence among participants aged 50 years and older. The secondary outcome investigated the association between macronutrients and retinal imaging biomarkers associated with AMD. The secondary outcome examined the association between macronutrient intake and retinal imaging biomarkers of AMD. Statistical analyses included univariable and multivariable linear regressions, incorporating complex sample weighting to estimate population-level effects.

Results: Of 2,390 participants included in the primary analysis, 229 (8.6%) had AMD. Univariable analysis of 24-hour dietary data showed that protein intake was associated with lower odds of AMD ($p<0.001$). Multivariable analysis revealed that polyunsaturated eicosatetraenoic acid intake was associated with reduced odds of AMD ($p=0.032$), while dietary fibre intake was associated to increased odds of exudative AMD ($p=0.003$). Secondary analysis showed that polyunsaturated docosahexaenoic acid ($p=0.029$) was associated with higher odds of hard drusen, whereas monounsaturated docosenoic acid ($p=0.038$), polyunsaturated eicosapentaenoic acid ($p=0.022$), and polyunsaturated docosahexaenoic acid ($p=0.024$) were associated with lower odds of large drusen. Saturated butanoic acid ($p=0.05$) and saturated hexanoic acid ($p=0.024$) were associated to large drusen formation. Additionally, fibre intake ($p=0.030$), carbohydrate intake ($p=0.042$), and total sugars ($p=0.047$) were associated with increased retinal pigment abnormalities.

Conclusion: Protective associations for AMD were observed with protein intake and specific fatty acids, such as polyunsaturated eicosatetraenoic acid, while other fatty acids, such as polyunsaturated docosahexaenoic acid, were associated with an increased AMD risk. The association between dietary fibre and exudative AMD is novel, highlighting the need for further research into macronutrient influences on AMD. These results underscore the importance of tailored dietary interventions in the prevention and management of AMD, with future studies needed to explore long-term effects.

Saba Samet **Resident** **Poster # 26**

Predictors of Primary Anatomic Reattachment with Pneumatic Retinopexy for Rhegmatogenous Retinal Detachment

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Introduction: Pneumatic retinopexy (PnR) is a minimally invasive procedure that offers a high-integrity retinal reattachment associated with superior functional outcomes compared to pars plana vitrectomy for rhegmatogenous retinal detachment (RRD). Despite these advantages, a significantly lower primary anatomic reattachment rate (PARR) is the rationale used by many surgeons to avoid PnR. Understanding the factors associated with primary anatomic reattachment (PAR) following pneumatic retinopexy for RRD is critical for optimizing patient selection and improving surgical outcomes. Identifying key predictors can lead to more personalized treatment strategies, better patient counselling, and improved overall visual and anatomical outcomes.

Methods: This retrospective study includes patients with primary RRD at St. Michael's Hospital, Toronto, Canada from November 2009 to September 2017 who underwent PnR with a minimum of 3 months of follow-up. The primary objective was to assess predictors of PAR at 3 months post-operatively.

Results: Five hundred fifty-four patients were included. Mean age was 59.7 (SD 11.9) years, with 70% (388/554) female and 60.5% (335/554) phakic. Regarding RRD characteristics, 56.3 % (312/554) were fovea-off RRD and mean extent of detachment was 4.9 (SD 2.4) clock hours. The proportion of males was 67.5% (277/410) in the PAR group vs 77.1% (111/144) in the failure group, p=0.03. When comparing groups based on lens status, the proportion of pseudophakic patients was 35.2% (140/398) in the PAR group and 45.3% (64/141) in the failure group, p=0.03. 54.9% (224/408) of patients were fovea-off in the PAR group vs 59.7% (86/144) in the failure group, p=0.3. The mean extent of RRD was 4.9 (SD 2.4) clock hours in the PAR group vs 5.6 (SD 2.7) clock hours in the failure group, p=0.01. Cryotherapy was used in 18.6% (76/407) of PAR cases vs 29.1% (41/141) in failure cases, p=0.009. 75.1% (308/410) of patients in the PAR group met PIVOT trial (Hillier et al) criteria vs 55.5% (80/144) in the failure group, p<0.001. PARR among patients meeting PIVOT criteria was 79.7% (308/388) vs 61.4% (102/166) in those with extended criteria. Secondary analysis within cases meeting PIVOT criteria found PAR of 79.8% (258/323) in patients with breaks above 9 and 3 vs 76.9% (50/65) in those with inferior breaks, p=0.4. Multivariable regression analysis identified RD extent and PIVOT criteria as the only statistically significant predictors of PAR (both p<0.001), with β=0.8 and 0.2, respectively.

Conclusion: Meeting PIVOT trial criteria and extent of RRD are important predictors of primary reattachment following pneumatic retinopexy for primary RRD.

Fooladi Seyedeh Sara **Graduate Student** **Poster # 27**

Harnessing the Potential of Mammalian Retinal Müller glia to Regenerate Cone Photoreceptors

Co-authors: Marek Pacal, PhD, Lunenfeld Tanenbaum Research Institute, Mt Sinai Hospital, Rod, Bremner, PhD, Laboratory Medicine and Pathobiology (LMP) , University of Toronto.

Introduction: Cone photoreceptors are responsible for visual acuity and colour vision. Their loss leads to blindness in various diseases including retinitis pigmentosa (RP). Zebrafish can regenerate their entire retina upon injury. This phenomenon happens through the dedifferentiation of Muller glia (MG) into a progenitor-like state, followed by division and subsequent differentiation, replacing the damaged cells. Mammalian MG have lost this regenerative ability and, despite extensive work, no study has ever reported their successful differentiation into mature cones. This project aims to harness the potential of mammalian retinal MG to regenerate cone photoreceptors.

MYCN is an oncoprotein best known for its ability to promote division. This protein is expressed in post-mitotic human cone precursors but is down-regulated in adult cones. The function of MYCN in cone precursors is still unknown. We wondered whether it may influence cone fate. In unpublished work, we discovered that overexpression of MYCN induces cone precursors in postnatal murine retinal progenitors. Indeed, scRNAseq analysis confirms that MYCN biases murine post-natal progenitors towards this lineage. Since the transcriptome of progenitors and MG is similar, a similar response can be anticipated in MG. (Blackshaw,2004) Therefore, we hypothesize that the transient expression of MYCN can initially facilitate MG differentiation into cone precursors, facilitating their subsequent maturation into cones.

Methods: To investigate the effects of MYCN overexpression in inducing cone lineage we use GlastCreER; Sun1-GFP mice where Tamoxifen administration leads to activation of Cre in MG. At birth, these mice are electroporated with a Cre-dependent plasmid containing MYCN. In MG, activated Cre removes the stop cassette, inducing permanent expression of MYCN from the electroporated plasmid and a green-fluorescent reporter from the Sun1-GFP transgene in the mice.

Results: Early results from collaboration with the Cayouette lab (IRCM, Montreal), suggest that MYCN can reprogram adult MG towards the cone lineage.

Conclusion: I will present our results tracking the effect of MYCN expression in post-natal murine retinal progenitors and adult MG on lineage transformation.

Sohat Sharma **Medical Student** **Poster # 28**

Comparison of Safety and Efficacy Regarding High Dose Aflibercept and Faricimab for Diabetic Macular Edema and Neovascular-Age-Related Macular Degeneration: A Systematic Review and Network Meta-Analysis

Co-authors: Andrew Mihalache, BSc, Department of Medicine, University of Toronto, Natasha Verhoeff, BSc, Department of Medicine, University of Toronto. Fahad Rasool Butt, BSc, Department of Medicine, Western University, Brendan Tao, BHSc, Department of Medicine, UBC, Marko M Popovic, MD MPH, Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Peter J Kertes, MD CM, Department of Ophthalmology and Vision Sciences, University of Toronto, Rajeev Muni, Department of Ophthalmology and Vision Sciences, University of Toronto.

Introduction: We performed a systematic review and network meta-analysis (NMA) to compare the functional outcomes (BCVA), anatomical outcomes (retinal thickness [RT]), and serious ocular adverse events (SAE) between high dose aflibercept and faricimab for the treatment of neovascular age-related macular degeneration (nAMD) and diabetic macular edema (DME).

Methods: A comprehensive search of MEDLINE and EMBASE was conducted of all studies from inception until October 2024. Eligible publications included randomized controlled trials that evaluated high dose aflibercept 8 mg or faricimab 6 mg. Aflibercept 2 mg Q8W was the reference treatment. Outcomes included BCVA, RT, and serious OAEs. A Bayesian network meta-analysis was performed to indirectly compare high dose aflibercept and faricimab using a random effects model.

Results: The search identified 10987 studies. Of these, 57 studies underwent full-text review, and 5 studies were included in the network meta-analysis. Our NMA indicated that 8 mg aflibercept Q12W had a BCVA WMD of -0.31 (95% CI=-1.71 to 1.08) and 8 mg aflibercept Q16W had a BCVA WMD of -1.30(95% CI=-2.73 to 0.13), while 6 mg faricimab had a BCVA WMD of -0.05(95% CI=-1.43 to 1.34), 6 mg faricimab Q16W had a BCVA WMD of 0.35(95% -0.90 to 1.60), and 6 mg faricimab Q8W had a WMD of 0.34(95% -1.05 to 1.72), all of which were non-significantly different in reference to 2 mg aflibercept. The functional visual outcomes were non-significantly different between high dose aflibercept and faricimab. Our NMA also indicated that 8 mg aflibercept Q12W had a mean reduction of 10.81(95% -0.20 to 21.83 um), 8 mg aflibercept Q16W had a mean reduction of 5.70(95% CI=-5.64 to 17.05 um), and 8 mg aflibercept Q8W had a mean reduction of 22.20(-6.49 to 50.89 um) in RT, while 6 mg faricimab had a mean reduction in RT of 9.81(95% 0.64-18.98 um), 6 mg faricimab Q16W had a mean reduction in RT of 7.40(-2.72-17.52 um), and 6 mg faricimab Q8W had mean reduction in RT of 18.41(95% CI=9.18-27.64 um), all in reference to 2 mg aflibercept. These differences were non-significant between high dose aflibercept and faricimab. The pooled analysis for serious OAEs showed that 8 mg aflibercept Q12W had a risk ratio of 2.44(95% CI=0.65-9.21), 8 mg aflibercept Q16W had risk ratio of 2.23(95% CI=0.49-10.05) while faricimab 6 mg personalized treatment interval had a risk ratio of 0.95(95% CI=0.49-10.05), 6 mg faricimab Q16W had a risk ratio of 0.61(95% CI=0.44-0.86), and 6 mg faricimab Q8W had a risk ratio of 1.10(95% CI=0.83-1.46), all of which were non-significantly different compared to 2 mg aflibercept Q8W.

Conclusion: Our results indicate that the safety and efficacy of high dose aflibercept and faricimab are relatively similar based on indirect comparisons derived from clinical trial data. Both drugs and their respective treatment regimens represent viable strategies to reduce treatment burden in patients who have diabetic macular edema or neovascular age-related macular degeneration.

Dana Taghaddos **Medical Student** **Poster # 29**

Artificial Intelligence for Screening, Diagnosis, and Treatment of Central Serous Chorioretinopathy: A Systematic Review

Co-authors: Andrew Mihalache MD(C), Temerty Faculty of Medicine, University of Toronto, Ryan Huang MSc MD(C), Temerty Faculty of Medicine, University of Toronto. Marko Popovic MD MPH FRCSC, Department of Ophthalmology and Vision Sciences, University of Toronto, Rajeev Muni MD FRCSC, Department of Ophthalmology and Vision Sciences, University of Toronto.

Introduction: This systematic review aims to evaluate the performance of artificial intelligence (AI) algorithms in the screening, diagnosis, segmentation, and treatment of central serous chorioretinopathy (CSR).

Methods: A literature search was conducted using Ovid MEDLINE, Embase, and the Cochrane Central from January 2005 to December 2024. Peer-reviewed studies reporting on at least 100 eyes with CSR and evaluating AI algorithms for CSR screening, diagnosis or treatment were included. The quality of included studies was appraised using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool.

Results: In this review, 9339 studies were screened, and 23 studies analyzing 6469 eyes with CSR were included. Across 14 studies reporting on AI algorithms for the diagnosis of CSR, the pooled mean sensitivity, specificity and accuracy of the AI models was 95.03%, 97.80%, and 93.24%, respectively. Across four studies reporting on AI algorithms for the screening of CSR, the pooled mean sensitivity was 96.02%, specificity was 98.85%, and accuracy was 98.56%. Three studies reported AI for segmentation of subretinal fluid in SRF. The accuracy was reported in one study, with a value of 98.44%, and the sensitivity and specificity were not reported. Two studies reported on AI algorithms for predicting treatment responses in eyes with CSR, which achieved a mean sensitivity of 100%, specificity of 81.32%, and accuracy of 78%. As per the QUADAS-2 tool, the overall quality of evidence from included studies ranged from low risk to high risk.

Conclusion: AI algorithms demonstrated high performance in CSR diagnosis and screening, whereas algorithms for predicting treatment responses in this setting were less accurate. Once performance metrics are optimized, AI integration into clinical settings could improve diagnostic efficiency and patient care for CSR.

Brendan Tao **Medical Student** **Poster # 30**

Face Masking and Risk of Post-Intravitreal Injection Endophthalmitis: A Network Meta-Analysis of 26 Million Injections

Co-authors: Peter J. Kertes MD, Department of Ophthalmology & Vision Sciences, University of Toronto, David T. Wong, MD, Department of Ophthalmology & Vision Sciences, University of Toronto. Radha P. Kohly, MD, PhD, Department of Ophthalmology & Vision Sciences, University of Toronto, Rajeev Muni, MD, MSc, Department of Ophthalmology & Vision Sciences, University of Toronto.

Introduction: Though mask mandates are lifted, ophthalmologists may question whether continued investment into face masks will influence their post-intravitreal injection endophthalmitis (PIE) rate. We sought to compare face masking protocols for PIE prophylaxis.

Methods: We included comparative studies of PIE incidence by masking policy (i.e. standard care [no restrictions], no-talking, physician masking, or universal masking [patient and physician]). A frequentist network meta-analysis (Mantel-Haenszel method with fixed-effects) synthesized direct and indirect evidence. Subgroup analysis excluded studies that systematically introduced new prophylactic techniques (e.g., prefilled syringes) during the observation period. The ROBINS-I and GRADE tools evaluated risk of bias and evidence certainty.

Results: We analyzed 17 studies (2,595,219 injections, 830 events; 0.032%). For the any PIE outcome (17 studies; 2,595,219 injections), compared with standard care, PIE incidence was significantly lower with no-talking (OR: 0.56, 95%CI [0.39, 0.82], I2: 0%) and physician masking (OR: 0.72, 95%CI [0.53, 0.99], I2: 0%) policies, which remained consistent in the subgroup analysis. Although PIE rates between standard care and universal masking did not differ in the main analysis (OR: 0.83, 95%CI [0.67, 1.02]), subgroup analysis revealed a significantly lower rate of any PIE with universal masking (OR: 0.70, 95%CI [0.55, 0.91], I2: 0%) compared to standard care. For the culture-positive (14 studies; 2,347,419 injections), Streptococcus (10 studies; 1,966,903 injections), and culture-negative (15 studies; 2,213,322 injections) outcomes, PIE rates between pairs of interventions groups generally did not reach significance, likely involving limited study power. As one exception, the incidence of culture-positive PIE was significantly lower with a no-talking policy (OR: 0.45, 95%CI [0.23, 0.92], single direct estimate) compared to standard care, though this result did not persist in subgroup analysis. As well, in subgroup analysis, universal masking had a significantly lower incidence of culture-negative PIE than standard care (OR: 0.68, 95%CI [0.47, 0.98], I2: 0%).

Conclusion: For all outcomes, by GRADE analysis, low- or very-low certainty evidence suggests that no-talking and physician masking policies may reduce culture-positive or clinical PIE rates, respectively, compared to standard care and universal masking. While data were only available for endophthalmitis, the overall comparative safety of these interventions remains unclear.

Brendan Tao **Medical Student** **Poster # 31**

Syringe-Filling Techniques for Post-Intravitreal Injection Endophthalmitis Prophylaxis: A Network Meta-Analysis of 41-Million Injections

Co-authors: Peter J. Kertes, MDCM, Department of Ophthalmology & Vision Sciences, University of Toronto, John Chen, MD, Department of Ophthalmology, McGill University. Wai-Ching Lam, MD, Department of Ophthalmology and Visual Sciences, University of British Columbia, Peng Yan, MD, Department of Ophthalmology & Vision Sciences, University of Toronto.

Introduction: We sought to compare the risk of post-intravitreal injection endophthalmitis (PIE) between manufactured prefilled syringes (PFS), compounded syringes, and traditional vial preparation of syringes (VPS). PIE is a rare but clinically devastating complication of intravitreal injection. Optimal syringe-filling technique may reduce the risk of PIE, yet there is wide variation between ophthalmologists or jurisdictions regarding utilized syringe-filling techniques. We hypothesized that PFS, requiring fewer preparatory steps, may confer significantly lower risk of PIE.

Methods: Medline, Embase, and the Cochrane Library from inception to June 5, 2024, for any study which primarily evaluated clinical PIE incidence (with or without culture results) stratified by syringe-filling technique (PFS, compounded syringes, VPS, and steroid injections). We conducted a frequentist network meta-analysis of rare events using the Mantel-Haenszel method with fixed-effects. Subgroup analysis of low risk of bias was conducted, where the Risk of Bias (ROB) In Non-randomized Studies of Interventions tool was used. The GRADE tool was used to summarize the certainty of evidence for prophylactic inferences between syringe-filling techniques.

Results: We included 20 studies (3,746 events; 41,611,960 injections; 0.009%; 1 per 11,108 injections). Compared to VPS, the risk of clinical PIE was significantly lower with either PFS (OR: 0.45, 95% CI [0.40-0.49]) or compounded syringes (odds ratio; OR: 0.69, 95% confidence interval (CI) [0.64-0.74]), whereas a greater risk of clinical PIE was observed with triamcinolone (OR: 3.44, 95% CI [3.03-3.89]) and dexamethasone implant (OR: 2.71, 95% CI [2.38-3.10]) injections. PFS syringes conferred significantly lower risk of clinical PIE than compounded syringes (OR: 0.65, 95% CI [0.58-0.72]). The risk of culture-positive PIE was significantly lower with PFS than with either compounded syringes (OR: 0.15, 95% CI [0.05-0.44]) or VPS (OR: 0.15, 95% CI [0.06-0.41]). No significant difference in culture-positive PIE was observed between VPS and compounded syringes (OR: 1.02, 95% CI [0.66-0.1.58]). Subgroup analysis of three low ROB studies, while lesser powered, revealed largely consistent findings.

Conclusion: Low- or very-low certainty evidence suggests a lower rate of PIE with manufactured PFS compared to compounded or VPS, and this conclusion was robust across included studies. As most studies did not conduct adjusted analyses, future studies should be designed to control for confounding factors of PIE incidence. Currently, provinces in Canada differ in their available syringe-filling techniques prior to intravitreal injection, but most commonly use compounded syringes. For safety, our results may support further consideration of publicly funded PFS techniques.

Godfrey Wong **VSRP Student** **Poster # 33**

Comparison of Multimodal Imaging with Predictions made by MERCI, a Machine Learning Algorithm for Hydroxychloroquine Toxicity Screening

Co-authors: Gareth, Mercer, MD, Ophthalmology, University of Toronto, Tom, Wright, PhD, Ophthalmology, University of Toronto. Brian, Ballios, MD, PhD, Ophthalmology, University of Toronto.

Introduction: Hydroxychloroquine (HCQ) a common drug prescribed for the treatment of autoimmune diseases such as Lupus and Rheumatoid Arthritis. It is recommended that patients on chronic HCQ treatment undergo annual ophthalmic screening to avoid irreversible vison loss due to HCQ retinopathy. Two diagnostic tests that are proven to detect early signs of toxicity are spectral domain optical coherence tomography (OCT) and the multifocal electroretinogram (mfERG). The machine learning algorithm, MERCI was designed to analyze mfERG and predict whether HCQ retinopathy is present. The purpose of the study was to identify the correlation of retinal structure integrity shown in OCTs to the predictive accuracy of MERCI.

Methods: A retrospective chart review of 440 mfERG reports were conducted, and the diagnosis of whether retinopathy was present or absent was recorded. MERCI was used to analyze the same mfERG tests, and the algorithm prediction was compared against the corresponding report's conclusion. Agreements between the MERCI prediction and the mfERG report diagnoses were assigned as true positives and true negatives. Discordance between the two were labelled as false positives and false negatives. The OCT of the eyes with mfERG prediction errors were evaluated for HCQ retinopathy. The severity and spread of the retinal disease were classified using a system proposed by Ahn, S.J. (2024).

Results: Of the 440 MERCI predictions, there were 66 (15.0%) true positives, 239 (54.3%) true negatives, 120 (27.3%) false positives, and 15 (3.4%) false negatives. Analysis of the OCTs from the eyes that generated a false positive on MERCI, found four OCTs that displayed disruption of the ellipsoid zone. The photoreceptor damage in three eyes were parafoveal and one was pericentral. Five OCTs of the false negatives had outer retinal changes, of which all were parafoveal.

Conclusion: Although MERCI was able to precisely identify HCQ toxicity in most mfERGs, approximately a third of predictions resulted in a discrepancy from the clinical diagnosis. As functional changes precede structural damage, the false positives may not be true prediction errors, but evidence that MERCI has a higher sensitivity to detecting early stage HCQ retinopathy. Prospective longitudinal data and correlating OCT changes to fundus autofluorescence can be used to determine the legitimacy of the errors.

Fay-Yi Zhai **Resident** **Poster # 34**

Molecular Diagnostic Yield and Barriers in Inherited Retinal Diseases: A Retrospective Cohort Study

Co-authors: Rita Kodida, MS, CCGC, CGC, Department of Ophthalmology & Vision Sciences, University of Toronto, Brian Ballios, MD, PhD, FRCSC, Department of Ophthalmology & Vision Sciences, University of Toronto.

Introduction: Inherited retinal diseases (IRDs) are a heterogeneous group of genetic ocular disorders resulting from mutations in over 300 distinct genes, with a combined prevalence estimated at 1 in 2,000 individuals. This study aims to assess our molecular diagnostic yield and identify barriers faced by patients who have not achieved a confirmed molecular etiology.

Methods: We conducted a retrospective cohort study of 406 patients clinically diagnosed with IRDs at the Adult Inherited Retinal Dystrophy Service from 2021 to 2024. Panel-based genetic testing was performed to identify molecular diagnoses, and diagnostic yield was calculated. Barriers preventing patients from obtaining a molecular diagnosis were also evaluated in this analysis.

Results: From Oct 2021 to Sep 2024, we received 685 referrals for IRDs. Of these, 573 cases were clinically confirmed as IRD by our clinic. Our analysis excluded 141 patients with pending genetic testing reports and 26 IRD patients who declined or deferred genetic testing.
We included 406 IRD patients in our study. Among these, 94 patients had a confirmed molecular diagnosis prior to referral, and an additional 138 patients received a confirmed molecular diagnosis through the genetic testing we organized. A diagnostic yield of 57% for panel-based genetic testing within our patient cohort was established. Notably, some diagnoses were achieved through repeat testing with different panels due to limited coverage or technical limitations of the initial panels. Additionally, 62 patients (15.8%) who received negative panel testing results would be eligible candidates for more comprehensive genetic testing methods such as whole exome sequencing (WES), whole genome sequencing (WGS), or long-read WGS. Furthermore, 112 patients (27.6%) had inconclusive results. Among these, 30 cases may be resolved by phasing two pathogenic variants in genes exhibiting an autosomal recessive inheritance pattern, and 10 exhibited phenotypes highly suggestive of the genes carrying variants of unknown significance (VUS). Testing first-degree relatives and conducting functional studies, such as RNA sequencing and proteomics, would be beneficial in confirming molecular diagnoses.

Conclusion: Panel-based genetic testing achieved a diagnostic yield of 57% in our IRD patient cohort, demonstrating its effectiveness in molecular diagnosis when appropriate panels are selected. However, our data highlights the need for sequential s, including testing family members, accessing more comprehensive genetic testing modalities, and incorporating research-based functional studies to enhance diagnostic accuracy and improve clinical management for patients with IRDs.

Jiajie Zhang **Graduate Student** **Poster # 35**

Stem cell-derived human retinal organoid model of USH2A-associated retinitis pigmentosa shows impaired retinal development and photoreceptor degeneration

Co-authors: Cassandra D'Amata, MSc, Donald K. Johnson Eye Institute, Krembil Research Institute., Brian G. Ballios, MD PhD FRCSC DABO, Department of Ophthalmology and Vision Sciences, University of Toronto.

Introduction: USH2A-associated retinitis pigmentosa (RP) is among the most prevalent autosomal recessive inherited retinal disorders (IRDs), in which loss of photoreceptors causes severe vision loss. Studying human USH2A disease mechanisms and therapies is challenging due to the lack of suitable USH2A disease models. Human induced pluripotent stem cell (iPSC)-derived retinal organoids (ROs) have shown promise for disease modeling, as they recapitulate human retinal development and pathophysiology in vitro. We have engineered isogenic USH2A-diseased iPSCs from healthy iPSCs and studied USH2A disease phenotypes in these ROs. I hypothesize that isogenic USH2A-ROs will show impaired photoreceptor development and maturation, allowing us to investigate USH2A disease mechanisms.

Methods: Isogenic USH2A-/--iPSCs and heterozygous USH2A+/- control iPSCs were generated by introducing the c.2299delG mutation into healthy iPSCs using CRISPR/Cas9. ROs were grown using an established 2D/3D protocol. TUNEL assay and Caspase-3 immuno-staining were used to assay cell death in ROs. EdU assay and pH3 immuno-staining were used to assay proliferation in ROs. ROs were immuno-stained for specific retinal markers in both cryosections and cleared whole-mount tissues.

Results: Isogenic USH2A-/-ROs showed reduced neuroepithelial thickness at an early developmental stage (week 6-9 of RO growth), with reduced proliferation compared to USH2A+/- and healthy ROs. USH2A-/-ROs showed reduced mature photoreceptor marker (Recoverin), a reduced rod (Crx+&Nrl+) population and an increased cone (Crx+&Nrl-) population at week 16. Increased apoptotic photoreceptors were also found in USH2A-/--ROs at week 16, with preferential cell deaths in the rod population. No significant differences were found between the USH2A+/- and healthy ROs. We also derived iPSC lines directly from an USH2A-diseased patient (USH2AdelG). At a late developmental stage (week 28), USH2AdelG-ROs showed reduced mature rod and cone photoreceptor markers (Rhodopsin and L/M-opsin, respectively). Additionally, whole-mount staining showed a reduced photoreceptor density and reduced photoreceptor layer thickness compared to healthy ROs.

Conclusion: Human isogenic USH2A-/-ROs show degenerative disease phenotypes including reduced mature photoreceptor layer thickness and photoreceptor density. Consistent with clinical human disease, rod photoreceptors are preferentially affected by the USH2A mutation in ROs, indicated by a reduced rod photoreceptor population and increased rod cell death. However, our results also suggest abnormal retinal development in USH2A disease may contribute to disease mechanism, with reduced neuroepithelial thickness, reduced retinal progenitor cell proliferation, and increased cell death. These are mechanisms that cannot be studied in human disease, and point to the value of our RO model for studying this common IRD.

Afreen Ahmad **Medical Student** **Poster # 36**

Cost and Availability of High Dose Oral Prednisone for Management of Optic Neuritis

Co-authors: Dr. Jonathan Micieli (MD), Faculty of Medicine, University of Toronto.

Introduction: Untreated optic neuritis can lead to worse prognosis and potential vision loss, especially in atypical cases. Early management is essential however barriers such as cost, availability, and pharmacist hesitancy can delay treatment. This study assesses the cost and availability of 1250 mg of oral prednisone for optic neuritis treatment across pharmacies in Toronto.

Methods: A cross-sectional study was conducted across 4 regions in Toronto, Ontario, Canada. Data was collected from 70 pharmacies on cost and availability for 3- and 5-day courses of prednisone. Pharmacy hesitancy was assessed based on the readiness of the pharmacist to dispense the required dose of medication.

Results: The average cost for a 3-day course of prednisone was $29.10 CAD, and for a 5-day course was $40.40 CAD. Availability was lowest in independent pharmacies (23.8%) and highest in chain pharmacies (47.6%). Although no significant association between availability and pharmacy type was found, $\chi 2$ (1, N = 63) = 3.66, p=0.06, the direction of the effect still shows an indication of chain pharmacies having higher stock. Chain pharmacies also exhibited the highest cost variability. Finally, pharmacist hesitancy to dispense the appropriate dose was high (40%), with 6 of the 70 pharmacies refusing to dispense the medication.

Conclusion: There is limited availability of high-dose prednisone across Toronto, with chain pharmacies offering the highest availability but at a higher cost. There is also significant hesitancy about dispensing this Prednisone dose among pharmacists. To our knowledge, this study is novel in exploring treatment barriers for patients with optic neuritis due to cost and availability. The implications of these barriers include delayed recovery and an increased risk of relapse in severe or untreated cases. In these cases, early initiation of treatment (i.e., within the first few days) is critical for optimizing outcomes. Clinicians should be aware of cost and availability trends when recommending treatment options for patients. This includes considering patients' financial limitations and access to specific pharmacy services, especially for those in rural or underserved areas. Additionally, neuro-ophthalmologists should aim to develop relationships with pharmacies to improve timely administration of this medication. Further research is needed to explore the pharmaceutical landscape in Canada and its impact on the treatment of conditions requiring high-dose generic medications like prednisone.

Yasir Al-Zubaidy **Graduate Student** **Poster # 37**

Investigating the roles of Vsx1 and Ey, the Drosophila homologs of vertebrate VSX2 and PAX6, in the developing fly visual system

Co-authors: Ted, Erclik, PhD, Department of Cell and Systems Biology, University of Toronto.

Introduction: The Visual system homeobox 2 (VSX2) and Paired box 6 (PAX6) transcription factors are expressed in the developing vertebrate retina and play important roles in eye development and disease. Mutations in VSX2 result in eye abnormalities such as microphthalmia and anophthalmia, while mutations in PAX6 lead to developmental defects in the iris, cornea, lens, and retina. While VSX2 and PAX6 are both known to regulate the proliferation and differentiation of retinal progenitor cells (RPCs), how the two genes interact with each other in RPCs is poorly understood. My work will study the VSX2 and PAX6 Drosophila orthologs, vsx1 and ey, in the developing medulla, which is the largest structure within the fly visual system. Due to the genetic, structural, and developmental similarities between the Drosophila medulla and vertebrate retina, this work will aid in understanding the developmental roles played by VSX2 and PAX6 in retinogenesis. The Drosophila medulla develops from neural progenitors that are patterned by spatial (Optix/Six3, Vsx1/Vsx2, Rx/Rx) and temporal (Hth/Meis1, Ey/Pax6, D/Sox2) transcription factors to generate different neuronal cell types. To date, however, it is not known whether the spatial Vsx1 and temporal Ey factors interact to diversify medulla neuronal fates.

Methods: To characterize the neuron types born from Vsx1-Ey progenitors, I am generating single cell clones using the split-Gal4 system and labelling the neurons using immunohistochemistry. Once the extent of neural diversity generated at this spatio-temporal address is understood, I will use an EdU-labelling technique to determine when each neuron type is born during neurogenesis. Lastly, complementary Loss-of-Function (LoF) and Gain-of-Function (GoF) genetic techniques will be employed to study the roles of Vsx1 and Ey in the specification of medulla neurons generated at this spatio-temporal address.

Results: Using the split-Gal4 system and a brainbow-like stochastic labelling technique I have identified at least six morphologically distinct neuronal types that are born in the Vsx1-Ey spatio-temporal window. These six neuron types, which have also been matched to the Drosophila brain's connectome, include Lpi3-4, Pm4, Tm5e, Tm33, Tm35, and Sm08. Future LoF and GoF experiments will determine whether Vsx1 and Ey are required for the specification of these cell types.

Conclusion: The above results demonstrate that medulla progenitors that coexpress Vsx1 and Ey generate distinct neuronal cell types. Based on these findings, it is anticipated that VSX2 and PAX6 may interact in vertebrate RPCs as well to promote the specification of distinct neural cell types.

Gur Rattan Pal (Gary) Chatha **Graduate Student** **Poster # 38**

Investigating the Role of Ultraspiracle, the Drosophila Homolog of the Retinoid X Receptor, in the Developing Fly Visual System

Co-authors: Teddy, Erclik, PhD, Department of Cell and Systems Biology, University of Toronto.

Introduction: The retinoid X receptor (RXR) family comprises ligand-activated transcription factors that are highly expressed in the developing and adult vertebrate retina. Null mutations in RXR lead to a shortened ventral retina, coloboma of the optic nerve, and a persistent retrolenticular membrane. To date, little is known about the downstream targets of the RXR family during retinal development. My work investigates the role of the Drosophila RXR homolog, ultraspiracle (usp), in the medulla neuropil of the developing fly visual system. Given the genetic and structural similarities between the mammalian retina and Drosophila visual system, the medulla serves as a great model in which to study the role of RXR homologs in neural retinal development.

Within the fly visual system, the medulla is the largest visual processing center, comprised of ~150 neuronal cell types. During development, medulla progenitors are temporally patterned by opposing gradients of the early Imp and late Syp RNA-binding proteins. Neural progenitors generate distinct neuronal cell types based on their levels of Imp and Syp expression. Our lab has previously found that USP together with its heterodimer binding partner EcR-B1 is required for the transition of the early Imp-dependent neuronal fates to late Syp-dependent neuronal fates. However, how USP/EcR-B1 regulate Imp/Syp-dependent patterning is unknown.

Methods: A time-course analysis was performed to examine the expression of EcR-B1/USP at various time points during medulla neurogenesis. The Gal4-UAS system was next used to generate recombinase-based Loss-of-Function (LoF) and Gain-of-Function (GoF) clones targeting these receptors. The expression of Imp/Syp and their downstream target genes was studied using immunohistochemistry and confocal microscopy.

Results: In medulla progenitors, I have found that USP/EcR-B1 signalling is initiated 48 hours after-larval-hatching (ALH), which coincides with the onset of medulla neurogenesis. Expression levels peak at 72 hours ALH and steadily decline up till the end of larval neurogenesis. Furthermore, I have shown that USP/EcR-B1 is required for the initiation of Syp expression in neural progenitors; in EcR-B1 LOF clones, Syp expression is lost at both intermediate and late developmental time points. Future experiments will determine whether USP/EcR-B1 signalling directly or indirectly activates syp transcription.

Conclusion: We anticipate these findings will contribute to our understanding of the role that RXR genes play in the developing retina. For example, my finding that USP/EcR-B1 signalling mediates temporal patterning through the activation of the syp gene suggests that RXR may regulate the vertebrate homolog of Syp, hnRNP Q1, in the developing retina as well.

Elina Farahani **Medical Student** **Poster # 39**

The Role of PFO Closure in Migraine Cessation and Stroke Prevention: A Case Study and Review of Current Evidence

Co-authors: Lam, Cindy, MD, FRSC, Department of Ophthalmology and Vision Sciences, University of Toronto.

Introduction: Migraines are one of the most prevalent neurological disorders, affecting over 1.1 billion individuals globally and representing the second highest non-fatal disease burden worldwide. While the precise etiology remains unclear, migraines with aura (MA) are well-established as an independent risk factor for ischemic stroke, particularly in females under 45 who smoke or use oral contraceptives. Increasing evidence suggests a potential link between right-to-left shunting via a patent foramen ovale (PFO) and both MA and stroke, though the mechanism remains disputed. Paradoxical embolism, transient hypoxia, and vasoactive metabolite bypass have all been proposed as explanations. To date, three randomized controlled trials have assessed the impact of PFO closure on migraine relief. While none met their established primary endpoints of migraine attack reduction, all three demonstrated increased incidence of migraine cessation in patients who underwent PFO closure. Despite this, PFO closure remains a non-standard intervention for migraine management. Here, we present a case of a patient with a history of MA who experienced complete migraine cessation following PFO closure after a suspected occipital lobe infarct.

Methods: A 43 year-old male with a history of MA presented with an episode of non-resolving visual symptoms following a migraine attack. Neurological and ophthalmologic assessments revealed a left-sided homonymous lower quadrantanopia with no other focal deficits. Initial CT and repeated MRI investigations were unremarkable and offered no explanation for his symptoms. A closer assessment of his imaging was later performed that revealed subtle T2/FLAIR signals in the right occipital lobe, indicating a likely prior infarct. A stroke workup identified the patient's PFO and he subsequently underwent percutaneous PFO closure.

Results: Following PFO closure in 2020, the patient experienced complete migraine cessation with no future incidences of stroke. This case supports the growing body of literature suggesting an association between PFOs and migraines, and highlights PFO as a potentially viable tool for migraine cessation and reduction in stroke risk.

Conclusion: The relationship between PFO and migraine remains contentious with conflicting evidence reported in literature. While RCTs such as the MIST, PREMIUM, and PRIMA trials failed to demonstrate significant migraine cessation following PFO closure, multiple observational studies have suggested a meaningful association. This discrepancy may stem from differences in patient selection and study endpoints. The three RCTs largely recruited patients with refractory migraines, which may represent a more complex and treatment-resistant phenotype. Additionally, the primary endpoints—such as complete migraine cessation or a predefined reduction in migraine days—may have been overly ambitious, failing to capture subtle but clinically meaningful improvements. This case report hosts limitations inherent to single-case observations, but highlights the need for further research into the PFO-migraine connection with refined selection criteria.

Angelica Hanna **Medical Student** **Poster # 40**

Natural history of non-arteritic anterior ischemic optic neuropathy

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Introduction: Non-arteritic anterior ischemic optic neuropathy (NAION) is a devastating condition with significant visual morbidity. This study aims to describe the presenting features and natural history of a large cohort of patients with NAION.

Methods: A retrospective chart review was conducted of all patients diagnosed with acute NAION (i.e. seen within 6 weeks of symptom onset and had disc edema) at two tertiary neuro-ophthalmology practices between January 2014 and December 2024. Patients were included if they had resolution of optic disc edema on a follow-up visit and had negative work-up for alternative etiologies of optic neuropathy.

Results: Overall, 256 eyes of 237 patients (55.5% female, mean age 63.7 ± 13.5 years) with acute NAION were followed for an average of 1.5 ± 1.6 years. Pain was a presenting feature in 15.3% of patients: 6.0% had headache, 7.7% ocular pain, and 2.0% both. At presentation, the mean visual acuity (VA) in the affected eye was 0.8 ± 0.8 logMAR (Snellen 20/123) and the visual field mean deviation (VFMD) was -13.3 ± 9.4 dB. The mean cup-to-disk ratio (CDR) in the fellow eye was 0.26 ± 0.20, with 27.3% of patients having a CDR of 0.3 or greater. At final follow-up, the mean VA was 0.9 ± 0.9 logMAR (Snellen 20/164) and the VFMD was -14.0 ± 10.3 dB. Compared to presentation, 36.8% of patients had decreased VA, 25.9% had improved VA (23.2% recovered at least 0.2 logMAR), and 37.2% had no change in VA at follow-up. Overall, 64 patients (25%) had a second episode of NAION, with 96.9% of recurrences in the fellow eye and 3.1% recurring in the same eye. The mean time to recurrence was 58 ± 91 months. Patients with recurrent NAION had a similar age at presentation (64.6 ± 13.0 years vs. 63.7 ± 14 years, p = 0.58), sex distribution (55.5% female in both groups, p = 0.56), and number of vascular risk factors (1.5 ± 1.1 vs. 1.3 ± 1.1, p = 0.24) compared to those with a single NAION episode.

Conclusion: Visual prognosis of NAION is generally poor, with 63% and 31% of patients having stable or worsening VA and VFMD, respectively. Up to 10% of patients with NAION present with ocular pain and up to 27% have normal CDR. NAION recurrence in the same eye or fellow eye occurred in 25% of cases. Sociodemographic and cardiovascular risk factors at baseline do not seem to hold prognostic value.

Samira Jafari **Research Fellow** **Poster # 41**

Structural Causes and Incidental Neuroimaging Findings in Pharmacologically Confirmed Horner Syndrome: A Retrospective Cohort Study

Co-authors: Edward Margolin MD, Professor, Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, ON, Canada, Jonathan A. Micieli, Assistant Professor, Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, ON, Canada.

Introduction: This study aimed to determine the prevalence and causes of pharmacologically confirmed Horner Syndrome (HS) in a cohort of 5000 patients and categorize incidental findings based on follow-up needs.

Methods: This retrospective cohort study included 134 patients (57.5% female, mean age 52.7 ± 18.0 years) diagnosed with HS and who underwent neuroimaging (MRI or CT) between July 2008 and June 2024 at a neuro-ophthalmology clinic. HS was classified as acute (<21 days), subacute (21 days to 3 months), or chronic (>3 months). Structural causes and incidental findings were categorized by follow-up requirements: none, routine, urgent, or emergency. Imaging and clinical data were independently reviewed by an ophthalmologist and neuro-ophthalmologist. Statistical analyses evaluated the prevalence and significance of findings.

Results: HS was acute in 20.2% (n=27), subacute in 10.4% (n=14), and chronic in 69.4% (n=93). Imaging modalities included MRI/MRA head/neck (55.2%), CT/CTA head/neck (41.8%), and others (3.0%). A cause for HS was identified in 14.9% (n=20), including structural and non-structural causes. Structural causes were identified in 10.6% (n=14) of patients, with the highest prevalence in acute (18.5%) and subacute (21.4%) cases, compared to chronic cases (6.5%). The most common structural causes were internal carotid artery (ICA) dissection (3.0%) and ICA aneurysm (2.2%). Non-structural causes included concussion (n=2), cluster headaches (n=1), and giant cell arteritis (n=2). Incidental findings were present in 35.6% (n=47) of patients. The most common were microangiopathic changes and brain atrophy (10%), sinus/mucosal changes (3%), and thyroid nodules (3%). Routine follow-up was required for 18.2% (n=24) of incidental findings, while urgent follow-up was needed for 1.5% (n=2). No cases required emergency follow-up.

Conclusion: Neuroimaging identified structural causes in approximately 1 in 10 HS cases, with ICA dissection and aneurysms being the most common causes. Acute and subacute HS cases were more likely to have structural causes than chronic cases. Incidental findings, present in about one-third of patients, were common but rarely required urgent or emergency follow-up. These findings highlight the importance of careful evaluation and follow-up in managing HS.

Angela Kwan **Medical Student** **Poster # 42**

Age-Related Variations in Orbital Apex Syndrome (OAS): Implications for Diagnosis, Prognosis, and Management

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Introduction: Orbital apex syndrome (OAS) is a rare yet clinically significant neuro-ophthalmic disorder that severely impacts health-related quality of life. Despite its clinical significance, data on its global incidence and demographic predispositions remain limited and poorly characterized. The syndrome's multifactorial etiologies, including neoplastic, inflammatory, infectious, vascular, and traumatic causes, pose significant challenges to timely diagnosis and optimal management. Understanding how OAS manifests differently across age groups is essential for improving recognition, prognosis, and treatment strategies. This study aimed to investigate age-related differences in the clinical presentation, progression, treatment, and outcomes of OAS in younger versus older patient populations.

Methods: We performed a retrospective review of medical records for patients diagnosed with OAS between 2017 and 2023 at a tertiary neuro-ophthalmology center affiliated with the University of Toronto. Data collected included ocular symptoms, underlying causes, visual acuity, imaging findings, treatment regimens, and outcomes. We compared clinical characteristics between two age groups: younger patients (<45 years, n=18) and older patients (≥45 years, n=57) using non-parametric statistical tests.

Results: A total of 57 patients with OAS were analyzed. Our findings revealed distinct age-related differences in etiology, clinical presentation, and outcomes. In younger patients, inflammation was the most common etiology, while neoplasia predominated in older patients, with neoplasia, accounting for 48% of cases overall (metastases 18%, nasopharyngeal carcinoma 15%). Younger patients had a higher prevalence of optic disc edema (28%) and optic atrophy (33%, p=0.03), while diplopia was more prevalent in the older cohort (53% vs. 38%, p=0.048). Recurrence was significantly higher among younger patients (55% vs. 12%, p=0.001) over a mean follow-up period of 36 months. Conversely, older patients had poorer final visual acuity (median 0.40 logMAR [IQR 0.275–2.0] vs. 0.25 logMAR [IQR 0.025–0.625], p=0.04) and higher mortality associated with their underlying disease.

Conclusion: Our study underscores the distinct age-related differences in OAS, with younger patients more prone to optic neuropathy and disease recurrence, and older patients experiencing more severe visual impairment and morbidity. These findings highlight the need for age-specific diagnostic and management strategies to optimize patient care. By elucidating these age-related manifestations, this study addresses critical gaps in the literature and provides the foundation for personalized treatment approaches. Given the complexity of OAS, a multidisciplinary approach is vital to ensure accurate diagnosis, effective risk stratification, and timely intervention, ultimately improving both visual outcomes and overall patient prognosis.

Tasha Miller **Medical Student** **Poster # 43**

New Onset Rapid Visual Loss from Myelin Oligodendrocyte Glycoprotein Antibody-Associated Optic Neuritis During Peripartum and Postpartum Periods

Co-authors: Arun Sundaram, MD, MSc, Hurvitz Brain Sciences Research Program, Sunnybrook Research Institute, Sunnybrook Health Sciences Centre, Department of Ophthalmology and Vision Sciences, University of Toronto, Division of Neurology, Department of Medicine.

Introduction: Managing acute visual loss during pregnancy is challenging. We describe a case series of myelin oligodendrocyte glycoprotein (MOG) antibody-positive optic neuritis (ON) with rapid vision loss in a pregnant and a postpartum patient.

Methods: Detailed chart review including medical history, examination, optical coherence tomography (OCT), visual fields and MR imaging was conducted.

Results: Case 1: A 32-year-old woman at 37 weeks gestation presented with bilateral vision loss and retrobulbar pain. Visual acuity was hand motion OD and 20/200 OS, with a relative afferent pupillary defect (RAPD) OD. Fundoscopy revealed bilateral disc edema, and OCT demonstrated bilateral retinal nerve fibre layer (RNFL) thickening. Contrast-enhanced MRI demonstrated increased T2 signal and enhancement of both optic nerves. She was treated with high-dose intravenous methylprednisolone, followed by oral prednisone, leading to complete visual recovery OU with normal visual fields. MOG antibody serology was positive. She delivered a healthy baby without complications and no more relapses during the pregnancy. Case 2: A 28-year-old woman presented 10 weeks postpartum with retrobulbar pain and rapid vision loss OS. Visual acuity was 20/20 OD and counting fingers OS, with a RAPD OS. Fundoscopy revealed left optic disc edema, and OCT showed circumferential RNFL thickening OS. Contrast-enhanced MRI showed enhancement in the orbital, intracanalicular, and prechiasmatic segments of the left optic nerve. Serological testing revealed MOG antibody positivity. She received 3 days of intravenous methylprednisolone followed by oral prednisone. Due to persistent visual impairment at 14 days, plasmapheresis was initiated and her vision recovered to 20/200 OS. Immunosuppressive therapy with mycophenolate was not initiated due to breastfeeding.

Conclusion: These cases highlight that pregnancy-related immune shifts can trigger the first attack of MOG antibody-positive ON. During pregnancy, elevated estrogen levels and shifts in T cells balance promote pro-inflammatory responses, which increase susceptibility to immune-mediated attacks. These immunological changes persist into the postpartum period, where decline in regulatory T cells and anti-inflammatory hormones like progesterone disrupts immune tolerance. Such hormonal and immune fluctuations can activate dormant autoimmune diseases like MOG-antibody-associated disease (MOGAD). Prompt treatment with corticosteroids, which are safe for use during pregnancy and breastfeeding as category C drugs, is critical to preserve vision. Plasmapheresis was initiated to restore vision in the postpartum patient. Immunosuppressive therapy with mycophenolate should be avoided during pregnancy due to the teratogenic side effects as a category D drug. These cases demonstrated the high risk for first attack of MOGAD during pregnancy and postpartum periods.

Manlong Xu **Resident** **Poster # 44**

Bilateral Simultaneous NAION with Resolution of Incipient NAION after Prompt Correction of Severe Anemia, A Case Series

Co-authors: Rahul A. Sharma, MSc, FRCS, Department of Ophthalmology & Vision Sciences, University of Toronto, Arun NE Sundaram, MD, FRCS(C), MPH, Department of Ophthalmology & Vision Sciences, University of Toronto.

Introduction: Nonarteritic anterior ischemic optic neuropathy (NAION) results from optic nerve head hypoperfusion. There is no proven effective treatment for NAION. Anemia is a known cause of NAION. Incipient or 'threatened' NAION is optic disc edema (ODE) without vision loss. It may resolve or progress to classic NAION in 25% cases.

Methods: Case series involving two patients for whom detailed review of charts including history, examination, visual fields (VF) and OCT was conducted.

Results: Case 1: A 46-year-old female with hypertension presented with acute painless visual loss OD. She had excessive vaginal bleeding for two months prior that, resulted in severe iron deficiency anemia with hemoglobin of 64 g/L. Visual acuities (VA) were 20/20 OU, with a RAPD OD. HVF 24-2 showed inferior altitudinal defect OD and a full field OS. Fundus exam showed ODE OU, worse OD. She received 3 units of RBC and 2 iron infusion over the next 2 months, and uterine leiomyoma that caused the bleeding was treated urgently by Gynecology, which normalized the hemoglobin. VA and VF worsened OD in 2 months with eventual optic atrophy, but ODE OS resolved with preserved vision. Case 2: A 63-year-old male with hypertension was referred for bilateral ODE. He reported blurred vision OS. VA were 20/30 OU, with a RAPD OS. HVF 24-2 revealed a full field OD and a partial inferior arcuate defect OS. Optic discs revealed edema OU, worse OS. His hemoglobin was 67 g/L. Urgent endoscopy identified gastrointestinal bleeding, which was treated. He also received 1 unit of RBC and 1 iron infusion urgently, and the hemoglobin steadily improved and normalized. ODE OU resolved in 2 months, with normal vision OD and mild residual inferior defect and superior optic disc pallor OS. Both patients had negative brain imaging and serological testing, and were diagnosed with NAION in one eye and incipient NAION in the contralateral eye from severe anemia.

Conclusion: In patients with severe anemia presenting with NAION, it is crucial to immediately correct the anemia, and also to identify the source and stop the bleeding to preserve vision in established NAION and to prevent the progression of incipient NAION. Treatment delays could result in bilateral visual loss within days to weeks in patients with bilateral ODE. Three of the four eyes had favourable outcome in our patients, and one eye with established NAION showed progressive visual loss despite aggressive measures to address the anemia.

Abrar Alsalamah **Clinical Fellow** **Poster # 45**

Expanding the clinical spectrum of PRPS1 in females: A report of two cases

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Introduction: Phosphoribosylpyrophosphate synthetase (PRS) I deficiency is an X-linked disorder presenting as a spectrum of clinical manifestations, including three distinct disorders: Arts syndrome, Charcot-Marie-Tooth type 5, and non-syndromic sensorineural hearing loss. While males typically exhibit severe symptoms, female carriers are often asymptomatic or present with milder phenotypes.

Methods: A retrospective case series of two unrelated female pediatric patients with multimodal retinal imaging, full-field electroretinography (ERG), and genetic analysis.

Results: Two unrelated female patients (9 and 8 years old) with de novo likely pathogenic heterozygous variants in the PRPS1 gene presented with bilateral optic atrophy and radially distributed retinal pigmentary changes. Interocular asymmetry and macular pseudocoloboma were noted in patient B. Both patients showed generalized retinal dysfunction on ERG. Asymmetric hearing loss was observed in both patients. Bilateral tongue fasciculations detected in patient A suggest the involvement of lower cranial nerve XII in addition to cranial nerves II and VIII. Mild upper limb dysmetria was identified in both patients.

Conclusion: These cases emphasize the importance of understanding the disease expression in females and underscore the need for further characterization of the PRPS1 clinical spectrum in females. The involvement of cranial nerve XII extends the cranial neuronopathy in this disorder.

Liran Hanan Hochma **Clinical Fellow** **Poster # 46**

Progression mapping of RPGR-associated Retinitis Pigmentosa using structural and functional metrics

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Introduction: RPGR-associated RP is characterized by progressive degeneration of photoreceptors. While various structural and functional measures have been proposed to monitor disease progression, the individual predictive value remains uncertain. This study aimed to assess the phenotype of molecularly confirmed patients with RPGR-associated retinitis pigmentosa and search for outcome measure of change.

Methods: 21 Patients, aged from 10 to 64 years old, were selected from a single center in-house database of genetically confirmed retinitis pigmentosa (RP) cases. Retrospective clinical records were assessed for functional (including best corrected visual acuity [BCVA] , Goldmann visual field [GVF] and refractive error) and structural (including optical coherence tomography [OCT] and fundus autofluorescence [FAF]) data. Data from right eyes was used for statistical comparison.

Results: Twenty patients met the inclusion criteria, 95% of whom were male. The mean age at first visit and follow up duration were 26.6 ±14.5 years and 4.1 ±3.9 years (2.4 ±0.9 visits), respectively. BCVA at first visit was 0.53 ±0.65 LogMAR and changed by mean 0.05 ±0.17/year. Mean spherical equivalent refractive error was -5.15 ±4.87D (range +1.25 – -14D) and 48% had high myopia.

Though annual change (Δ) in BCVA was not greater for those >20 years vs ≤20 years (p=0.728), final VA was significantly worse for older patients (0.89 ±0.27 vs 0.14 ±0.05, p=0.027). Five patients (24%, 10 - 35 years) had residual I4e field area at any time point and this did not predict rate of change in any measure. Presence of residual GVF III4e isopter area was seen in younger patients (17.7 ±9.0 vs 34.7 ±13.9 years, p=0.004). Though annual rate of change in CRT1mm (-2.3 ±9.9µm), CRT1-3mm (-1.6 ±7.8µm) and CRT3-6mm (-1.8 ±8.6µm) was not related to age at first presentation, patients presenting at <30-years-old had thinner final CRT3-6mm (242.4 ±25.0 vs 313.1 ±67.2µm, p=0.049). Horizontal EZ width reduced by -68.3 ±263.9µm/year. Those with ORF15 variants did not have significant differences in any structural or functional measures.

Conclusion: RPGR-RP is an aggressive juvenile onset form of RP. In depth analysis found that no single measure predictive of outcomes. Multimodal measures, in the context of age at first presentation, rather than one specific functional or structural measure are the most useful in predicting change.

Frances Argento **VSRP Student** **Poster # 47**

Characterizing the Consent Preferences of Participants in a Pediatric Biobank

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Introduction: The Kids Eye Biobank at the Hospital for Sick Children houses an international collection of biological specimens, images, and clinical data for use in future research. Pediatric ophthalmology patients with a wide range of eye and vision conditions are enrolled in the Kids Eye Biobank. Establishing biobanks with comprehensive datasets is essential for advancing equitable health research in genomics and precision medicine. Participant characteristics may influence their participation choices. This study aimed to (i) define participant consent preferences and (ii) investigate associations between participant characteristics and consent preferences.

Methods: A broad informed consent model was utilized. Main study participation entailed the storage and sharing of participant data with academic researchers. Participants had additional options, including the sharing of resources with for-profit companies, research to develop cell lines or organoids, and sharing of whole genome sequencing (WGS) data. Participants also made communication decisions, including the desire to be notified of incidental genetic findings or future research studies. Participant date of birth, diagnosis, gender, race, religion, date of enrollment, consent decision-maker, and consent preferences were collected from the Kids Eye Biobank's records. Chi-Square Test was used to investigate associations between participant characteristics and consent preferences. All findings were interpreted with Kids Eye Biobank patient partners.

Results: Between June 2020 and August 2024, 312 patients were approached and 276 (88%) were enrolled. Of the enrolled participants, 79% had a substitute decision-maker and 64% were diagnosed with a malignant neoplasm affecting the eye. Demographic data was available for 81% of participants: 52% were girls/women, 50% identified as belonging to a visible racial minority group, and 75% reported belonging to a religious group.

Participants with malignant neoplasms (e.g., retinoblastoma, optic glioma) opted in to more research choices compared to individuals with benign neoplasms, including research to develop cell lines ($p = 0.005$) and sharing of WGS data ($p = 0.028$). Participants belonging to a visible racial minority opted in less to research of cell lines ($p = 0.02$) or to receive future communications ($p = 0.01$) compared to other participants. No significant associations were identified between age, gender, religion or decision-maker with consent preferences.

Conclusion: Understanding characteristics associated with participant consent preferences may help us refine communication strategies and expand the Kids Eye Biobank population. This is essential for advancing high-impact precision child health research. More research is needed to further unpack the findings of this study.

Andrew Yim **Graduate Student** **Poster # 48**

Elucidating the underlying mechanisms of unique TEAD interactomes across distinct target-gene specificity in YAP binary classes

Co-authors: Joel Pearson, PhD, Ophthalmology and Vision Sciences, Laboratory Medicine and Pathobiology, University of Toronto, Suying Lu, PhD, University of Toronto. Rod Bremner, PhD, Ophthalmology and Vision Sciences, Laboratory Medicine and Pathobiology, University of Toronto.

Introduction: Retinoblastoma is a small cell ophthalmic pediatric cancer that originates when the RB1 tumour suppressor gene is inactivated during retinal development. From retinoblastoma, the Bremner lab has discovered the binary pan-cancer model, stratifying tumours based on the opposite expression and pro- or anti-cancer activity of one cotranscriptional activator, YAP. While most solid cancers express YAP (YAPon) to facilitate division, YAP was found to be epigenetically silenced (YAPoff) in retinoblastoma. Forced YAP expression in YAPoff retinoblastoma activated silenced extracellular matrix (ECM)/adhesion genes, and induced cytostasis. The DNA binding protein TEAD targets distinct loci in YAPon or YAPoff contexts, preferentially binding AP1 (FOS/JUN dimers) at cell cycle loci, or homeobox proteins and corepressors respectively to give rise to these contrasting phenotypes. We aimed to outline the mechanism underlying repression of this YAP/TEAD mediated anti-cancer program in YAPoff cancers.

Methods: We screened the TEAD interactome in YAPon lines and YAPoff retinoblastoma with immunoprecipitation assays (ChIP-seq, BioID and affinity purification-MS), and validated for homeobox and corepressor binding targets with Western analysis. A CRISPRi strategy to deplete TEAD family paralogs (TEAD1-4) was developed to validate cytostasis and cellular adhesion, then tested in YAPoff lines.

Results: BioID confirmed distinct YAP/TEAD partners in YAPoff and YAPon tumours, with ~28% and ~30% respectively being unique to A549 YAPon cells and YAPoff SCLC (H209) and retinoblastoma (Y79) lines. The JUN/FOS/ATF leucine-bZIP and NCOA1-3 proteins that bridge TEAD to AP1 in YAPon tumours were, with the exception of JUND, nearly undetected in YAPoff cells, which instead show several top Homeobox (Hox) and Zinc finger (Znf) hits. Of note, MYT1, a repressor family protein, promotes the neural/NE lineage and complexes with a network of corepressors including histone demethylase KDM1A/LSD1, and CoREST members RCO1-3, HDAC1, and GSE1, suggesting that MYT1 and TEAD cooperate to silence YAPon programs. Western analysis validated the exclusive binding of MYT1 to TEAD in tested YAPoff lines. Interactome analysis revealed TEAD pull down of MYT1 in both H209 and Y79, and its paralog ST18 in H209. Remarkably, deletion of MYT1 in the YAPoff WERI-RB1 retinoblastoma context induced YAP protein expression. Likewise, siRNA targeting of TEADs 1, 3, & 4 reactivated YAP protein expression, inducing growth arrest and increasing adhesion in YAPoff cells. YAP silencing therefore critically involves the cooperation between TEAD and MYT families.

Conclusion: Retinoblastoma was the founding cancer of our binary cancer model, from which our study revealed that YAP drives cytostasis given a unique TEAD target repertoire. We identify the novel function of the TEAD/homeobox/CoREST interactome in the repression of an anti-cancer adhesion program in YAPoff cancers, elucidating a targetable pathway for exposing novel therapeutic strategies in retinoblastoma and other YAPoff class tumours.

Victoria Leung **Medical Student** **Poster # 49**

Nasolacrimal system disorders associated with medication use: A Population-Based Pharmacovigilance Study

Co-authors: Andrew Mihalache, MD(C), Temerty Faculty of Medicine, University of Toronto, Marko M. Popovic, MD, MPH, Department of Ophthalmology and Vision Sciences, University of Toronto. Georges Nassrallah, MD, FRCSC, Department of Ophthalmology and Vision Sciences, University of Toronto.

Introduction: Nasolacrimal system disorders encompass a range of conditions affecting tear production, drainage, and associated structures, leading to symptoms such as epiphora, recurrent infections, and inflammation. The prevalence of nasolacrimal duct obstruction (NLDO) increases with age and has been associated with idiopathic fibrosis, trauma, infections, and systemic inflammatory diseases. However, evidence linking certain medications to NLDO is limited, primarily consisting of case reports. The aim of this study was to comprehensively investigate associations between drugs and reports of nasolacrimal system disorders using population-based, real-world data from the U.S. Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS).

Methods: A pharmacovigilance analysis of NLDO-related events reported to the FAERS database from October 2003 through October 2024 was conducted using Open Vigil 2.1 (Kiel, Germany) data-mining software. Drug-specific reports encompassing NLDO-related events were compared to background rates for all other drugs in the FAERS database. Disproportionality analyses were performed using reporting odds ratios (RORs) and Bayesian confidence propagation neural network algorithms to identify significant safety signals.

Results: Seventeen pharmacological agents were disproportionately associated with high NLDO reports. Notably, sodium iodide i-131 (2.46%, n=23/936; ROR=387.4, 95%CI=[254.7, 589.2], IC025=5.6), netarsudil (1.88%, n=30/1597; ROR=339.3, 95%CI=[234.9, 490.2], IC025=5.8) and docetaxel (0.52%, n=269/51285; ROR=160.0, 95%CI=[138.2, 185.2], IC025=5.9) showed the highest disproportionate reporting of NLDO. These were followed by iodide i-131 (0.83%, n=5/606; ROR=116.8, 95%CI=[48.3, 282.3], IC025=2.8), carboxymethylcellulose (0.15%, n=7/4748; ROR=40.3, 95%CI=[16.7, 97.1], IC025=2.2), and ketotifen (0.15%, n=8/5267; ROR=31.8, 95%CI=[11.9, 85.0], IC025=1.9). The most common drug classes associated with NLDO were radiopharmaceuticals, ophthalmic agents, antibiotics, chemotherapy agents, and anti-inflammatory agents.

Conclusion: This study is the first pharmacovigilance analysis of drug-associated NLDO using FAERS data, identifying significant associations between NLDO and specific pharmacological agents. These findings suggest medications may contribute to nasolacrimal system dysfunction, potentially through fibrosis, inflammation, or direct toxicity. Given the implications for ocular health and quality of life, clinicians should consider these potential adverse effects, especially in patients at higher risk for NLDO. Future studies are warranted to better understand the causal relationships and develop preventative strategies.

Shaikhah Abohaimed **Resident** **Poster # 50**

Retrospective Case Series of Conservative Management for Chronically Inflamed Anophthalmic Sockets with Pegged Integrated Orbital Implants

Co-authors: Webb, Michael, Nijhawan, Navdeep.

Introduction: Purpose: Integrated implants were introduced and popularized for their improved prosthesis motility. Placing a peg in the integrated implant post-operatively was also thought to improve motility of the prosthesis. However, peg implants were shown to have their own host of complications, other than those caused by the implant itself, including include discharge, pyogenic granulomas, peg extrusion, clicking, and implant infection. Given the integrated nature of these implants, resection may be challenging and leave the patient's orbit volume deficient and thus significantly reduce cosmesis. The purpose of this retrospective case series is to assess the success of a stepwise conservative approach to the management of peg associated complications in an effort temporize or even eliminate the need for implant resection.

Methods: Methods: In this retrospective case series, the charts of all patients with chronic anophthalmic socket inflammation with a pegged integrated orbital implant seen by the principal investigator between 2019 to 2022 were retrieved. Data concerning demographic features, physical exam findings, conservative management used and whether or not they eventually required implant resection was collected. Descriptive statistics were then calculated.

Results: Results: Nine patient charts were collected. Median age was 49 years (34-65) with a median time since eye removal surgery of 20.5 years (10-26). 7/9 patients had a history of eye trauma. On initial presentation, 3/9 had pyogenic granuloma, 4/9 had significant pain, and 5/9 had discharge. 8/9 patients were started on conservative management which involved topical antibiotic and steroid ointment with oral antibiotic. One patient required immediate peg and sleeve excision. Eventually, 5/9 patients required peg sleeve excision and only one patient required implant resection. 7/9 patients had resolved socket complaints at last follow-up. Mean follow-up time was 2.8 years (standard deviation 1 year).

Conclusion: Conclusions: Adequate conservative management may temporize or even eliminate the need for implant resection in most cases of chronic anophthalmic socket inflammation with pegged integrated implants. This offers such patients a viable management option to retain the prosthesis motility afforded by their implant and alleviates the need for further surgery to reconstitute lost orbital volume resulting from implant resection.

Natalie Chen **Medical Student** **Poster # 51**

Defining Supportive Care Needs for Retinoblastoma: A Pilot Study

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Introduction: Survivors and caregivers affected by retinoblastoma (RB) experience unique stressors related to vision loss, facial appearance following treatment procedures, and secondary cancers. Enhancing psychosocial support has been deemed a priority by the RB community, but their supportive care needs (SCN) remain largely unknown. This study aims to identify the proportion and predictors of unmet SCNs amongst RB survivors and caregivers.

Methods: Participants (RB survivors ≥16 years and caregivers of children with RB) responded to a virtual survey that (i) collected demographic/clinical information and (ii) assessed SCNs and distress using validated questionnaires. Descriptive statistics were generated for survivors and caregivers; caregiver-survivors were included in both groups to reflect dual roles. Univariate analysis was conducted to identify associations between distress levels, demographic or clinical variables with the degree of unmet SCNs.

Results: There were 93 participants (29 survivors, 59 caregivers, 5 caregiver-survivors). The proportion of participants with ≥1 unmet SCN was 79% (survivors) and 95% (caregivers). The most common SCN was “uncertainty about the future” (survivors, 88% unmet) and “knowing whom to direct questions to” (caregivers, 33% unmet). Predictors found to have significant associations with degree of unmet SCNs in both groups included age and distress levels. Older survivors ($p=0.020$) and caregivers ($p=0.040$) had fewer unmet SCNs, while survivors ($p=0.047$) and caregivers ($p=0.0039$) with distress experienced greater unmet SCNs. Among survivors, women ($p=0.030$) had greater unmet SCNs compared to men. Among caregivers, those with a longer time since diagnosis ($p=0.011$) had less unmet SCNs. No other significant demographic or clinical predictors were identified.

Conclusion: Most RB survivors and caregivers reported ≥1 unmet SCN. Predictors including age and time since diagnosis had a negative association with degree of unmet SCN, while distress levels and identifying as a woman had a positive association. It is pertinent for medical teams to consider how these predictors may impact SCNs when providing tailored support to members of the RB community.

Youwei, Jeremy Hu **Clinical Fellow** **Poster # 52**

To investigate the accuracy of intraocular lens (IOL) formulas for pediatric patients lacking capsular support implanted with an iris claw IOL (Artisan aphakia IOL, Ophtec BV)

Co-authors: Kamiar Mireskandari, MD, Ophthalmology and Vision Sciences (Sick kids), University of Toronto, Asim Ali, MD, Ophthalmology and Vision Sciences (Sick kids), University of Toronto.

Introduction: To investigate the accuracy of intraocular lens (IOL) formulas for pediatric patients lacking capsular support implanted with an iris claw IOL (Artisan aphakia IOL, Ophtec BV).

Methods: Setting Department of Ophthalmology and Vision Sciences, the Hospital for Sick Children, Toronto, Ontario, Canada. Design: Consecutive retrospective case-series . 41 eligible eyes with lens subluxation from ectopia lentis or microspherophakia from 24 pediatric patients (mean age 10.63 ± 3.99 years) that underwent lensectomy and iris claw intraocular lens implantation were included in the study. The prediction errors (PEs) of the spherical equivalent of six formulas: Barrett Universal II (BU II), Emmetropia Verifying Optical (EVO), Hoffer-Q, Holladay 1, T2 and SRK/T were compared.

Results: All formulas compared yielded myopic PEs before the mean PEs were zero-ed out. After which, SRK/T had the lowest median absolute error (MedAE) at 0.317 diopters, followed by T2 (MedAE: 0.345 D), Holladay 1 (MedAE: 0.406D), EVO (MedAE: 0.415 D), BUII (MedAE: 0.480 D), Hoffer-Q (0.571D). T2 formula has the highest percentage of cases within ± 0.25 D accuracy (43.9%), while SRK/T has the highest percentage within ± 0.5D (65.9%).

Conclusion: SRK/T and T2 formulas are the best performing IOL formulas for pediatric eyes undergoing Artisan aphakia lens with ectopia lentis or microspherophakia in our series.

Farheen Khan **VSRP Student** **Poster # 53**

Evaluation and Adaptation of the FACE-Q Patient-Reported Outcome Measure for Ophthalmology Patients

Co-authors: Ashwin, Mallipatna, MD, Department of Ophthalmology and Vision Sciences, University of Toronto, Karen, Wong-Riff, MD, PhD, Department of Plastic and Reconstructive Surgery, University of Toronto. Asim, Ali, MD, FRCSC, Department of Ophthalmology and Vision Sciences, University of Toronto, Helen, Dimaras, PhD, Department of Ophthalmology and Vision Sciences, University of Toronto.

Introduction: There is a dearth of validated patient-reported outcome measures (PROMs) that evaluate treatment outcomes of patients with corneal anesthesia (CA), retinoblastoma (RB), and strabismus (SB). Previous studies identified appearance-based outcomes as important to CA and RB patients, and it is hypothesized that such outcomes may also be important to SB patients. FACE-Q | CRANIOFACIAL (FACE-Q) is a validated PROM that evaluates appearance-based outcomes of craniofacial patients. This mixed-methods study aims to adapt and validate FACE-Q for use in CA, RB, and SB patients.

Methods: Content validity was assessed through two rounds of cognitive debriefing interviews with CA, RB and SB patients ≥ 8 years old (n=7 per condition per round) to refine seven FACE-Q scales and checklists measuring eye-related (3/7), appearance-based (2/7) and psychosocial outcomes (3/7). The need for additional scales was also evaluated. FACE-Q was iteratively modified based on participant feedback and additional input from an expert panel of clinicians, scientists, and patient advocates. An additional round of interviews was conducted to develop a novel preliminary scale evaluating the appearance of ocular prostheses (OP). The modified PROM, FACE-Q: Ophthalmology, was then field-tested. CA, RB, SB, and OP patients ≥ 8 years old were recruited to complete the FACE-Q: Ophthalmology online via REDCap. New participants (n=200) were recruited for psychometric validation (i.e., Rasch analysis to evaluate item fit, reliability, and validity).

Results: Of the 61 items in the original FACE-Q, 82% were comprehensible and relevant to CA, RB, and SB patients. Cognitive debriefing interviews (n=38) led to adapting five scales generically and creating condition-specific versions of two eye-related checklists. Modifications included removing irrelevant concepts, subdividing checklists, and rewording existing content to enhance comprehensibility and inclusiveness of experiences of visually impaired patients. A novel, preliminary 17-item scale was developed with input from the additional round of interviews (n=6 RB; n=4 eye trauma) to evaluate the appearance of OP. To date, 135 participants (2% CA, 40% RB, 20% SB, and 11% non-RB OP) completed the pilot FACE-Q: Ophthalmology. Psychometric validation results are pending.

Conclusion: The study highlights the importance of a rigorous PROM adaptation process with patient input to enhance relevance, comprehensibility, and comprehensiveness. The newly added concepts relevant to CA, RB, SB, and OP patients indicate the potential for a more meaningful assessment of treatment outcomes. Though psychometrical validation is pending, preliminary insights highlight the promise of the FACE-Q: Ophthalmology in capturing patient perspectives and improving their quality of care.

Mariana Akemi Matsura Misawa **Clinical Fellow** **Poster # 54**

Morning Glory Disc Anomaly in Children: Optical Coherence Tomography as a Prognostic and Management Tool

Co-authors: Michael J. Wan, MD, Department of Ophthalmology and Vision Sciences, Hospital for Sick Children, University of Toronto, Kamiar Mireskandari, MBChB, PhD, Department of Ophthalmology and Vision Sciences, Hospital for Sick Children, University of Toronto.

Introduction: This study reports a series of Morning Glory Disc Anomaly (MGDA) cases in which Optical Coherence Tomography (OCT) was used to guide amblyopia management by assessing the extent of foveal involvement and its correlation with visual prognosis.

Methods: We retrospectively reviewed medical records of patients from 2000 to 2024. Inclusion required a confirmed MGDA diagnosis via high-quality fundus photographs and OCT imaging. Patients with retinal detachment, inability to cooperate with visual acuity testing, or suboptimal imaging were excluded. OCT findings guided discussions with parents on visual prognosis and the benefits versus challenges of patching therapy. Cases were categorized as: no or minimal foveal involvement with preserved external retinal layers, partial foveal involvement with an identifiable fovea and varying external retinal preservation, and absence of an identifiable fovea. This stratification informed treatment decisions.

Results: Six patients (five unilateral, one bilateral) were included in the study. OCT findings of foveal involvement predicted visual outcomes in all cases. Two patients with visual acuity (VA) of 20/20 and 20/32+2, showing minimal foveal involvement and intact inner segment/outer segment (IS/OS) junctions, were managed with observation. One patient with VA of 20/125 and retinal pigment epithelium (RPE) loss in the nasal fovea but intact external retina under the foveal pit underwent patching, improving to 20/80. OCT of another patient with VA of 20/125 revealed disrupted foveal architecture with absence of the IS/OS junction beneath the foveal pit. Due to partial foveal involvement and preserved temporal retina, patching therapy was initiated, but the patient had poor compliance, and vision remained stable. A bilateral case with VA of 20/160 in one eye and retinal detachment in the other (excluded from the study) showed partial foveal pit involvement with preserved retina temporally. Given the poor vision in the fellow eye, amblyopia treatment was not required. Finally, a patient with light perception and an absent foveal pit had poor prognosis. After careful consideration, it was decided not to proceed with occlusion therapy.

Conclusion: OCT is a valuable tool for assessing foveal involvement in MGDA and guiding amblyopia management. In cases with minimal foveal disruption, OCT supports continued therapy, while in severe cases, OCT helps inform decisions to not initiate or discontinue therapy, reducing unnecessary stress for both the child and the family. Sedation or general anesthesia may be required to obtain adequate OCT imaging in severe cases.

Aminat Adama **Graduate Student** **Poster # 55**

Investigation of an Early Transcriptomic Response Induced by LXB4 Neuroprotective Activity Activity

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Introduction: Glaucoma remains a predominant global cause of irreversible blindness, and there continues to be a need to develop neuroprotective strategies to prevent optic nerve degeneration and retinal ganglion cell (RGC) loss across all forms of the disease. We have previously illustrated the neuroprotective activity of the lipid mediator Lipoxin B4 (LXB4). LXB4 promotes the survival of apoptotic RGCs in both acute and chronic models, with higher potency than its more well studied isomer, LXA4. Despite this potency, downstream activity of LXB4 in neuronal cells has yet to be elucidated. Here, we describe early targets of LXB4 transcriptional activity.

Methods: Bulk RNA Sequencing: HT22 neuronal cells were seeded at 1x106 cells/well in high glucose DMEM media overnight. 4 groups; LXA4, LXB4, 15-HETE (an inactive lipoxin precursor) and vehicle were treated at 1µM for 1h in biological replicates. Total RNA was then isolated 1h after treatment, followed by purification and sequencing on an Illumina platform. Data was analyzed bioinformatically for differential gene expression and LXB4-specific transcripts were identified. For validation studies HT22 cells were treated with 1µM LXB4 or vehicle at various timepoints and in combination with neurotoxic injury. In parallel, mRNA was isolated from treated cells for qPCR analyses. The regulation of early LXB4 targets in RGCs was confirmed in-vivo via intravitreal injection of C57BL/6 mice prior to neurotoxic insult and results were quantified by immunofluorescence imaging. Bulk RNA sequencing (following in-vivo LXB4 neuroprotection): C57BL/6 mice (aged 6-8 weeks) were intravitreally injected with 10µM LXB4 and Vehicle 1-hour prior to 10mM kainic acid (KA) insult. After defined timepoints retinas were dissected and RGCs isolated using CD90.2 magnetic microbeads. Total RNA was collected from isolated RGCs, then purified and sequenced on an illumina platform. Bioinformatic analysis was performed to identify injury-dependent genes specific to LXB4 neuroprotection.

Results: Bioinformatic analyses resulted in 242 LXB4-specific genes being identified ($p<0.01$). Of these, the top 10 LXB4-responsive genes prioritized in subsequent analyses. Of these, the top hit was TERT. Validation by qPCR identified a significant 2-fold increase in TERT expression following LXB4 treatment compared to vehicle and/or injury alone. In-vivo assessment of TERT demonstrates similar changes following LXB4 treatment after 3h of neurotoxic injury that is sustained after 20h.

Conclusion: LXB4 neuroprotective signaling results in rapidly increased expression of TERT in-vitro and in-vivo. Additional characterization of LXB4 transcriptional signalling in the context of early injury is ongoing.

Fakhera Salem Alderei **Clinical Fellow** **Poster # 56**

5- Fluorouracil bleb needling efficacy in patients of different ethnic backgrounds

Co-authors: Dr. Catherine Birt, Professor, Department of Ophthalmology and Vision Sciences, University of Toronto.

Introduction: Antimetabolites agents such as 5 Fluorouracil (5- FU) or Mitomycin C (MMC) have been used in bleb needling to help in modulating wound healing and reducing scarring following glaucoma surgery. Despite that, the rate of bleb failure has been reported to be 10 to 20 %. There are many factors that could affect the efficacy of 5- FU bleb needling, yet to the best of our knowledge this is the first study to examine the efficacy of 5-FU bleb needling in different ethnic backgrounds.

Methods: This is a retrospective descriptive cohort study. The research took place at Sunnybrook Health Sciences Centre in Toronto, Canada. The electronic medical records of patients who attended the Ophthalmology Clinic at Sunnybrook Health Sciences Centre data between 2021 and 2024 received 5- FU bleb needling post trabeculectomy or phacotrabeculectomy were reviewed. 108 participants were enrolled in this study. The inclusion criteria for this study were previous trabeculectomy or cataract combined with trabeculectomy, patient-reported ethnic background available on chart, age from 18 to 90 years old, received a 5- FU bleb needling, and a minimum of 6 months follow up post bleb needling. The exclusion criteria for this study were having other types of filtration procedures than trabeculectomy and lost to follow up. The procedure of 5- FU bleb needling was performed as follows. The eye was identified and prepped with betadine, xylocaine gel, phenylephrine 2.5%, and moxifloxacine eye drop. A lid speculum was placed and 0.1cc of 5FU on 1 cc syringe with 30g needle was used. Bleb was needled until flow was established. Then a subconjunctival air pocket created, 0.1 cc 5FU injected posteriorly and then lid speculum was removed. Patient were followed 10 days, 3 months and 6 months after the 5- FU bleb needling. The results of IOP, visual acuity, eye examination and number of the medications were documented in every visit. The primary outcome is to compare the results of the 5- FU bleb needling in controlling IOP among patients of different ethnicities (as self-reported), matched for age within 5 years. Five patients from each of the study ethnicities – Caucasian, African, South Asian, and East Asian will be age matched with a Caucasian patient. The data was summarized using descriptive measures. This included using percentages for categorical variables such as ethnicity and gender while means and standard deviations for continuous variables including age. The main objective of this study was to determine if there is an association between 5- FU bleb needling success rate and the racial background. A chi-square test was used to determine if there was a significant relationship between different ethnicity background and the efficacy of 5- FU bleb needling. Results of IOP reduction were considered significant at $p<0.05$.

Results: The results of IOP, visual acuity, eye examination and number of anti-glaucoma medications were documented in every visit. The results showed that 5- FU bleb needling was more often performed for patients who had combined cataract and trabeculectomy surgery. The ethnicity was 45% for Caucasian, 23%, 16%, and 16 % East Asian, African, and South Asian respectively. The mean age was 72.66. The gender was 53% male and 47 % female. The mean baseline IOP before the procedure was 22.6 ± 7.3 mmHg. The IOP range was 2 to 32 mmHg 10 days after the 5- FU bleb needling. Between 5 to 33 mmHg and 4 to 40 mmHg in 3 month and 6 months post 5- FU bleb needling, respectively. The successful reduction in IOP was statistically significant at $p<0.05$ for Caucasian followed by East Asian, African, and then South Asian ethnicity.

Conclusion: The formation of scar tissue is one of the most common causes of bleb failure post trabeculectomy or combined cataract and trabeculectomy surgery. Antimetabolites agents such as 5 Fluorouracil (5- FU) or Mitomycin C (MMC) have been used in bleb needling to help in modulating wound healing and reducing scarring. It was found that 5- FU bleb needling was performed more often for patients who had combined cataract and trabeculectomy surgery. The success of 5- FU bleb needling in reducing IOP was noticed to be the highest among Caucasian population followed by East Asian, African, and then South Asian ethnicity. The association between 5- FU bleb needling success rate and ethnicity could influence postoperative decision making.

Mohammad Javad Ghanbarnia **Research Fellow** **Poster # 57**

Outcomes of SIBS microshunt implantation in the second-operated eyes of patients with failed vs successful surgery in the contralateral eye

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Introduction: The purpose of this study was to investigate the outcomes of SIBS microshunt implantation in the second-operated eyes of patients who underwent bilateral SIBS microshunt implantation.

Methods: In this single centre, retrospective, cohort study all consecutive patients who underwent bilateral SIBS microshunt implantation between October 2015 and October 2019, were included. Primary outcome measure was the cumulative proportion of complete success at 18 months defined as 1) no 2 consecutive intraocular pressure (IOP) >17 mmHg or clinical hypotony, without glaucoma medications; and (2) ≥20% reduction from decision IOP. Surgical reoperations and reduction of visual acuity to no light perception were also counted towards failure. Secondary outcome measures included complete success with IOP thresholds of 14 and 21 mmHg, IOP and medication reduction after 18 months, post-surgery adverse events and interventions. Identical success criteria were applied to both eyes when evaluating surgical success based on each of the three complete success definitions.

Results: A total of 146 eyes of 73 patients were included in this study. Median (IQR) age at the time of first and second surgery was 57.0 (49.5-65.5) and 58.0 (52.0-66.0) years, respectively. Median decision IOP and classes of medications for the second operated eyes between patients with failed vs successful first surgeries were comparable (24.0 [19.0-30.5] mmHg and 4.0 [3.0-4.0] classes vs 22.0 [19.0-27.5] mmHg and 4.0 [3.0-4.0] classes, P>0.050). At the last visit, median IOP and medication classes significantly decreased to 14.0 (11.0-17.0) mmHg and 0.0 (0.0-3.0) classes in the group with failed first surgery and to 13.0 (10.2-16.0) mmHg and 0.0 (0.0-1.0) classes in the group with successful first surgery compared to baseline (P<0.001). After 18 months of follow-up the cumulative probability of complete success for the second operated eyes of patients with failed vs successful first surgery based on IOP thresholds of 14, 17 and 21mmHg, was 36.3% vs 63.8%, 40.4% vs 66.7% and 42.3% vs 66.9% respectively. Higher rate of distinct post-operative complications was observed in patients with failed compared to successful first surgeries (73% vs 21.9%). The rate of distinct post-operative interventions was 31.7% and 28.1% in patients with failed and successful first surgeries, with 6 and 4 needlings performed in each group, respectively.

Conclusion: SIBS microshunt implantation resulted in significant reduction in IOP and medication burden in the second-operated eyes of both groups with failed and successful first surgery. However, individuals with failed first surgery had lower rate of surgical success and higher rate of complications in their second operated eyes.

Mohammad Javad Ghanbarnia **Research Fellow** **Poster # 58**

Incidence, risk factors and outcomes of hypotony following SIBS microshunt Implantation

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Introduction: Purpose: To investigate the incidence, risk factors and outcomes of early and late-onset hypotony following polystyrene-isobutylene-styrene (SIBS) microshunt implantation in patients with glaucoma.

Methods: In this single centre, retrospective study, all consecutive patients undergoing SIBS microshunt implantation between 2015 and 2019 with at least 1 month of follow up were included. Numeric hypotony was defined as IOP<6mmHg in at least one post-operative visit during the early (within the first 3 months) or late (3 months and beyond) post-operative periods without any clinical signs of hypotony. Clinical hypotony was defined as numeric hypotony plus clinical signs such as choroidal effusion, hypotony maculopathy or shallow anterior chamber. For individuals with hypotony in more than one visit, the first instance of detected hypotony was considered. The first detected clinical sign was recorded as a distinct clinical sign and the first instance of an intervention was recorded as a distinct intervention. Potential risk factors for early clinical hypotony were evaluated in univariable and multivariable binomial logistic models through generalized estimating equation to account for inter-eye correlation.

Results: In total, 416 eyes from 347 patients with median (IQR) age of 61.0 years (52.0-69.0) were included. Median follow up time was 29.5 months (15.4-41.1). Incidence (95% CI) of early post-operative hypotony was 42.3% (37.5-47.2%), including 32.4% numerical and 9.8% clinical hypotony. Incidence (95% CI) of late hypotony was 5.5% (3.5-8.2%) including 3.4% numerical and 2.2% clinical hypotony. Most (88.6%) early hypotony cases occurred during the first post-operative week. Early hypotony was transient and resolved without intervention in 84.7% of eyes. Interventions were required in 10.2% of early hypotony cases all of which involved eyes with clinical hypotony. Median (IQR) time to detection of the first clinical signs and time to the first intervention in eyes with early hypotony were 6.0 days (5.0-29.0) and 12.5 days (2.75-50.75), respectively. Interventions were required in 21.7% of eyes with late hypotony. Median (IQR) time to detection of the first clinical signs and time to the first intervention in eyes with late hypotony were 113.0 days (97.0-194.5) and 113.0 days (99.0-335.0), respectively. After adjusting for confounders, diabetes mellitus (OR 2.59; 95%CI 1.17-5.73) and previous subconjunctival filtering surgery (OR 2.17; 95% CI 1.01-4.36) were significantly associated with increased odds of early clinical hypotony.

Conclusion: Early hypotony is a common transient event following SIBS microshunt implantation, resolving without clinical complications in most cases. Late hypotony is uncommon but requires more interventions. Diabetes mellitus and previous subconjunctival filtering surgery were significantly associated with early clinical hypotony.

Zi Yi Huang **VSRP Student** **Poster # 59**

The Effect of De-insuring Routine Eye Exams in Ontario on Optometric Glaucoma Diagnostic Billings

Co-authors: Graham Trope, MB, PhD, Department of Ophthalmology and Vision Sciences, University of Toronto, Wendy Hatch, OD, MSc, Department of Ophthalmology and Vision Sciences, University of Toronto. Yvonne Buys, MD, Department of Ophthalmology and Vision Sciences, University of Toronto, Ya-Ping Jin, MD, PhD, Department of Ophthalmology and Vision Sciences, University of Toronto.

Introduction: In 2004, Ontario de-insured routine eye exams (REEs) for individuals aged 20-64, with exceptions for those on social assistance or with specifically defined conditions. We assessed the effect of Ontario's delisting of REEs on new glaucoma diagnostic billings by optometrists (ODs).

Methods: We analyzed Ontario Health Insurance Plan (OHIP) billing data from 1998-2019 to determine the annual number of patients with a new glaucoma billing (diagnostic code 365) by ODs per 10,000 population. Analyses were stratified by age group, urban/rural residency, income quintile, and OHIP-defined major vs all exams by ODs. Changes in billings before vs after the 2004 policy change were statistically tested using segmented regression analysis.

Results: In policy affected groups, the number of individuals with a new glaucoma billing by ODs at major exams per 10,000 population decreased significantly from 2004 to 2005: 10.4 (95% CI: -10.9, -9.9; p<.0001) for the 20-39 group and 38.8 (-40.9, -36.8; p<.0001) for the 40-64 group. This represents an immediate reduction of 3,835 newly billed glaucoma patients in the 20-39 group and 15,500 in the 40-64 group. In the policy unaffected 65+ group, the number of patients with a new glaucoma billing per 10,000 was stable after 2004 (+0.10, p=0.9). The percentage of new glaucoma billings by ODs at major exams among all patients with a new glaucoma billing by ophthalmologists and ODs decreased immediately from 2004 to 2005: 11.0% (p<.0001) from 34.9% in 2004 for Ontarians aged 20-39, and 9.9% (p<.0001) from 32.5% for those aged 40-64. The 65+ group saw little change from 20.3% after 2004 (+0.5%, p=0.5). From all exams by ODs, the number of patients with a new glaucoma billing per 10,000 population decreased significantly for all age groups from 2004 to 2005: 28.3 (-29.6, -27.1; p<.0001) for those aged 20-39, 104.1 (-108.2, -100.1; p<.0001) for those aged 40-64, and 30.5 (-38.9, -22.0; p<.0001) for those aged 65+. This corresponds to an immediate reduction of 10,167 new glaucoma billings for the 20-39 group, 42,086 for the 40-64 group, and 5,380 for the 65+ group. Similar patterns were observed in Ontarians residing in rural vs urban areas and in the lowest vs the highest income quintiles.

Conclusion: Ontario's delisting of REEs was associated with significantly reduced optometric glaucoma diagnostic billings at major exams in the policy affected 20-64 groups, irrespective of sociodemographics. Further studies are required to determine if these reductions represent an increase in actual undetected glaucoma.

Patrick Xiang Ji **Medical Student** **Poster # 60**

Ocular Surface Disease with Preserved Vs Preservative-Free Prostaglandin Analogue Drops: A Systematic Review and Meta-Analysis

Co-authors: Andrew Mihalache, MD(C), Temerty Faculty of Medicine, University of Toronto, Xiaole Li, MD(C), Temerty Faculty of Medicine, University of Toronto. Michael Balas, MD, Department of Ophthalmology and Vision Sciences, University of Toronto, Principal Investigator: David J Mathew, MBBS, MS, FRCS (Ophth)(Glasg), PhD.

Introduction: Prostaglandin analogues (PGAs) are first-line treatments for reducing intraocular pressure (IOP) in patients with glaucoma and ocular hypertension. Eyedrops with preservative (such as benzalkonium chloride)-containing (PC) formulations, have been associated with ocular surface disease (OSD). Preservative-free (PF) PGAs offer an alternative that may mitigate the risk of OSD, thereby improving patient comfort, adherence, and long-term treatment outcomes. This systematic review and meta-analysis aims to compare the incidence and severity of OSD, as well as the efficacy in IOP reduction, between PC and PF PGA eyedrops.

Methods: A systematic search was performed across OVID MEDLINE, Embase, and Cochrane Library databases for studies published until October 2024. Continuous outcomes were analyzed using standardized mean differences (SMD) with 95% confidence intervals (CI), while risk ratios (RR) were calculated for dichotomous outcomes. A random-effects model was applied to all outcomes in the meta-analysis.

Results: Thirteen studies were included, encompassing 702 eyes treated with PC-PGAs (57.5±12.3 years; 55.5% females) and 699 eyes tread with PF-PGAs (57.3±12.0 years; 50.2% females). PF-PGAs had significantly lower OSDI scores within six months of treatment compared to PC-PGAs (SMD=0.56; 95% CI: [0.12-1.00]; $p<0.05$; n=157 per group). Additionally, PF-PGAs were associated with significant reductions in lid margin abnormality scores (LAS) beyond six months of treatment (SMD=0.86; 95% CI: [0.49-1.23]; $p<0.001$; PF: n=61; PC: n=63). No significant differences were observed between PF and PC groups for other OSD-related parameters, including tear break-up time (SMD=-0.63; 95% CI: [-1.60-0.34]; p=0.20), Schirmer's test results (SMD=-0.08; 95% CI: [-0.52-0.36]; p=0.72), ocular staining score (SMD=0.66; 95% CI: [-0.30-1.61]; p=0.18), or OSDI (SMD=0.10; 95% CI: [-0.75-0.95]; p=0.82) beyond six months of treatment. Both PF- and PC-PGAs achieved comparable IOP reductions when measured within 2-12 weeks of treatment (SMDs=-0.12 to -0.03; p values=0.34-0.88). There were also no significant differences in rates of hyperemia (RR=0.92, 95% CI: [0.65-1.31]; p=0.65), punctate keratitis (RR=1.04; 95% CI: [0.55-1.97]; p=0.91), or pruritus (RR=0.96; 95% CI: [0.45-2.06]; p=0.92) between PC and PF groups.

Conclusion: This study highlights the potential benefits of PF-PGAs in mitigating short-term OSD symptoms compared to PC formulations, particularly within the first six months of treatment. However, the diminished advantage beyond six months implies that other factors may impact long-term outcomes. Both formulations achieved comparable IOP reductions, reaffirming that PF-PGAs are similarly efficacious as PC-PGAs. Future research studies with larger sample sizes and standardized reporting methods are warranted to elucidate the clinical advantages of PF-PGAs in mitigating adverse events over a longer course of treatment.

Chris Zajner **Medical Student** **Poster # 61**

Visual Acuity Outcomes After Trans Scleral Cyclophotocoagulation: A Systematic Review and Meta-analysis

Co-authors: Michael Balas, MD, Department of Vision Sciences, University of Toronto, David Mathew, MD MMBS, FRCS, Department of Vision Sciences.

Introduction: The aim of this systematic review and meta-analysis is to evaluate best-corrected visual acuity (VA) outcomes following Trans Scleral Cyclophotocoagulation (TSCPC) in patients with refractory glaucoma. While individual studies have reported various outcomes, no comprehensive review of the literature has yet been conducted.

Methods: The full protocol was registered on PROSPERO (42023485891). The electronic databases OVID MEDLINE, and EMBASE were searched using keywords related to TSCPC and visual acuity outcomes (start date to May 12, 2024). Meta-analysis was completed using random effects models and risk ratios to calculate pooled estimates.

Results: In total, 86 studies with 5,915 eyes were included. Weighted mean patient age was 48.8±4.3 years, with 53.0% males (n=3135). Follow-up periods of the studies consisted of 19.8% with less than 1 year follow-up, 38.4% with between 1-2 years, and 40.7% with more than 2 year follow-up. Weighted mean pre-operative VA was 1.17±0.30 logMAR (20/295 Snellen), and 1.40±0.20 (20/502 Snellen) post-operatively. Meta-analysis did not show a statistically significant difference between VA before TSCPC and at last follow-up (Standardized Mean Difference: -0.15, 95% confidence interval: -0.34 to 0.04). At the final follow-up, 37.8% of patients maintained their VA, with 9.0% showing a 1-line improvement,15.8% improving by 2 or more lines, 25.1% decreasing by 1 line, and 12.3% decreasing 2 lines or more. The mean pre-operative IOP was 30.9±8.0 mmHg, which dropped to 17.2±6.5 mmHg, with 70.0% of patients achieving an IOP below 22 mmHg. The average number of glaucoma eye drops decreased from 3.03±1.00 pre-operatively to 2.05±1.11.

Conclusion: These results support the role of TSCPC as a viable treatment option for patients with refractory glaucoma, providing effective IOP control and reduction in eye drops without a marked deterioration in VA.

Jenny Zhang **VSRP Student** **Poster # 62**

Spatially Heterogenous Glial Cell Activation In The Hypertensive Human Optic Nerve Head

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Introduction: Rapid neuroinflammatory responses in the human optic nerve head (ONH) and lamina cribrosa (LC) to elevated intraocular pressure (IOP) remain unclear due to the unique biomechanical properties of this tissue. To investigate these changes, we generated a model of acute IOP elevation in perfused whole-globe human eyes. This model was used to characterize the ONH glial molecular mechanosensitive responses in spatially resolved manners.

Methods: Whole-globe human eyes were received from the Eyebank of Canada within 24h of enucleation according to an Ethics Board-approved protocol. Physiological fluid flow was restored in the eyes by infusion of synthetic aqueous humor into the posterior chamber over 6 hours. For each pair, one eye was maintained at normal IOP of ~15 mmHg, and the contralateral eye maintained an elevated IOP of ~40 mmHg. Four pairs of fixed perfused eyes were used for spatial transcriptomics of the ONH on the Visium platform (10x Genomics). Processing and visualization of spatial sequencing data were performed on SpaceRanger and R. Clustering, differential expression analysis, and pathway module score calculation were performed using Seurat vignettes.

Results: All eyes maintained physiological or elevated IOP for 6 hours. Clustering of spatial spot transcriptomes revealed distinct expression profiles of neighboring ONH subregions that correspond to established anatomical features (eg: neuroretinal rim, prelamina, LC, and retrolaminar optic nerve). Differential expression analysis of the LC cluster identified significantly upregulated genes related extracellular matrix components (p.adjusted = 0.00071) and glial migration (p.adjusted = 0.012) upon pressure insult. Remarkably, integration of our previous mRNA sequencing data from a different cohort of dissected ONH from the same model, revealed a significant increase in the expression score of pressure-induced gene signature in the LC cluster ($p = 0.0026$), but not in any of the other ONH subregion clusters ($p = ns$).

Conclusion: Spatial transcriptomic profiling of the ex vivo human ONH provides direct evidence to support the long-held hypothesis that the LC is the initial site of neuroinflammatory responses following IOP elevation.

Sonia Anchouche **Resident** **Poster # 63**

Aqueous Humour Cytokine Levels in Fuchs Endothelial Corneal Dystrophy

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Introduction: Purpose: Fuchs endothelial corneal dystrophy (FECD) is characterized by progressive corneal endothelium dysfunction and apoptosis of corneal endothelial cells and development of guttae. Although the pathogenesis of FECD is incompletely understood, genetic, endocrine, and environmental factors have been implicated in disease progression. Few reports have assessed the intraocular cytokine levels of patients afflicted with this disease. This study aims to characterize the expression of pro- and anti-inflammatory factors in the aqueous humour of patients with FECD.

Methods: Prospective cohort study. Patients with a diagnosis of either FECD with or without cataract, or cataract only requiring surgical intervention were prospectively enrolled in this study. An anterior chamber paracentesis was performed before surgery and aqueous humour was collected for analysis. The primary outcome of this study is aqueous cytokine expression of interleukin (IL)-1α, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12, IL-13, IL-15, transforming growth factor (TGF)-α, TGF-β (TGF-β-1/-2/-3), FMS-related tyrosine kinase 3 ligand (Flt3L), vascular endothelial growth factor A (VEGF-A), Tumor necrosis factor (TNF)- α, TNF-β, and granulocyte-colony stimulating factor (GCSF) which was measured using multiplex bead array assays. Additionally, we recorded relevant demographic and clinical data for each included participant.

Results: Results: A total of 53 eyes from 45 patients (38 women; 7 men) with FECD were included in this study. 36 healthy eyes from 18 patients undergoing cataract extraction with intraocular lens implant (CE IOL) served as the control group. The average age of the included patients with FECD was 70. Of the FECD phakic patients who underwent surgery, 85% (34/40) of eyes underwent combined Descemet Membrane Endothelial Keratoplasty (DMEK) and CE IOL and 15% (6/40) underwent combined Descemet's Stripping Only (DSO) and CE IOL. 100% (13/13) of the pseudophakic FECD eyes underwent DMEK. Aqueous cytokine expression analysis demonstrated increased expression of TGF-β2 in phakic FECD patients undergoing DMEK + CE IOL when compared to the cataract control group ($p = 0.0040$) and pseudophakic FECD patients undergoing DMEK only ($p = 0.0405$). There is increased expression of TGF-α ($p = 0.0273$), IL-2 ($p = 0.0221$) and IL-22 ($p = 0.0251$) in the cataract control group when compared to the phakic FECD patients. Pseudophakic FECD patients undergoing DMEK had higher expression of GCSF ($p = 0.0314$), FLT3L ($p = 0.0208$) and IL-8 ($p = 0.0425$) when compared to phakic FECD patients undergoing DMEK and CE IOL. There were no statistically significant differences in expression of the remaining cytokines in all three patient groups.

Conclusion: Conclusions: There are distinct inflammatory signatures in FECD phakic patients and pseudophakic FECD patients. Future studies are needed to investigate their contribution to FECD pathogenesis.

Kathrine Bhargava **VSRP Student** **Poster # 64**

Altered levels of aqueous humor cytokines in glaucoma patients undergoing endothelial keratoplasty promote apoptosis in corneal endothelial cells

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Introduction: Glaucoma patients, particularly those that have undergone glaucoma surgery, have poor endothelial keratoplasty (EK) graft survival rates. While various mechanisms have been suggested, the causative etiology remains unknown. Here, we collect aqueous humor (AH) from glaucoma patients undergoing EK and measure levels of 48 cytokines to characterize their AH environment. We also investigate the ability of Tumor Necrosis Factor alpha (TNFα) and Interleukin 6 (IL-6) to promote apoptosis in corneal endothelial cells.

Methods: We prospectively recruited 14 subjects with glaucoma undergoing EK, and 17 subjects undergoing cataract surgery alone as a control group. AH samples were collected at the beginning of surgery, then processed using a 48-analyte bead assay (Millipore). Kruskal-Wallis and Dunn's multiple comparison tests were used to determine significance. For the in vitro apoptosis assay, corneal endothelial cells (HCEC-21T) were treated with various concentrations of TNFα, IL-6, or a combination of TNFα and IL-6. Apoptosis was detected using live-imaging with a caspase 3/7 dye over 72 hours. A Two-Way ANOVA test was used to determine significance.

Results: Twenty-two cytokines (CD40L, CXCL9, EGF, Eotaxin, Flt3L, G-CSF, GM-CSF, GROα, IL-5, IL-6, IL-8, IL-10, IL-12p40, IL-15, IL-17F, IL-22, IP-10, MCP-1, M-CSF, MDC, MIP-1β, and TNFα) showed statistical significance in the glaucoma group compared to the control group. We next investigated the pro-apoptotic effect of TNFα and IL-6 in HCEC-21T. TNFα significantly increased apoptosis at all doses (125, 250, 500, and 1000 ng/mL: 11.53%, 11.12%, 11.49%, and 13.69% respectively), compared to control (6.37%, $p<0.05$). IL-6 showed no difference in apoptosis at all doses (125, 250, 500, and 1000 ng/mL: 2.84%, 2.52%, 2.68%, and 2.16% respectively) compared to control (1.84%, $p>0.05$). To test for a synergistic effect, HCEC-21Ts were treated with a combination of TNFα (125ng/mL) and IL-6 (125ng/mL), resulting in an increase in apoptosis compared to TNFα alone (16.32% vs 11.84%, $p<0.05$) or IL-6 alone (16.32% vs 6.05%, $p<0.05$).

Conclusion: The AH environment of glaucoma patients is enriched in cytokines that are directly cytotoxic to corneal endothelial cells. Therapeutics targeting TNFα and IL-6 signaling could be developed to increase EK graft survival in these high-risk corneal transplant patients.

Narisa Dhupar **Graduate Student** **Poster # 65**

Differential expression of NEAT1 in the central corneal endothelium leads to an altered oxidative stress response in Fuchs endothelial corneal dystrophy

Co-authors: Judy Yan, PhD, Biological Sciences, Sunnybrook Research Institute, Ness Little, BSc, Laboratory Medicine and Pathobiology, University of Toronto. Chao Wang, PhD, Immunology, University of Toronto, Stephan Ong Tone, MDCM, PhD, Laboratory Medicine and Pathobiology, University of Toronto.

Introduction: Fuchs endothelial corneal dystrophy (FECD) is characterized by progressive corneal endothelial cell (CEC) loss and guttae formation that preferentially affects the central corneal endothelium (CE) compared to the peripheral. However, the reasons underlying this distribution pattern remains unknown. Here, we spatially dissected the central and peripheral CE isolated from healthy and FECD cadaveric donors and performed bulk RNA sequencing (RNA-seq).

Methods: The central 8-mm and peripheral CE from healthy (N=3) and FECD (N=3) cadaveric donors were dissected for bulk RNA-seq. Differentially expressed genes (DEGs) were grouped in categories by molecular and biological function. Validation experiments on the long non-coding RNA (lncRNA) nuclear enriched abundant transcript 1 (NEAT1) were done using RNAscope, both gain-/loss-of-function assays, and cell viability assays with hydrogen peroxide (H_2O_2) solution.

Results: DEG analysis of transcriptomic profiles demonstrated an enrichment of genes involved in collagen and extracellular matrix between the central and peripheral CE in both normal and FECD CE, as well as between the normal and FECD CE. We identified NEAT1 as a top DEG, where its expression was decreased in the center CE compared to the periphery. We confirmed decreased NEAT1 expression in the central CE with RNAscope. To investigate spatial differences in susceptibility to oxidative stress, we treated normal cadaveric CE (N=3) with 1.9mM H_2O_2 solution and observed decreased cell viability in the central vs. peripheral CE (42.4% vs. 74.1%, $p<0.05$). We also detected decreased NEAT1 expression in 3 FECD cell lines (FECD-SVF5-54F, -SVF6-61M, and -SVF7-74F) compared to 2 normal cell lines (HCEC-SVN1-67F, -SVN4-68F). FECD cells displayed increased susceptibility to 3.8mM H_2O_2 and decreased cell viability compared to normal CECs (45.4% vs. 94.3%, $p<0.001$). NEAT1 knockdown in normal and FECD cells increased H_2O_2-mediated cell death compared to control cells (61.6% and 25.0%, $p<0.001$), while NEAT1 overexpression in FECD cells completely rescued them from H_2O_2-mediated cell death relative to control cells (61.9%, $p<0.0001$).

Conclusion: We demonstrate that altered NEAT1 expression in the central CE leads to increased oxidative stress and cell death compared to the peripheral CE. As such, NEAT1 is implicated as an important antioxidant in the CE. This provides novel insight into FECD pathogenesis and why the center is more affected than the periphery. Antioxidants targeting NEAT1 signaling could be developed into novel therapeutics for FECD.

Ryan Huang **Medical Student** **Poster # 66**

Comparative Outcomes of Single vs Multiple Cyanoacrylate Tissue Adhesive Applications in the Management of Corneal Thinning and Perforation

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Introduction: Cyanoacrylate glue is commonly used to treat corneal thinning and perforation; however, some cases necessitate multiple applications due to persistent leakage, displaced glue, or progressive thinning. This study aims to compare outcomes between patients treated with a single cyanoacrylate tissue adhesive (CTA) patch for corneal thinning or perforation and those requiring multiple CTA applications.

Methods: We conducted a single-center, comparative cohort study of patients with corneal thinning or perforation treated with either a single or multiple CTA applications in Toronto, Canada, between 2006 and 2024. Primary outcomes were the need for tectonic penetrating keratoplasty (PKP) and the best-corrected visual acuity (BCVA) at final follow-up. Associations between the number of CTA applications with baseline characteristics (age, sex, initial BCVA), perforation characteristics (underlying cause, location, and area), and final outcomes were analyzed using univariable and multivariable logistic regression models, adjusted for age, sex, underlying cause, and location of defect on Stata 17.0.

Results: Overall, 189 patients (median age: 69.0 years; 42% female) were included, with 116 (61%) in the single CTA application group and 73 (39%) in the multiple CTA application group (mean: 2.3 ± 0.6), over a median follow-up of 4.4 months. Baseline characteristics were similar between groups. Central and paracentral corneal defects were more likely to require multiple glue applications than peripheral defects (OR=2.92, 95%CI=1.31-6.51, P=0.009), while corneal defects caused by trauma were less likely to require multiple CTA applications compared to other underlying causes (OR=0.24, 95%CI=0.08-0.69; P=0.005). Patients receiving multiple CTA applications (47%, n=34/73) were more likely to require PKP (OR=2.70, 95%CI=1.42-5.15, P=0.003) than those treated with a single glue patch (26%, n=30/116); however, no difference was observed in final BCVA between groups (median: 2.0 logMAR [single] vs. 2.0 logMAR [multiple]; P=0.838).

Conclusion: Multiple CTA applications were more frequently required for central/paracentral defects and were associated with a greater likelihood of PKP. Given that there was no significant difference in final BCVA between groups, a conservative, stepwise management approach can be pursued without compromising long-term visual outcomes, allowing flexibility in surgical planning.

Ness Little **VSRP Student** **Poster # 67**

Adeno-associated virus mediated expression of Bcl-xL attenuates apoptosis in Fuchs Endothelial Corneal Dystrophy

Co-authors: Judy Yan, PhD, Sunnybrook Research Institute, Narisa Dhupar, BSc, Department of Laboratory Medicine and Pathobiology, University of Toronto. Stephan Ong Tone, MD, PhD, Department of Laboratory Medicine and Pathobiology & Department of Ophthalmology and Vision Sciences, University of Toronto; Sunnybrook Research Institute.

Introduction: Fuchs Endothelial Corneal Dystrophy (FECD) is characterized by corneal endothelial cell loss and the formation of corneal guttae. Currently, there is a global shortage of donor corneas and new strategies are needed to reduce the need for corneal transplantation. While adeno-associated viruses (AAVs) have the capacity to deliver anti-apoptotic genes to human corneal endothelial cells (HCECs), this has not been fully explored as a therapeutic strategy for FECD. This laboratory-based study investigated the ability of AAV-mediated expression of Bcl-xL to attenuate apoptosis in FECD HCECs.

Methods: 17 AAV2 serotypes were screened for transduction efficiency by green fluorescent protein (GFP) expression in normal HCECs. The four AAV2 serotypes with the highest transduction were screened in FECD HCECs, as well as ex vivo specimens from healthy cadaveric donors and FECD patients. Apoptosis was induced using 17μM etoposide or 60μM menadione in FECD HCECs transduced with AAV2/5-Bcl-xL (AAV2/5-CAG-eGFP-P2A-BCLXL), control AAV2/5 (AAV2/5-CAG-eGFP), or no AAV.

Results: AAV2/2, 2/5, 2/6, 2/DJ showed the highest transduction efficiencies in normal (92.20%±10.65, 28.15%±6.00, 33.63%±12.30, 38.05%±12.40) HCECs. AAV2/2 and AAV2/5 transduction remained high in FECD HCECs (44.90%±21.69, 33.22%±19.05), healthy cadaveric donor tissues (56.83%±16.86, 46.86%±14.93), and FECD ex vivo specimens (80.72%±19.70, 66.80%±10.95). AAV2/5-Bcl-xL transduced FECD HCECs with high efficiency (72.71%±10.19) and significantly attenuated etoposide (23.96%±11.54; p=1.55x10-5) and menadione (76.92%±9.54; p=3.40x10-4) induced apoptosis when compared to both AAV2/5-transduced (70.42%±14.35, 90.66%±3.66) and non-transduced HCECs (71.68%±18.70, 90.68%±5.56).

Conclusion: AAV2/2 and AAV2/5 transduced normal and FECD HCECs and ex vivo tissues with high efficiency. AAV2/5-Bcl-xL transduction attenuated both etoposide and menadione-induced apoptosis in FECD HCECs. Future studies may explore using AAVs to deliver other anti-apoptotic genes, target the Bcl-xL pathways as a treatment for FECD, or to attenuate apoptosis related to prolonged corneal donor tissue storage.

Andrew Mihalache **Medical Student** **Poster # 68**

Incidental Ocular Surface Squamous Neoplasia in Pterygia: A Meta-Analysis

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Introduction: Accurately differentiating pterygium from ocular surface squamous neoplasia (OSSN) is critical for effective management. Misdiagnosis can result in inappropriate treatment, increasing the risk of recurrence or tumor progression. This meta-analysis evaluates the prevalence and risk factors for incidental OSSN in clinical specimens of pterygia.

Methods: A systematic literature search was conducted using Ovid Embase, MEDLINE, the Cochrane Library, and Web of Science from January 2000 to February 2025. Included studies analyzed ≥100 clinically diagnosed pterygium specimens via histopathology. Studies were not considered if they explicitly reported pterygium samples that were either not submitted for histopathologic analysis or excluded due to missing data. A random-effects meta-analysis was performed to estimate the prevalence of incidental OSSN in pterygium specimens. Risk factors were evaluated using the Mantel-Haenszel and inverse variance methods, while meta-regression analyzed the influence of publication year, geographic proximity to the equator (km), and country-level estimates of population-weighted average daily ambient UV radiation levels (J/m^2) obtained from the World Health Organization. Subgroup analyses were stratified by continent and leave-one-out sensitivity analyses were performed to assess the robustness of findings.

Results: Twelve studies, comprising 8,688 specimens, identified 202 cases of incidental OSSN (pooled prevalence=1.32%, 95% CI=0.41%–4.21%). Meta-regression analysis revealed that a higher OSSN prevalence was associated with locations closer to the equator ($p<0.01$) and those with greater UV exposure ($p=0.01$), whereas publication year had no effect ($p=0.98$). Age ($p=0.18$), sex ($p=0.45$), and lesion location ($p=0.60$–0.82) did not significantly differ between cases of incidental OSSN cases and benign pterygia. The prevalence of incidental OSSN also did not significantly differ between primary and recurrent pterygium samples ($p=0.23$). Regional analyses revealed considerable variation in the prevalence of incidental OSSN among clinically diagnosed pterygium specimens: Europe (0.29%), Asia (0.76%), North America (1.03%), Oceania (8.57%) and South America (14.97%). The leave-one-out sensitivity analysis, which sequentially excluded individual studies from the primary analysis, yielded a pooled prevalence ranging from 1.06% (95% CI=0.32%–3.56%) to 1.95% (95% CI=0.71%–5.33%), depending on the study omitted.

Conclusion: This meta-analysis identified a 1.32% pooled prevalence of incidental OSSN in clinically diagnosed pterygia specimens, highlighting the potential influence of UV exposure and equatorial proximity. The overlap in demographic and lesion characteristics between benign pterygia and OSSN underscores diagnostic challenges. Future research should focus on enhancing non-invasive diagnostic techniques, investigating immunologic risk factors, and addressing the geographical disparities in this context.

Miller Tasha **Medical Student** **Poster # 69**

Regional differences in corneal endothelial cell densities in Fuchs endothelial corneal dystrophy

Co-authors: Stephan Ong Tone, MDCM, PhD Department of Ophthalmology and Vision Sciences, University of Toronto, Department of Laboratory Medicine and Pathobiology, University of Toronto.

Introduction: Fuchs endothelial corneal dystrophy (FECD) is the most prevalent primary corneal endothelial dystrophy and a leading cause of corneal transplantation. It is characterized by the progressive decline of corneal endothelial cells and the formation of guttae, which impairs the cornea's ability to maintain clarity, leading to corneal edema and a decline in visual acuity. This study aims to quantify regional variations in endothelial cell density (ECD) in both the central and peripheral corneal endothelium in FECD, as determined by specular microscopy. We also investigated the impact of FECD stage, biological sex, and previous intraocular surgery on ECD.

Methods: Charts were reviewed from a single provider located in an academic centre practice from 2023-2024 to identify patients with a diagnosis of FECD and specular microscopy images (Konan Specular CellCheck20Plus). Specular images were acquired from the central, superonasal (SN), superotemporal (ST), inferonasal (IN), and inferotemporal (IT) regions of the cornea. Clinical data such as age, sex, FECD stage, pachymetry, ocular history, and diabetic status were collected.

Results: 274 eyes of 141 subjects were included in the study. The mean age was 70.57 years (range: 41–95), and 66.7% of participants were female. 115 eyes (67.8% female) had no previous intraocular surgery, while 159 eyes (65.6% female) had a history of cataract surgery. Among patients with no previous intraocular surgery, central ECD was lower than that of all peripheral regions in FECD stage 4 or greater surgery (central: 478.61 cells/mm2, ST: 1810.8 cells/mm2, SN: 1436.1 cells/mm2, IT: 967.01 cells/mm2, IN: 1472.7 cells/mm2; $p<0.01$). In stage 5 or greater, the central-inferotemporal differences were no longer observed, and inferotemporal ECD was lower than all other peripheral regions (ST: 1415.5 cells/mm2, SN: 1371.4 cells/mm2, IT: 695.47 cells/mm2, IN: 1211.4 cells/mm2; $p<0.01$). ECD was significantly lower ($p<0.05$) in all peripheral regions of patients with a history of cataract surgery. No differences in ECD were found between biological males or females in any corneal region or at any disease stage.

Conclusion: In more advanced stages of FECD, central ECD is more severely affected than peripheral regions. Peripheral regional differences in ECD were also observed, where the inferotemporal region was more affected than other peripheral regions. A history of intraocular surgery was associated with lower ECDs. No sex differences in ECDs were found across all stages and regions. These regional differences in ECD offer new insights into the pathogenesis of FECD.

Judy Yan **Undergraduate Student** **Poster # 70**

Transforming Growth Factor-Beta Promotes Endothelial-to-Mesenchymal Transition and Alters Corneal Endothelial Cell Migration in Fuchs Endothelial Corneal Dystrophy

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Introduction: Fuchs endothelial corneal dystrophy (FECD) is a progressive corneal disease characterized by corneal endothelial cell (CEC) loss and guttae formation. Elevated levels of TGF-β1/-β2 have been reported in the aqueous humor of FECD patients, and have been implicated with abnormal extracellular matrix (ECM) production, endothelial-mesenchymal-transition (EMT), the unfolded protein response and cell death. However, how TGF-β signaling affects cell migration in FECD remains unknown.

Methods: Aqueous humor (AH) samples from FECD patients (N=37) and control patients undergoing cataract surgery alone (N=17) were analyzed for TGF-β1/-β2 levels using a TGF-β Magnetic Bead Multiplex Assay. Immortalized CECs isolated from FECD patients and normal donors were treated with TGF-β1 or TGF-β2, and RNA sequencing was performed to identify differentially regulated pathways. EMT markers were assessed via western blotting. Morphological changes and (filamentous) F-actin expression were examined under low- and high-confluence conditions using immunofluorescence staining. Migration was assessed using scratch assays to evaluate wound closure rates and migration patterns, and single-cell tracking was used to measure individual cell migration speeds.

Results: We found that TGF-β2 levels were significantly elevated in the AH of FECD patients compared to controls ($p<0.01$). RNA sequencing identified the EMT pathway as one of the top dysregulated pathways in FECD CECs when TGF-β1 and TGF-β2 treatment was added. Western blotting confirmed that EMT markers FN1, αSMA, ZEB1 and SNAI1 were upregulated in both normal and FECD CECs following TGF-β1/-β2 treatment ($p<0.05$). The addition of TGF-β also showed increased F-actin expression and more EMT-like phenotype in confluent conditions ($p<0.05$). TGF-β1 and TGF-β2 significantly enhanced wound closure as detected by scratch assay ($p<0.05$), and mean speed as detected by single cell analysis ($p<0.001$) for both normal and FECD cells.

Conclusion: Increased TGF-β signalling promotes EMT and alters cellular migration in both healthy and FECD CECs. These findings highlight TGF-β as a potential therapeutic target for modulating CEC migration.

Lina Chen **Research Associate** **Poster # 71**

Aqueous Cytokine Levels in Uveitic Macular Edema: Baseline Profiles and Changes Following Intravitreal Aflibercept Injection

Co-authors: Michael, Balas, Manlong, Xu, Stephan, Ong Tone, Panos, Christakis.

Introduction: This study is to evaluate baseline cytokine levels and their changes following intravitreal aflibercept (IVA) injections in patients with recurrent uveitic macular edema (UME) as compared to healthy controls.

Methods: Seven patients with UME and 18 age-matched healthy controls underwent routine cataract surgery were included. Eyes with a history of macular hole, infectious uveitis, proliferative retinopathy, or retinal detachment were excluded. Central subfield thickness (CST) was measured monthly from baseline. 60-80µl of anterior chamber aqueous humor (AH) was extracted via paracentesis. The concentrations of 17 cytokines in the aqueous humor (AH) were measured using the MILLIPLEX Human Angiogenesis/Growth Factor Magnetic Bead Panel 1 at baseline and follow-ups. IVA re-treatments were performed at the time of UME recurrence until the last recurrence at the endpoint of the study. Cytokine levels between patients and healthy controls, and between baseline and different timepoints were compared using the Wilcoxon signed-rank test. Spearman's correlation was applied to measure the association between cytokine levels and CST.

Results: The average age of patients was 69.6 years (SD 15.2) and 5 out of 7 were females; 4 to 8 samples were collected from each study eye during the 5.1 to 25.5 months of follow-up. At baseline, patients with UME had a CST ranged from 267 to 923 um (median 471um). These patients also had significantly higher G-CSF ($p<0.001$) and VEGF-A ($p<0.05$), and lower EGF ($p<0.05$) compared to healthy controls. At one month following the initial IVA treatment, the baseline G-CSF ($R=0.71$, $p=0.088$) and IL-8 ($R=0.68$, $p=0.10$) showed moderate correlations with CST reduction, though not statistically significant. At the last recurrence of UME, there was a significant decrease in VEGF-A (-151.5 pg/ml, $p<0.05$), and notable decrease in Leptin (-830.6 pg/ml, $p=0.53$) and G-CSF (-1276.7 pg/ml, $p=0.67$) when compared to the baseline. Most other cytokines, including VEGF-C, VEGF-D, FGF-1, Endoglin, EGF, PLGF, Follistatin, Angiopoietin-2, Endothelin, and BMP-9 exhibited no significant change.

Conclusion: Patients with UME had significantly elevated G-CSF and VEGF-A, and lower EGF levels compared to healthy controls. While initial response to IVA treatment showed moderate, albeit non-significant, correlations between baseline G-CSF and IL-8 levels and reduction in CST, repeated IVA was associated with a significant decrease in VEGF-A at the final UME recurrence. Leptin, G-CSF, and a range of angiogenic and growth factors showed no significant change over time. These findings highlight the role of VEGF-A and G-CSF in UME pathophysiology and suggest that targeted anti-VEGF therapy may help modulate the inflammatory and angiogenic milieu in this patient population.

Angelica Hanna **Medical Student** **Poster # 72**

Factors Associated with Late Presentation for Cataract Surgery: A Case Control Study

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Introduction: Cataracts are the leading cause of reversible blindness worldwide. Despite the safety and efficacy of cataract surgery, some patients delay assessment until severe vision loss occurs, impacting quality of life and making surgery more complex—even in a universal healthcare system. This study examines the characteristics of patients presenting with advanced cataracts and their postoperative outcomes.

Methods: A case-control study was conducted using a chart review of patients seen at Prism Eye Institute between January 2022 and July 2024. Consecutive patients presenting for cataract assessment with a best corrected visual acuity (BCVA) of 20/200 or worse were considered “late presenters”. Consecutive patients presenting with BCVA greater than 20/200, was also assessed, as a control group of “early presenters”. Patients for which cataract was not the reason for vision loss were excluded. Patient age, sex, socioeconomic status, and comorbidities were compared. BCVA at postoperative week one and intraoperative complications were also assessed. (UofT REB #00047423)

Results: 250 late presenters and 250 controls were collected and analyzed. There were no sex differences between groups (53% female late presenter group and 56% female control group, p=0.419). The median ages of patients in the late and early presenter groups were 69.0 and 71.5 years, respectively, with the late presenter group being slightly younger (rank-biserial correlation = 0.14, p=0.001). There was no difference in the patient’s neighbourhood-based income (p=0.3). Patients presenting late for cataract surgery had significantly more systemic comorbidities compared to those who presented earlier (rank-biserial correlation = 0.14, p=0.002). Compared to controls, patients in the late presenter group were significantly more likely to have diabetes (OR 1.91, 95% CI 1.29 - 2.84). Late presenters were also significantly more likely to have a physical disability compared to early presenters (2.4% vs 0%, p = 0.03). At postoperative week one, late presenters had a median BCVA of 20/40 while early presenters had a median vision of 20/25 (p<0.001). Late presenters were significantly more likely to have intraoperative complications including retained lens fragments, posterior capsule rupture and corneal edema, compared to early presenter controls (OR = 2.77, 1.20 – 6.39).

Conclusion: Compared to early presenters, late presenters for cataract surgery are more likely to have multiple systemic comorbidities, diabetes and physical disabilities. Patients presenting late for cataract surgery are more likely to have intraoperative complications and worse postoperative vision. Further research is required to reduce disparities and system wide efforts are required to minimize late presentation for cataract surgery.

Angelica Hanna **Medical Student** **Poster # 73**

Follow up After Cataract Surgery: A Survey of Practice Patterns at the Kensington Eye Institute

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Introduction: Cataract surgery is one of the most frequently performed surgeries in Canada. Advances in surgical techniques have significantly improved patient outcomes and surgical safety. Evidence suggests that in person assessment immediately after surgery may not be necessary. Globally, practice patterns for follow up after surgery vary. The purpose of this study was to explore the current follow-up practices of ophthalmologists in Toronto after routine cataract surgery.

Methods: A survey of practice patterns of cataract surgeons at the Kensington Eye Institute was conducted through in-person interviews. Surgeon demographic information was collected. Follow up practices including time points of postoperative assessments, virtual versus in-person visits, and components of the routine postoperative assessments were collected. Descriptive statistics were used to summarize findings. (UofT REB Protocol #00047423)

Results: 29 cataract surgeons were interviewed. 65% were male and 35% were female. The mean time in practice was 16 years (range 1-39 years). 35% were comprehensive ophthalmologists and 65% had subspecialty training. 73% of surgeons performed an assessment on or before postoperative day one, with 35% performing their first assessment on the day of surgery and 38% preforming the first assessment on postoperative day 1. 97% of surgeons had a follow up within the first week of surgery. A total of 35% of surgeons used a phone call for their first postoperative assessment and the remaining 65% had in-person assessments. Of the 35% who used a virtual first postoperative assessment, 50% called on the day of surgery and 50% called on postoperative day one. 64% of surgeons reported that they routinely performed two total assessments with patients and the remaining 36% reported three total postoperative assessments. None of the surgeons used a virtual follow up modality for postoperative assessments two or three. 45% of surgeons did not routinely use any intervention to prophylactically lower the intraocular pressure after surgery, however 36% of surgeons used a single application of a topical pressure lowering drop immediately postoperatively, and 24% of surgeons routinely prescribed a topical pressure lowering agent for several days after surgery. 85% of surgeons reported routinely performing a posterior segment exam, with 72% reporting that they performed a dilated exam before discharging their patients.

Conclusion: There is significant variability in postoperative cataract surgery practice patterns with no single current standard of care. Building further evidence through high quality studies and streamlining follow up after cataract surgery may have significant implications for patient experience, safety and overall health system efficiency.

Setting the Foundation for the Development of a Patient- and Provider-Informed Cataract Surgery Care Model

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Introduction: Purpose of this study is to refine and pilot-test our previously created appropriateness and prioritization tool, assessing its practicality and effectiveness within a multi-cultural Canadian healthcare context.

Methods: This is a Prospective mixed-methods study approach using qualitative semi-structured interviews and quantitative interviews. Demographic and clinical characteristics were also collected for recruited patients. In stage one, patients provide detailed feedback on the 3-item abridged questionnaire's (Catquest-9SF) clarity, wording, and layout. Their qualitative insights informed improvements to the tool. In stage two, a refined tool was presented. We recorded completion time and noted any assistance required. We analysed the tool's responses for variations, missing values, and correlations between demographics and visual acuity. Based on visual acuity, PROMs only, and the tool's responses, three distinct waiting lists were generated to assess prioritization for cataract surgery. This feedback optimized the tool's clarity and utility, preparing it for larger scale testing.

Results: A total of 60 patients were enrolled, of which 48.3% were female, with a mean age of 70.9 years. In stage one (n=20), all patients understood the three questions presented and expressed preference to complete questionnaire at Ophthalmologist consult and in written format. 10% (2 patients) required assistance in completing the questionnaire. In stage two (n=40) the mean time to complete the questionnaire was 85.5 seconds, and 18.3% (11 patients) needed assistance in completing the questionnaire which mostly was due to language barrier. The median for visual acuity in the worst eye was 0.42 logMAR. (IQR: 0.23-0.61). There was a significant positive correlation between the questionnaire's scores and visual acuity. (Spearman correlation coefficient = 0.5168, P = 0.00002).

Conclusion: The abridged questionnaire demonstrated practicality in a clinical setting, with short administration time, and clear comprehension among patients in the Canadian healthcare context. Its correlation with visual acuity supports the tool's effectiveness in assessing the impact of cataract severity on visual function. Our findings suggest that this tool could help create more tailored waiting lists, potentially enhancing patient-centered care and optimizing surgical outcomes. Larger-scale testing in clinical practice is to follow.

Carmen Balian **Research Associate** **Poster # 75**

Documenting the subjective patient experience of first versus second eye during immediate sequential bilateral cataract surgery

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Introduction: To examine the subjective experience after immediately sequential bilateral cataract surgery.

Study Design: Prospective intraindividual observational study

Methods: Patients completed a questionnaire immediately after bilateral cataract surgery at a single multisurgeon facility.

Results: 200 patients who underwent immediately sequential bilateral cataract surgery completed the questionnaire while in recovery. Surgery was rated as taking longer in the first eye by 41 patients (20.5%) and in the second eye by 83 (41.5%); 57 (28.5%) reported no difference and 19 (9.5%) were unsure. Discomfort and pressure were reported by 21 patients (10.5%) as worse for the first eye, 106 (53%) for the second eye, 69 (34.5%) as no difference and 4 (2%) unsure. Reported pain level during surgery in the second eye was significantly greater than the first eye ($P < 0.001$). Of the 61 patients who rated the second eye surgery as taking longer and being more uncomfortable, only 8 (13.1%) were more relaxed during the second procedure.

Conclusion: These results can help surgeons when counselling patients regarding expectation for immediately sequential bilateral cataract surgery.

Moiz Lakhani **Medical Student** **Poster # 76**

Drugs Associated with Floppy Iris Syndrome: A Real-World Population-Based Study

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Introduction: Intraoperative floppy iris syndrome (IFIS) has been associated with a higher rate of severe intraoperative complications and increased visual morbidity during cataract surgery in females compared to males. This pharmacovigilance analysis aims to identify FDA-approved drugs that are disproportionately associated with IFIS and to elicit whether there are sex differences in these reports. Understanding these differences is crucial for optimizing the preoperative planning of cataract surgery.

Methods: This study evaluated cases of IFIS submitted to the Food and Drug Administration Adverse Event Reporting System (FAERS) from Q4 2003 to Q1 2024. We evaluated the disproportionality of IFIS reports through various metrics, including reporting odds ratios (RORs), proportional reporting ratios (PRRs), relative risk reductions (RRRs), chi-squared ($\chi 2$) values, p-values (with a Bonferroni-adjusted significance threshold of 0.0011), and Bayesian confidence propagation neural network (BCPNN) information components (ICs). Drug-specific reports of IFIS were compared to those for all other drugs in the database, and only signals for positive adverse drug reactions (i.e., $n > 2$, $\chi 2 > 4$, $PRR > 2$) in accordance with Evans criteria were considered. Subgroup analyses based on sex were performed. This study utilized de-identified public data, which did not require institutional ethics approval.

Results: A total of 12,345,128 unique adverse event reports were retrieved, including 649 cases of IFIS (0.0053%). The drugs with the highest disproportionality of IFIS reports were imipramine (ROR = 251.66, 95% CI = 157.53 - 402.02), tamsulosin (ROR = 171.44, 95% CI = 143.12 - 205.36), and chlorpromazine (ROR = 91.30, 95% CI = 49.91 - 167.03) all of which were $p < 0.0001$, $IC025 > 0$. Additionally, α1-blockers, tricyclic antidepressants (TCAs), and atypical antipsychotics were the most over-reported drug classes for IFIS, followed by carbonic anhydrase inhibitors, corticosteroids, 5α-reductase inhibitors, β-blockers, prostaglandin analogs, and β2-agonists. Notably, IFIS was disproportionately reported among females using brinzolamide (ROR = 409.63, 95% CI = 196.78 - 852.73) and salbutamol (ROR = 67.12, 95% CI = 28.37-158.80) both of which are $p < 0.0001$, $IC025 > 0$; however, these associations did not hold in males.

Conclusion: Our novel pharmacovigilance analysis identified α1-blockers, TCAs, and atypical antipsychotics as the drug classes most disproportionately associated with reports of IFIS. These associations, along with the sex differences identified, should be considered during perioperative counseling and surgical planning for patients undergoing cataract surgery.

David Mikhail **Medical Student** **Poster # 77**

Quantitative Analysis of Instrument Motion Paths in Cataract Surgery Throughout a Resident's Training

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Introduction: With an aging population, there is an increasing need for efficient, objective tools to train resident ophthalmologists to perform cataract surgery. Traditional assessments relying on subjective feedback lack standardization, prompting the development of data-driven motion tracking to quantify surgical skill. This study aimed to objectively quantify the motion paths of surgical instruments during cataract surgery across a resident's training period, identifying patterns of skill acquisition and proficiency development.

Methods: A total of 100 cataract surgery videos performed by a single resident from their 6th to 760th case were collected. Advanced motion tracking software (Computer Vision Annotation Tool [CVAT]) was utilized to annotate and track the trajectories of 11 surgical instruments on a frame-by-frame basis. Six key motion parameters – total path length, average velocity, average acceleration, root mean square (RMS) jerk, average angular change, and workspace coverage – were extracted for each instrument in each video. Monotonic trends were assessed using the Mann-Kendall test and Theil-Sen slope estimation, with Spearman's correlation measuring the association between case number and performance metric values. Pettitt's change-point analysis identified significant transitions in the resident's skill progression.

Results: All 11 instruments demonstrated statistically significant reductions in at least one motion parameter. Path length consistently decreased across training, with the largest reductions seen in the cannula (-11.8%, 95% CI: [-17.4%, -6.8%], $p<0.001$), phacoemulsification handpiece (-11.5%, 95% CI: [-14.1%, -8.7%], $p<0.001$), and cystotome (-8.9%, 95% CI: [-11.8%, -5.9%], $p<0.001$). The cystotome also showed the greatest improvement in average angular change (-1.70°, 95% CI: [-2.22°, -1.16°], $p<0.001$). Pettitt's analysis a significant shift in surgical efficiency around case 300 for most instruments, although improvements in certain advanced tasks (e.g., lens implantation) emerged later.

Conclusion: This large-scale, frame-by-frame motion tracking study revealed distinct, instrument- and task-specific learning curves in cataract surgery that underscore both increasing efficiency and refined precision. The shift around case 300 may signify a key milestone in the resident's proficiency. These findings underscore the potential of objective, video-based motion tracking analytics to provide data-driven resident feedback, thereby guiding targeted instruction and standardizing cataract surgery training.

Ryan Huang **Medical Student** **Poster # 78**

Loss to Follow-up in Patients with Neovascular Age-Related Macular Degeneration Receiving Intravitreal Anti-VEGF Injections

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Introduction: Intravitreal anti-vascular endothelial growth factor (anti-VEGF) therapy represents the standard of care for neovascular age-related macular degeneration (nAMD). However, effective treatment relies on consistent patient follow-up, as treatment interruptions can lead to disease progression and irreversible vision deterioration. This study aims to investigate the demographic, clinical, and treatment-related risk factors associated with being lost to follow-up (LTFU) among patients with nAMD receiving anti-VEGF intravitreal injections (IVIs).

Methods: We conducted a multicenter, retrospective review of patients with nAMD treated with anti-VEGF IVIs over a 10-year period in Toronto, Canada from January 2012 to December 2021. The primary outcome was the proportion of patients LTFU, defined as the absence of an ophthalmic visit within one year of the last appointment with the treating retinal specialist. Univariable and multivariable logistic regression analyses were conducted to examine associations between demographic, clinical, and treatment-related factors with LTFU rate.

Results: Among 2,556 patients with nAMD, 527 (21%) were LTFU over a mean follow-up of 65 ± 15 months. In the multivariable analysis, males (vs females, odds ratio [OR]=1.40, 95%CI=1.15-1.88; p<0.001), patients living further from the point of care (>200 vs ≤20 km, OR=2.51; 95%CI=1.60-4.22; p<0.001), and those with multiple comorbidities (≥3 vs none, OR=1.39; 95%CI=1.07-1.91; p=0.01) were more likely to be LTFU. Compared with White patients, Black patients (OR=2.07, 95%CI=1.48-3.19; p<0.001) and Hispanic patients (OR=1.70, 95%CI=1.23-2.46; p<0.001) were also more likely to be LTFU. In contrast, older patients (≥90 years vs age <70 years, OR=0.53, 95%CI=0.38-0.69; p<0.001), those with worse baseline visual acuity (>20/200 Snellen vs 20/40 Snellen or better, OR=0.72, 95%CI=0.45-0.96; p=0.03), pseudophakia (vs phakia, OR=0.80, 95%CI=0.60-0.98; p=0.04), bilateral eye involvement (vs unilateral involvement, OR=0.72, 95%CI=0.50-0.90; p=0.01), and those with a high anti-VEGF IVI burden in the first year following treatment initiation (vs low treatment burden, OR=0.55, 95%CI=0.37-0.70; p<0.001) were less likely to be LTFU. On optical coherence tomography (OCT), patients with baseline intraretinal fluid (vs none, OR=0.71, 95%CI=0.55-0.97; p=0.03) and subretinal fluid (vs none, OR=0.75, 95%CI=0.59-0.96; p=0.02) were also less likely to be LTFU.

Conclusion: Male sex, greater travel distance, those with multiple comorbidities, and Black or Hispanic race/ethnicity increased LTFU risk, while older age, worse baseline visual acuity, pseudophakia, bilateral disease, presence of fluid on OCT, and higher treatment burden were protective. These findings can inform the development of targeted retention strategies for high-risk patients to optimize long-term visual outcomes in patients with nAMD.

Moiz Lakhani **Medical Student** **Poster # 79**

Association of Glucagon-like Peptide-1 Receptor Agonists with Ischemic Optic Neuropathy and Retinal Detachment: A Global Population-Based Study Across 180 Countries

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Introduction: Despite the proven efficacy of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) for treating type 2 diabetes and obesity, the risk of reported ocular adverse events (AEs) has raised concerns regarding their ophthalmic safety. We conducted a real-world, population-based disproportionality analysis to investigate the association between optic nerve and retinal AEs and GLP-1 RAs.

Methods: This global, observational pharmacovigilance study analyzed ocular data from the US FAERS (Jan 2004–Sept 2024) and WHO VigiBase (Jan 2004–Dec 2024) databases, focusing on new-generation GLP-1 RAs, semaglutide and tirzepatide. Reports of optic nerve and retinal AEs were analyzed using OpenVigil 2.1 (FAERS) and VigiAccess (VigiBase). Disproportionality metrics included reporting odds ratios (RORs), 95% confidence intervals (CIs), chi-squared ($\chi 2$) values, p-values, and Bayesian confidence propagation neural network (BCPNN) information components (IC). A p-value < 0.05 indicates statistical significance, and a positive signal was defined as IC025 > 0. The controls were all other drugs for FAERS and metformin for both databases.

Results: In FAERS, 12,936,341 AE reports were retrieved, with 76,444 (0.59%) involving newer GLP-1 RAs. Semaglutide showed significantly higher odds of ischemic optic neuropathy (ION) (ROR=11.12, 95%CI=8.15-15.16) and retinal detachment (ROR=2.44, 95%CI=1.70-3.52) compared to all other drugs (all P<0.0001, IC025≥0.63). Compared to metformin, the RORs were higher and statistically significant for both AEs. In Vigibase, 35,000,000 AE reports were extracted, with 117,173 involving newer GLP-1 RAs. Semaglutide was associated with significantly higher odds of ION (ROR=66.83, 95%CI=16.31-273.74) and retinal detachment (ROR=8.44, 95%CI=4.19-17.00) compared to metformin (all P<0.0001, IC025≥0.80). Other optic nerve and retinal AEs were predominantly associated with semaglutide, with no significant risk for tirzepatide.

Conclusion: The widespread use of GLP-1 RAs and their potential link to serious ocular AEs underscores the need for ongoing global pharmacovigilance among the general population. This study is the first global observational post-market surveillance analysis to report an association between semaglutide and a diverse set of optic nerve and retinal adverse events, using data from both the US FAERS and WHO Vigibase databases. While semaglutide shows a disproportionately higher association with certain optic nerve and retinal AEs, further post-marketing surveillance is needed to clarify these associations.

Xiaole Li **Medical Student** **Poster # 80**

Outcome-Reporting Bias in Ophthalmology Clinical Trials Between 2014–2023

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Introduction: Outcome-reporting bias (ORB) in randomized controlled trials (RCTs) occurs when trial endpoints are selectively or inadequately reported. Recognizing ORB is important because it can exagerrate intervention benefits, compromise clinical guidelines, and lead to suboptimal patient care and resource allocation. This cross-sectional study investigated the prevalence and extent of ORB in seminal ophthalmic RCTs.

Methods: Following PRISMA guidelines, we systematically searched Embase, MEDLINE, and CENTRAL for ophthalmic RCTs published in the ten highest-impact ophthalmic and general medical journals between 2014 and 2023. Incompletely reported outcomes were defined as those lacking sufficient data for meta-analysis, while unreported outcomes were those present in trial protocols but absent from the primary publication. A logistic regression was performed for the association between publication year and incomplete reporting. The association between statistical significance (favoring the exxperimental intervention) and completeness of reporting was calculated as an odds ratio (OR) for eligible trials, which were then synthesized via meta-analysis. Discrepancies between pre-specified primary and secondary outcomes in trial protocols and their final publications were also analyzed.

Results: Among 9,436 screened records, 260 ophthalmic RCTs met inclusion criteria. Of these, 167 (64.2%) had at least one incompletely reported outcome, and 124 (47.7%) had at least one unreported outcome. Primary outcomes were incompletely reported in 30 (11.5%) trials and unreported in 2 trials (0.1%), while secondary outcomes were incompletely reported in 146 (56.2%) trials and unreported in 108 trials (41.5%). For primary outcomes, 10.2% (SD ± 29.0%) were incompletely reported, while only 0.4% (SD ± 4.7%) were unreported. Among secondary outcomes, 42.2% (SD ± 38.4%) were incompletely reported, and 25.9% (SD ± 34.0%) were unreported. No significant temporal trend was observed for incompletely reported ($P = 0.44$) nor unreported outcomes ($P = 0.15$). Statistically unfavorable outcomes were more likely to be incompletely reported than statistically favorable outcomes (OR: 3.31, 95% CI: 2.41–4.56, $P < 0.001$). Discrepancies between protocol-specified and published outcomes were identified in 121 (46.5%) trials. Of 32 trials (12.3%) with discrepancies in primary outcomes, 23 (71.9%) omitted protocol-specified primary outcomes and 9 (28.1%) reclassified a primary outcome as secondary in the final publication. Among 105 (44.4%) trials with discrepancies in secondary outcomes, 94 (90.0%) omitted protocol-specified secondary outcomes and 20 (19.0%) reclassified a secondary outcome as primary.

Conclusion: Selective outcome-reporting bias remains prevalent in ophthalmic RCTs. Strengthening adherence to pre-specified protocols and improving transparency in outcome reporting are essential to mitigate ORB and enhance trial validity.

Xiaole Li **Medical Student** **Poster # 81**

Use of Patient-reported Outcomes in Ophthalmology Clinical Trials Between 2014–2023

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Introduction: Patient-reported outcomes (PROs) evaluate health and functional status, and patient-reported outcome measures (PROMs) are standardized tools for measuring these outcomes. PROs provide valuable insights into treatment efficacy, safety, and practicality that would not otherwise be captured by traditional clinical endpoints. However, the state of PRO integration in ophthalmology RCTs is unknown. Therefore, this cross-sectional analysis aims to investigate the use, interpretation, and reporting of PROs and PROMs in ophthalmic randomized controlled trials (RCTs) between 2014–2023.

Methods: Following PRISMA guidelines and using Embase, MEDLINE, and CENTRAL, we systematically searched the top ten highest impact factor ophthalmic and medical journals for ophthalmic RCTs published between 2014–2023. We assessed the frequency of PRO inclusion as endpoints and evaluated the quality of PRO reporting using the CONSORT PRO extension. Multivariable analysis was performed to explore the relationship between PRO utilization and study-level and journal-level characteristics.

Results: Of 9436 records screened by six independent reviewers, 333 ophthalmic RCTs met eligibility criteria. Of the included ophthalmic RCTs, 87 (26.1%) incorporated at least one PRO and 28 (8.4%) used PROs as primary outcomes. Most studies (83/87, 95.4%) leveraged PROMs to measure PROs, with ophthalmology-specific PROMs being the most common (61/83, 73.5%). Minimal important differences (MIDs) were rarely applied (2/87, 2.3%) for PRO interpretation. At least 8 of the 13 CONSORT PRO Extension items were reported in 29 (33.3%) studies. Trials with primary PRO outcomes adhered better to these guidelines than those with secondary PRO outcomes ($P < 0.001$). Lack of PRO utilization was associated with lower 5-year journal impact factor (aOR 0.99, 95% CI 0.98–1.00, $P = 0.037$) and pharmaceutical interventions compared to health service interventions (aOR 0.15, 95% CI 0.03–0.67, $P = 0.013$).

Conclusion: The use and interpretation of PROs, which offer a meaningful adjunct to objective trial endpoints, is limited in high-impact ophthalmic RCTs. Future trials should incorporate robust, validated PROMs tailored to specific ocular conditions and establish MIDs for interpretation. Collectively, these efforts will contribute to the advancement of patient-centered care in ophthalmology.

Aswen Sriranganathan **Medical Student** **Poster # 82**

Parametric Trends in US Cost-Effectiveness and Cost-Utility Studies in Ophthalmology

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Introduction: Cost-effectiveness analyses (CEA) and cost-utility analyses (CUA) rely on input parameters such as willingness-to-pay (WTP) thresholds, which are frequently derived from outdated economic data and do not reflect current economic and health landscapes.

Methods: A cross-sectional analysis performed to (1) evaluate the frequency of input parameters used in CEAs within ophthalmology and (2) examine temporal trends in studies conducted in the United States. Data were extracted from the Tufts Medical Center CEA Registry (1993-2022), including all studies assessing diseases of the eye and adnexa. Primary outcome measures collected were willingness-to-pay thresholds, funding sources, intervention types, and disease classifications.

Results: A total of 82 US-based CEAs met the inclusion criteria, covering a range of ophthalmologic diseases and interventions. All studies assessed outcomes in quality-adjusted life years (QALYs). WTP thresholds of $50,000 (41%) and $100,000 (39%) were most frequently reported, with $150,000 emerging in 9% of studies since 2019. Discounting at 3.0% for costs and QALYs was universally applied. Government (33%), nonprofit (29%), and pharmaceutical (17%) funding predominated. Pharmaceutical-funded studies often employed higher WTP thresholds of $100,000 (29%) and $150,000 (29%). The most common intervention types were surgical (40%) and pharmaceutical (40%), while diseases of the choroid and retina (43%) were most frequently studied. Healthcare perspectives (17 studies) were more commonly reported than societal perspectives (6 studies).

Conclusion: US-based ophthalmology CEAs commonly use $50,000-$100,000 WTP thresholds and a 3.0% discount rate, with higher thresholds emerging recently. Public and nonprofit funding predominates, focusing on retinal diseases and surgical or pharmaceutical interventions. Reassessing fixed WTP thresholds and incorporating societal perspectives could improve CEAs' relevance and equity, ensuring alignment with evolving economic and healthcare landscapes.

Dana Taghaddos **Medical Student** **Poster # 83**

Parental Leave in Surgery: A Systematic Review of Policies, Practices, and Career Equity

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Introduction: Appropriate parental leave policies are critical for promoting work-life balance and career satisfaction among medical professionals. However, surgical specialties pose unique challenges due to their intense training demands, long working hours, and the need for sustained clinical competence. This systematic review examines parental leave practices in surgery, exploring policy awareness, utilization, and their impact on career progression, job satisfaction, and gender equity.

Methods: A systematic search of PubMed, Embase, Scopus, and Web of Science was conducted for studies published between January 2000 and August 2024. Eligible studies included male and female surgeons, fellows, and residents who had taken or were eligible for parental leave. Data extraction included demographics, parental leave characteristics, policy awareness, financial support, and perceived career impacts. Study quality was assessed using the CLARITY Risk of Bias Instrument and the Newcastle–Ottawa Scale.

Results: Thirty-eight studies, encompassing 11,785 surgical participants, met inclusion criteria. Only 19.0% of respondents utilized parental leave, with higher rates among females (66.8%) than males (9.1%). Maternity leave averaged 12.2 weeks, while paternity leave averaged 2.2 weeks. Financial compensation during leave was available to 53.2% of participants. Awareness of parental leave policies was reported by 43% of participants, while 31.2% stated that the policies were readily accessible. Negative experiences, stigma, and concerns about career advancement were common, especially among female respondents. Qualitative analyses revealed themes of training disruptions, lack of institutional support, and financial obstacles, alongside social pressures and cultural biases discouraging leave utilization.

Conclusion: Parental leave policies in surgical specialties remain insufficiently utilized and inadequately supported, with gendered disparities and cultural barriers further complicating access. Addressing these issues requires transparent policy communication, financial support, and cultural reforms to normalize parental leave and mitigate stigma. Future research should focus on longitudinal studies to assess long-term impacts and identify interventions that promote equity and work-life balance in surgical professions.

Elizabeth Wei **Medical Student** **Poster # 84**

When should we declare an endophthalmitis outbreak? A Poisson model of post-cataract surgery endophthalmitis outbreak projections

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Introduction: Acute endophthalmitis is a rare, sight-threatening post-operative complication of cataract surgery, and the detection of outbreaks are a crucial public health concern. Currently, there are no established guidelines on the threshold to declare a post-operative endophthalmitis (POE) outbreak. It can be challenging for surgical centers to determine whether a POE outbreak is likely, particularly given the low incidence. Under-calling an outbreak can lead to further transmission, while over-calling can lead to an unnecessary use of healthcare resources. This study aimed to develop an evidence-based, online tool that uses a Poisson model to determine the likelihood of an endophthalmitis outbreak.

Methods: A systematic review was conducted to determine the 6-week risk of acute POE following standalone cataract surgery. Due to the rare incidence of POE, a Poisson probability model was selected to calculate the cumulative probability of observing a certain number of POE cases following standalone cataract surgery. Customizable variables included in the calculator were the number of POE cases observed, number of cataract surgeries performed, duration of observation (e.g., 1 month), and reference standard POE risk. Significance was defined as $p<0.05$, $p<0.01$, or $p<0.001$.

Results: A total of 2,561 articles were identified from MEDLINE, EMBASE, and Cochrane Library. 2,080 articles underwent title and abstract screening, and 92 articles underwent full-text screening. From the 25 articles included in the final systematic review, the risk of POE following standalone cataract surgery was 0.063% (range: 0.019-0.10%). The online clinical tool computes and visualizes the cumulative probability of ≥ X number of POE cases following cataract surgery, according to the user inputs. For example, the model demonstrates that for a center that performs 1,000 cataract surgeries in a month, the probability of at least 1 POE case occurring in a month is not statistically significant ($p=0.24$), and therefore outbreak is unlikely at a 95% confidence interval. In contrast, the probability of at least 3 POE cases occurring in a month at this center is statistically significant ($p<0.01$), and thus, there is strong evidence for outbreak declaration at a 95% confidence interval.

Conclusion: The Poisson model represents an evidence-based way to determine whether the number of POE cases observed are outside expectations for the number of cataract operations performed over a specified time period. This online tool provides a helpful real-time clinical tool for ophthalmologists and public health agencies to guide POE outbreak decision making.

Winnie Yu **Medical Student** **Poster # 85**

The impact of delisting public funding for routine eye exams on the prevalence of common ocular conditions in Ontario, Canada

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Introduction: Routine eye exams under the Ontario Health Insurance Plan (OHIP) were delisted in November 2004 for individuals aged 20-64 years who were healthy with no pre-existing eye conditions. This study aimed to assess the impact of delisting routine eye exams on the annual prevalence of common ocular conditions in adults 40-64 and 65+ years between 1997-2021.

Methods: A population-based, retrospective cohort study was conducted using health administrative data of adults ≥40 years who were eligible for OHIP between 1997-2021. OHIP diagnostic codes and fee codes submitted by ophthalmologists or optometrists were used to identify common ocular conditions, namely cataracts, retinopathies and glaucoma. Segmented linear regression was used to determine the change in prevalence before and after the delisting of eye exams. Linear regression was used to derive prevalence trends.

Results: Annual prevalence rates of adults aged 40-64 years with 1+ common ocular condition increased by 1.9% per year ($p<0.0001$) from 5.9% in 1997 to 19.6% in 2004. Since 2005, annual prevalence increased 0.2% per year ($p<0.0001$) to 21.0% in 2021. The number of additional individuals in this age group who could potentially have 1+ ocular condition and were not seen for an eye exam due to the delisting of routine eye exams was estimated to be 1.5 million (n=1,532,249) in 2021. Prevalence of cataracts was reported to be 2.1% in 1997 and 6.2% in 2021 ($\beta=0.1$, $p<0.0001$), retinopathies was 1.4% in 1997 and 7.8% in 2021 ($\beta=0.2$, $p<0.0001$) whereas glaucoma was 2.1% in 1997 and 8.1% in 2021 ($\beta=0.2$, $p<0.0001$). In adults aged 65+ years, prevalence of having a common ocular condition was 29.1% in 1997, increased 5.1% per year ($p<0.0001$) to 2004 and continued to rise at 0.6% per year ($p<0.0001$) to 78.9% in 2021. In those aged 65+, the annual prevalence rates of cataracts increased from 20.0% in 1997 to 66.6% in 2021 ($\beta=1.5$, $p<0.0001$). Retinopathies also rose from 3.9% in 1997 to 34.8% in 2021 ($\beta=1.3$, $p<0.0001$) and glaucoma was 7.3% in 1997 and 31.1% in 2021 ($\beta=1.0$, $p<0.0001$).

Conclusion: Annual prevalence of common ocular conditions significantly increased over time. However, the increase in having 1+ common ocular condition appeared to have slowed significantly in the cohort of adults aged 40-64 since 2005, with approximately 1.5 million Ontarians likely undetected with a common ocular condition. This illustrates the impact that delisting eye exams on OHIP may have on the accessibility of early diagnosis and management of common ocular conditions.

Winnie Yu **Medical Student** **Poster # 86**

The introduction of pediatric ophthalmology in rural Northwestern Ontario

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Introduction: Disparities in accessing healthcare services continue to exist in rural and remote regions of Canada as fewer providers, especially subspecialty services, are available outside of major urban city centres. This study aimed to analyze the availability of pediatric ophthalmology and strabismus services in Northwestern Ontario (NWO), a region with remote populations, large geographic distances, vulnerable demographics and physician shortages, over a period of ten years.

Methods: A retrospective chart review was conducted using physician billing records submitted by permanent ophthalmologists with hospital privileges at the main ophthalmology clinic in NWO, Port Arthurs Health Center (PAHC), between January 2015 and December 2024. There was no pediatric ophthalmologist in the region prior to 2019. Billing records were compared before and after a pediatric ophthalmologist joined PAHC in November 2019. Three ocular conditions, commonly associated with the pediatric ophthalmology and strabismus subspecialty, were identified based on ICD-9 diagnostic codes including strabismus (378), amblyopia (368) and refractive error (367). Each billing record was considered a visit. In the event of multiple billing records for a given patient on the same day, only the first record was considered. The number of clinic visits and surgeries performed for these conditions were compared between the two time periods (before and after availability of a pediatric ophthalmologist in the region) using appropriate statistical tests.

Results: There were a total of 4,969 clinic visits identified for the three mentioned conditions during the study period, with 780 visits in 2015-2019 and 4,189 in 2020-2024. There were significant differences observed in the number of clinic visits for all three ocular conditions examined with a greater proportion of visits occurring in 2020-2024 as compared to 2015-2019 ($p<0.0001$). There were 693 recorded visits for strabismus in 2015-2019 which rose to 3,743 in 2020-2024. For amblyopia, there were 9 records in 2015-2019 and 199 in 2020-2024 whereas refractive error had 78 records during 2015-2019 and 247 in 2020-2024. There was a steady increase in the number of strabismus surgeries performed since the availability of a pediatric ophthalmologist from 0 in 2015-2019 to 282 in 2020-2024.

Conclusion: This study highlights the need for specialized ocular care in the NWO region and the impact a sub-specialist can have in managing these patients closer to their home. Findings from this study can be used to advocate for the availability of other subspecialty ophthalmic care not only in the NWO region but also in other rural and remote regions in Canada.

Danielle Solish **Resident** **Poster # 87**

Becoming a Micro-Revolutionary: A Workshop on How to Respond to Microaggressions and Facilitate Bystander Training

Co-authors: Marko Popovic MD MPH FRCSC, Radha P. Kohly MD PhD FRCSC.

Introduction: Purpose: There is a significant gap in medical education resources and curricula aimed at addressing mistreatment towards healthcare professions. The aim of this study was to evaluate the effectiveness of a workshop and toolkit designed to empower healthcare professionals to become "micro-revolutionaries", defined as individuals who engage in “mini-actions” in response to microaggressions, advocating for change on an interpersonal level.

Study Design: Cross-sectional, quasi-experimental design with pre- and post-questionnaires.

Methods: Adapted from the literature, we developed a 60-minute workshop to prepare students, residents, allied healthcare professionals and staff physicians on how to recognize and respond to microaggressions, both as a victim and a bystander. A novel framework entitled “ACT FIERCE” was developed to provide a toolkit to attendees on responding to microaggressions. The workshop utilized an interactive lecture, group discussion, and role-play scenarios to practice the framework. Participants completed pre- and post-questionnaires regarding the learning objectives of the workshop and their preparedness to respond to microaggressions.

Results: The workshop and respective surveys were conducted at five sessions across three ophthalmology and two internal medicine departments. Eighty-six participants completed the pre-workshop questionnaire, and seventy-one participants completed the post-workshop questionnaire. In the pre-workshop questionnaire, 60.5% of participants reported that they had never received previous training on microaggressions and 76.7% of all participants reported that they have experienced at least one microaggression and did not respond to it. After completing the workshop, 78.9% of attendees felt that the training helped prepare them to respond to microaggressions, with 94.3% reporting that they would use the ACT-FIERCE strategy in the future. Participants reported greatest improvements in responding directly to microaggressions when responding as a bystander when colleagues are questioned, and providing support and following up when others face these micro-insults.

Conclusion: Despite the high proportion of individuals experiencing microaggressions in healthcare environments, there is scant guidance on how to address them or intervene on behalf of others. This interactive workshop fills this void by preparing healthcare professionals on how to become a micro-revolutionary and respond to microaggressions. Our findings demonstrate the effectiveness of widespread delivery of the workshop and adoption of the ACT FIERCE framework across diverse institutions.

Bryan Guo **Graduate Student** **Poster # 88**

Investigating Cytotoxic Retinal Release by Activation Switch 2 Rhodopsin Mutants

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Introduction: Rhodopsin is the principal photoreceptor in rod cells that mediates dim-light vision. Mutations in its rhodopsin gene accounts for ~30-40% of cases of autosomal dominant Retinitis Pigmentosa (RP). Although pathogenic mechanisms have been identified for many rhodopsin variants, many more remain uncharacterized, classified as variants of uncertain significance (VUS). One mechanism is that is commonly pointed to is protein misfolding, exemplified by variant P23H. Many classes of disfunction have been proposed to explain disease mechanisms, yet many mutants remain unclassified. It is possible that some mutations produce functional receptors yet still cause visual disease. One alternative explanation of disease is the idea that uncontrolled release of rhodopsin's ligand, a cytotoxic retinal chromophore, can cause visual degeneration over time. This study investigated variants within or in close proximity to Activation Switch 2 (AS2), one structural region that impacts the ability of rhodopsin to maintain its active state conformation. We propose that these mutants destabilize the active state and prompt premature release of rhodopsin's ligand retinal.

Methods: Mutants were generated in human rhodopsin via site-directed mutagenesis. Mutant proteins were purified and assayed. UV-Vis spectroscopy was used to quantify protein expression and identify shifts in peak absorption in mutants. Fluorescence spectroscopy measured the rate of retinal release, corresponding to stability of the activated rhodopsin. Retinal release was also measured in the presence of an arrestin peptide to determine the ability of each mutant to be bound and stabilized. Mechanisms were proposed by interpreting these results in conjunction with protein structure modeling and known clinical data.

Results: One AS2 variant, A298D, had been found in a patient but did not have an identified disease mechanism. Other variants tested (A260T, A298T, I305V) were VUS. This study identified which of these variants had accelerated retinal release, indicating decreased active state stability and greater potential for causing disease by free chromophore. Structure modeling also helped confirm these experimental results.

Conclusion: We speculate that these mutants may contribute to visual degeneration by interrupting key interactions in AS2, causing aberrant release of cytotoxic retinal. This may represent an alternative mechanism of visual disease by rhodopsin mutation.

Cynthia Larche **Medical Student** **Poster # 89**

Assessing the impact of ophthalmology locum clinic rotation in Northeastern Ontario

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Introduction: The purpose of this study is to assess the rotating locum ophthalmology clinic's impact on healthcare accessibility and patient care in Northeastern Ontario.

Methods: For this descriptive cross-sectional study, we recruited 100 patients from three one-week visits with the locum team. Telephone survey and medical chart data analyzed for demographics, access to care, clinical data, and patient care experiences.

Results: Average patient age was 71.5 years, 52% female. Patients had limited access to ophthalmologists (last visit M=5.4 years ago) and optometrists (M=9.8 months ago), often relying on emergency departments. Travel distance was significant (round trip M=171 km) with an average out-of-pocket cost of $89.25. Nearly half applied for a Northern Health Travel Grant but faced delays. The locum clinic improved access but wait times for consultations and surgeries increased. Most patients were referred for cataract surgery, with many having severe vision impairments and multiple comorbidities. Recommended treatments included surgery (n=59), pharmaceuticals (n=5), and laser therapy (n=2). Patients attended an average of 2.4 appointments. High satisfaction with clinic services was reported, though suggestions were made for better scheduling, financial support, and communication.

Conclusion: The study's participant demographics align with provincial cataract patient trends, revealing barriers to eye care and a reliance on emergency departments due to limited ophthalmic services. The locum clinic's added capacity is essential for the region. Patients traveled significant distances, facing financial challenges, especially those without NHTG access. The clinic is more cost-effective than alternatives in distant cities. Increasing wait times at the clinic point to a need for expanded capacity to prevent negative health outcomes. Most referrals were for cataracts, with some requiring urgent care. Visual acuity data indicate severe vision impairments, emphasizing the need for timely intervention.
High patient satisfaction and low travel-related stress underscore the clinic’s positive impact. Patient recommendations for additional locum clinics in other specialties highlight a broader need for accessible specialist care. Suggestions for improvements offer actionable insights for enhancing clinic operations. The locum clinic model effectively fills a critical gap in ophthalmologic care for Northeastern Ontarians, offering accessible, high-quality services and reducing patient financial burdens. Expanding clinic capacity, improving logistics, and addressing patient concerns will further enhance the clinic's impact and serve as a model for other specialties.

Ghaliah Nsour **Clinical Fellow** **Poster # 90**

Correction of Abnormal Head Position in Pediatric Nystagmus using Yoked Low-value Prism Glasses: a Retrospective Study

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Introduction: Nystagmus involves abnormal head positions (AHP) towards the null point for improving visual acuity. While surgical interventions are the standard therapy, the use of yoked prisms was conceptualized in the past, excluded for its side effects. Our team used low-value prisms in children to mitigate AHP.

Methods: Prisms were tailored to the direction of head turn. 31 children were reviewed. Outcomes were binocular best corrected visual acuity (BBCVA) and AHP measures with and without prisms.

Results: 31 patients averaging 10.3 ± 3.6 y/o, 16 male, 14 diagnosed with idiopathic infantile nystagmus syndrome, 6 with oculocutaneous albinism, and 9 with other secondary nystagmus were reviewed. Prism's average prescription was 3.9 ± 1.25 prism diopters. BBCVA for distance averaged 0.44 ± 0.22 logMar, improving to 0.41 ± 0.23 logMar ($p= 0.001$, small size effect). AHP reduced from 16.9 ± 9.90 to 4.6 ± 5.80 for distance vision ($p<0.0001$) and 12.7 ± 12.90 to 3.8 ± 6.20 for near vision ($p<0.0001$), both large size effects. The angle of the prisms most frequently prescribed was 1800 (26 cases), 2 cases at 1350, 1 case at 300, and 2 cases at 900.

Conclusion: Our study found a significant improvement in AHP using low-value prisms in a pediatric population. Allowing the use of primary gaze position, prisms may be a therapeutic option to reduce the physical and social difficulties from nystagmus.

Cynthia Larche **Medical Student** **Poster # 91**

Impact of Interprocedural Intraocular Lens Selection Alteration on Refractive Outcomes in Delayed Sequential Bilateral Cataract Surgery: A Retrospective Study in Northern Ontario

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Introduction: Immediately sequential bilateral cataract surgery (ISBCS) offers multiple advantages about which much has been written. It requires only a single operating room visit and half the postoperative visits, rendering the surgical journey more manageable for patients and their families, yet many ophthalmologists prefer delayed sequential bilateral cataract surgery (DSBCS). In Canada, just over a third of ophthalmologists do not perform ISBCS, with a second third doing so only in occasional cases. Approximately half state they want to assess the first eye's refractive outcome before operating on the second, as DSBCS provides a potential opportunity to alter intraocular lens (IOL) selection for the second eye, typically pre-determined by preoperative optical biometry (e.g., IOL Master or Lenstar). In Northeastern Ontario, a persistent large backlog for cataract surgery led the region's only full-time ophthalmologist, a retinal specialist who has preferred DSBCS, to investigate whether second-eye IOL adjustments genuinely improved refractive outcomes.

Methods: Design: Retrospective comparative-effectiveness study.
Methods: Cases of patients undergoing DSBCS with monofocal IOLs, whose first-eye IOL was targeted for plano based on preoperative optical biometry, performed between January 2022 and December 2023 were reviewed. Exclusion criteria included cases with intraoperative aberrometry or non-monofocal IOLs. Second-eye IOL adjustments were evaluated using postoperative spherical equivalent error (SEE) in the first eye and compared against predicted outcomes with biometry-suggested IOLs. Statistical analyses were performed using Microsoft Excel, SciPy and statsmodels.

Results: Of 688 total DSBCS cases, 116 met the inclusion criteria. No significant difference in postoperative SEE was observed between thirty-five cases with second-eye IOL modifications (mean SEE±standard deviation = 0.55±0.49 diopters) and eighty-one unmodified cases (mean SEE±standard deviation = 0.42±0.41 diopters). Among the thirty-five IOL-modified cases, the mean difference between actual postoperative SEE and biometry-predicted SEE was 0.02D (95% CI: -0.11D to +0.15D; TOST p=0.0006). These findings confirm clinical equivalence between methods.

Conclusion: Interprocedural IOL adjustments during DSBCS did not significantly enhance refractive outcomes. Results align with broader studies suggesting no refractive advantage for DSBCS over immediately sequential bilateral cataract surgery (ISBCS). Adoption of ISBCS could address surgical backlogs, particularly in this Northern region, without compromising safety or efficacy.

Nishanthini Karuppiah **Clinical Glaucoma Fellow** **Poster # 92**

A comparative study of the effects of 5FU needling versus no 5FU following AGV

Co-authors: Professor. Catherine Birt, MD, Department of Ophthalmology, UofT, Professor. Christoph Kranemann MD, Department of Ophthalmology, UofT. Fakhra Alderei, MD, Department of Ophthalmology, UofT.

Introduction: Implantation of Ahmed glaucoma valve (AGV) is an effective surgical technique to reduce intraocular pressure in patients affected with glaucoma. The aim of the study was to compare the effects of 5FU(5- Flurouracil) needling versus no 5FU following AGV.

Methods: Thirty eyes who underwent 5FU post AGV implantation were recruited in this retrospective study as cases and compared with controls, which were thirty eyes with no 5FU needling post AGV. Cases were matched according to ethnicity, diagnosis, gender and age within 5 years. Using a 30 gauge needle, the tenon's capsule over the plate was needled and bleb reformed to restore aqueous flow. Patients were examined at day 1, 10 days, 3 months, 1 year and final visit. Procedure outcome was determined on the basis of the recorded IOP(Intraocular pressure levels and number of AGM(Anti glaucoma medication) used. Complete success was defined as having no further anti-glaucoma medications and no intervention within 2 years of follow up. Qualified success was the result of medications restarted and having no intervention within 2 years.

Results: The mean interval between AGV implantation and needling was 13 months. The mean follow up time was 24 months after needling. Both groups had statistically significant mean IOP at day 1, day 10, 3rd month and 1 year, but a similar mean IOP (5FU AGV: 16.8 mm Hg; AGV 14.8 mm Hg; $p = 0.324$) at the final visit. The difference in mean IOP pre and post needling was 7.5 mm Hg (34.5%). AGV -5FU group always had higher medication use, and also at the final visit (5FU AGV: 3.52 AGV 2.5; $p = 0.028$). The Kaplan-Meier survival analysis revealed 100%, 91%, and 70% cumulative predictive success rates in the 5FU AGV group versus 100%, 95%, and 95% in the AGV group at 1, 2 and 5 years respectively.The cumulative proportion of cases receiving either qualified or complete success at 24 months was 76.6 %. Failure was noted in 23.3% patients out of which 28.6 % was attributed due to retinal complications. No severe complications were noted after the procedure.Seven patients had repeated needlings in which 2 had 5FU needling twice and 5 had needling thrice. Hence, a qualified sucess of 71.4% and complete sucess of 28.6% was acheived in patients with repeated needling.

Conclusion: Needling over the plate of an AGV supplemented with 5FU is an effective and safe choice in patients with elevated IOP due to encapsulation or fibrosis. Success rates were higher in patients with repeated needling.

Mostafa Ibrahimi **Graduate Student** **Poster # 93**

TRACR a molecular tool to study retinal connectivity

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Introduction: To investigate retinal connectivity in photoreceptor transplantation, degeneration, and development, we use TRACR (TRanssynaptic Anterograde Circuit Readout), a ligand-receptor system based on a synthetic Notch receptor. TRACR detects synaptic interactions using (i) a GFP ligand at the presynaptic terminal (Sender), (ii) a postsynaptic Notch-based Receiver with an anti-GFP nanobody and tTA, and (iii) a Reporter gene under a TRE promoter. Synaptic interactions trigger tTA release, activating Reporter expression in postsynaptic cells. We hypothesize that TRACR enables high-throughput detection of photoreceptor synapses.

Methods: Sender and Receiver AAVs were injected subretinally in neonatal Reporter mice. Eyes were sectioned, and markers were assessed via immunohistochemistry.

Results: Sender was selectively expressed in photoreceptors and Receiver in ON bipolar cells. Reporter activation in Receiver+ cells required Sender expression in presynaptic photoreceptors. Eliminating Sender cells via MNU treatment or in RD1s significantly reduced Reporter expression. Reporter activation was also attenuated by rod-selective neurosecretion inhibition.

Conclusion: Reporter activation depends on trans-synaptic interactions and sustained neurosecretion. TRACR provides a robust, high-throughput method to study synapse formation, degeneration, and transplant-associated synaptogenesis.

Mohammed Ayan Chhipa **Graduate Student** **Poster # 95**

Single-Cell RNA-Sequencing Explores the Mechanism of Novel Anti-Angiogenic Inhibitors for the Treatment of Age-related Macular Degeneration

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Introduction: Age-related macular degeneration (AMD) is a leading cause of vision loss in older adults. One severe form, neovascular AMD, is characterized by abnormal, leaky blood vessels and is typically treated with intravitreal injections targeting vascular endothelial growth factor (VEGF). Given the limitations of current therapies, novel treatments are needed. We have characterized APX2009, a small molecule inhibitor of apurinic/apyrimidinic endonuclease 1/reduction-oxidation factor 1 (APE1/Ref-1), which modulates transcription factors involved in angiogenesis, inflammation, and cell growth. APX2009 is a more potent derivative of clinical candidate APX3330, recently shown to be safe and effective in a Phase 2b diabetic retinopathy trial (NCT04692688).

Methods: To elucidate the downstream effects of Ref-1 inhibition, we performed single-cell RNA sequencing (scRNAseq) in the laser-induced choroidal neovascularization (L-CNV) mouse model, which recapitulates some features of neovascular AMD. Following L-CNV, intraperitoneal injections of APX2009 were administered twice daily for 7 days. After enucleation, the retina and RPE-choroid-sclera complex underwent scRNAseq. To validate differentially expressed genes, human retinal endothelial cells (HRECs) were treated with APX2009 for 24 hours followed by qPCR analysis.

Results: scRNAseq revealed that in mouse choroidal endothelial cells, L-CNV increased expression of immunity-related GTPase M1 (Irgm1) and proto-oncogene JunD, which was normalized by APX2009 treatment. Irgm1 plays a role in immune regulation and cellular stress responses, which may influence extracellular matrix remodeling (ECM) and neovascularization. JunD is part of the Activator Complex 1 (AP1), which regulates cell growth and differentiation. Additionally, Matrix Metalloproteinase 3 (Mmp3) was downregulated in the RPE. Mmp3 is an enzyme that breaks down the ECM, thus creating space for new blood vessel formation.

Conclusion: With APX2009 treatment, we confirm the differential expression of genes that may be implicated in reducing angiogenesis. Using qPCR, we continue to investigate these differentially expressed genes to delineate the molecular mechanisms of novel anti-angiogenic treatments.