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

**66<sup>th</sup> Annual Research Day**

**And**

**43<sup>rd</sup> Clement McCulloch Lecture**

**Friday, May 24, 2024,  
7:30 AM – 5:00 PM**

**St. Michael's Hospital  
Li Ka Shing Knowledge Institute  
209 Victoria Street  
Toronto, Ontario  
M5B 1T8**



Ophthalmology & Vision Sciences  
**UNIVERSITY OF TORONTO**

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## Chair's Message

### Department of Ophthalmology and Vision Sciences 66<sup>th</sup> Annual Research Day



It is a pleasure for me to welcome you to the University of Toronto Department of Ophthalmology and Vision Sciences 66th Annual Research Day. Vision science is fundamental to who we are and what we do. We have established ourselves as leaders in providing the most advanced vision care and continue to break new ground. Our research output is amazingly productive and prolific and have made us a world leader. Our commitment to scientific discovery and the collaborations that are fostered between clinicians, clinician-scientists, and discovery scientists translate ultimately into health benefits for our patients. As academic ophthalmologists and research scientists, we are at the forefront of discovery and knowledge translation, putting forward new treatment and diagnostic methodologies to continually refine our understanding and management of ophthalmic conditions. A mission of the Department of Ophthalmology and Vision Sciences at the University of Toronto is, in no small part, to train ophthalmologists in research and critical thinking irrespective of their ultimate career path. We hope this research training will lead to lifelong critical thinking and ongoing inquiry, a deeper understanding of vision science, and a quest for better treatments of eye disease. A primary goal of the Department is the provision of high-quality, compassionate, cutting-edge clinical care, through the translation of high-impact research and the promotion of discovery research to drive our profession forward. This year, under the leadership of Dr. Matt Schlenker, the research day program is extensive and rich. The program will begin at 7:30 AM and there will be 3 sessions during the day. During each session, we will feature the trainee presentations that scored highest by the abstract reviewers along with expert presentations. In addition, all other submitted abstracts will be provided an opportunity to share their work during the poster session. We hope this approach will bring a unique experience to everyone. Our guest speaker this year is Dr. Ula V. Jurkunas.

In addition to our visiting guest speaker, our local faculty, Drs. Clara Chan, Matt Schlenker and Jeremy Sivak will be sharing their exciting work with us. Dr. Matthew Schlenker, our Director of Resident Research, has devoted much energy and thought to planning this important event and we are grateful to him for his hard work contributing to the success of this day. I also would like to express my gratitude to all the supporting staff for the assistance they provided Dr. Schlenker in the preparation of the program and manual. A special thanks to Mano Chandrakumar, Sandra Gauci, Maggie Lam, Ryan Lue, and Helena Medeiros for all their efforts.

I would like to thank our sponsors Bayer, Novartis, and Sun Pharma, without whom this event could not take place, for the educational grant.

I hope and trust that you will enjoy today's sessions, and leave having gotten a taste of the broad spectrum of the Department's research enterprise. Hopefully, you will also leave curious and with some ideas of where we should go next. Thanks for attending and we look forward to having you back next year.

Peter J. Kertes, MD CM, FRCS

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**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, and many cross institution and discipline collaborations 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 66th Ophthalmology Departmental Research Day and the 43d Clement McCulloch Lecture. We would like to welcome Dr. Ula V. Jurkunas, MD, a renowned clinician-scientist and Cornea Surgeon. Dr. Jurkunas has conducted award-winning research into pathophysiology of Fuchs endothelial corneal dystrophy as well as pioneered the development of cultivated epithelial cell transplantation for the treatment of limbal stem cell deficiency.

This scientific gathering would not be possible without the generous support from our sponsors Novartis, Bayer, and Sun Pharma. 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 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 of 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

*UHN-Toronto Western Hospital  
Kensington Eye Institute  
Trillium Health Partners*

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**Evaluation of  
Presentations**

An evaluation form is filled out by each judge for every presentation. To avoid possible conflicts of interest, a judge who is listed as a co-author in a paper will not evaluate that paper. Marks are given for presentation, quality of work, and clinical or scientific relevance. Emphasis is placed on the quality of the work including the clarity of the published abstract. A numeric score is given to each candidate and the scores are averaged to determine the winner of each award. While some may question the value of competition on Research Day, our department feels that there should be a formal recognition for 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.

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

*UHN-Toronto Western Hospital  
Kensington Eye Institute  
Trillium Health Partners*

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## Research Day 2024 Committees

### **Organizing Committee**

Mano Chandrakumar  
Mariana Collazos  
Sandra Gauci  
Peter Kertes  
Helena Medeiros  
Rajiv Muni  
Prem Nichani  
Saba Samet  
Matt Schlenker  
Valerie Wallace

### **Abstract Reviewers**

Brian Ballios  
Yaping Jin  
Keyvan Koushan  
Michael Reber  
Jeremy Sivak  
Gary Yau

### **Session Moderators**

Kenneth Eng  
Matthew Schlenker  
Jeremy Sivak  
David Wong

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**Dr. Clement  
McCulloch**

**Professor and Chair  
Department of  
Ophthalmology 1961 - 1982**



Dr. McCulloch graduated from the University of Toronto, Faculty of Medicine in 1939. He then continued his Ophthalmological training at the Columbia Presbyterian Hospital in New York City for three years where he worked with Dr. Phillip Thygeson on the pathophysiology of external diseases such as trachoma. He enlisted in the Royal Canadian Air Force and served on the central Medical Board. During this period, he served with a research unit and further demonstrated his love for research, looking at retinal effects of high altitude flying and the optics of night vision. At the conclusion of the Second World War, he returned to Toronto, as chief of the Ophthalmology service at the Toronto Western Hospital. He established an Ophthalmology training program there which later became integrated into the University of Toronto teaching program under the direction of Dr. A J Elliott. In 1961, Dr. McCulloch became Chair of the University department. It was his goal to elevate the standard of practice in Toronto to be on a par with other major centres. Research was a major priority, and he went to all efforts to support those staff members who were interested in the acquisition of new knowledge. He is known for the friendly way he ran the department. The monthly hospital chiefs' meetings were always held in the informal atmosphere of one of the members' home. The lively debate often gave a very personal atmosphere to the shaping of policy. During his 21 years of leadership, the University of Toronto was noted for its commitment to research. Dr. McCulloch encouraged excellence in all the subspecialty fields.

Dr. McCulloch published over 80 articles in international journals on a variety of topics from the ultrastructure of zonules to crystalline dystrophy of the cornea. His scientific works have been collated and published by the University of Toronto Press. His invaluable experience and breadth of knowledge is appreciated by our department. In 1980 a group of Dr. McCulloch's friends set up a fund to establish an annual lectureship in Ophthalmological research. These funds have helped to support the University of Toronto annual research day and Clement McCulloch lecture.

Dr. McCulloch passed away in early 2007. With this lectureship, Dr. McCulloch's legacy will continue to live on.

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## 43<sup>rd</sup> Clement McCulloch Lecture

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### **Ula V. Jurkunas, M.D.**

Associate Professor of Ophthalmology,  
Associate Director of Cornea and  
Refractive Surgery Service  
Co-Director Cornea Center of Excellence,  
Department of Ophthalmology, Schepens  
Eye Research Institute of Massachusetts  
Eye and Ear, Harvard Medical School



Dr. Ula Jurkunas is a clinician scientist and corneal surgeon at Mass. Eye and Ear. At Schepens Eye Research Institute of Mass. Eye and Ear, she conducts basic science research on stem cell transplantation and Fuchs endothelial corneal dystrophy, a disease that accounts for over 20,000 corneal transplants each year in the United States. In addition, she teaches residents and fellows about ocular surgical procedures, as well as the clinical management and diagnosis of corneal and refractive conditions. Dr. Jurkunas is an Associate Director of Cornea and Refractive Surgery Service and a Co-director of the Harvard Ophthalmology Cornea Center of Excellence. After earning her medical degree from the University of Louisville, Dr. Jurkunas completed her ophthalmology residency at Boston University. She then completed subspecialty training in cornea, external diseases, and refractive surgery at Mass. Eye and Ear, serving as Chief Cornea Fellow for one year.

Dr. Jurkunas was one of the first in our department to benefit from the prestigious K12 Harvard Vision Clinical Scientist Development Program, an award funded by the NIH/NEI. As a K12 scholar, she conducted award-winning research into the pathophysiology of Fuchs endothelial corneal dystrophy.

Today, Dr. Jurkunas heads a fully-staffed and RO1-NIH funded laboratory, which studies the mechanisms involved in the corneal endothelial degeneration seen in Fuchs dystrophy. Her studies focus on the role of oxidative stress in cell-extracellular matrix interactions, estrogen metabolism, DNA damage and repair, and mitochondrial biogenesis in Fuchs dystrophy.

Moreover, she has pioneered the development of cultivated epithelial (stem) cell transplantation for the treatment of limbal stem cell deficiency. The latter studies have led to the translational development of stem cell therapy in corneal disorders. She has recently received approval for an Investigational New Drug (IND) application to the FDA and has completed a Phase I/II study using stem cells to treat corneal blindness. She has received numerous awards, including Research to Prevent Blindness Award, ARVO Alcon Early Clinician-Scientist Research Award, Alcon Research Institute Award, AAO Achievement Award, and ARVO Foundation/Pfizer Ophthalmics Carl Camras Translational Research Award.



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**66<sup>th</sup> Annual Research**

**Day and**

**43<sup>d</sup> Clement McCulloch**

**Lecture**

**Program**

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**PROGRAM**

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8:10 -9:29 AM            Session moderator: Dr. David Yan  
8 minute presentation- 3-minute discussion

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7:30	8:00	Continental Breakfast	
8:00	8:05	Department Chair's Welcome	Peter Kertes, MD CM, FRCS
8:05	8:10	Annual Ophthalmology Research Day Chair Welcome	Matthew Schlenker, MD, MSc, FRCS
8:10	8:30	<b>Perspectives from an ophthalmic surgeon, clinician, researcher.</b>	<b>Clara Chan, MD, FRCS Faculty</b>
8:30	8:41	Cost-Utility Analysis of Cultured Human Corneal Endothelial Cells Compared to Endothelial Keratoplasty for Endothelial Dysfunction.	Tina Felfeli, MD Resident
8:42	8:53	Refractive Outcomes of Penetrating Keratoplasty in Children.	Emily Witsberger, MD Fellow
8:54	9:05	Early Surgeon Experiences of the Xen63 versus Xen45 Gel Stents: An International Multicenter Study.	Ahmed Abdelaal, MD Fellow
9:06	9:17	Intraocular Pressure Comparisons with iCare HOME versus iCare IC200.	Jenny Qian MD Resident
9:18	9:29	A retrospective study of Biofeedback training in Low Vision patients.	Mariana A M Misawa, MD Fellow
9:30	10:15	Coffee Break + Poster Sessions (Even numbered posters are judged)	

10:15-12:00 PM

Session Moderator: Dr. Kenneth Eng

8 minute presentation- 3-minute discussion

10:15	10:35	TBA	<b>Jeremy Sivak, PhD Faculty</b>
10:36	10:47	Area Under the Curve visual acuity following Rhegmatogenous Retinal Detachment Repair with Pneumatic Retinopexy vs Pars Plana Vitrectomy.	Sue Ellen Demian, MD Research Fellow
10:48	10:59	Outer retinal recovery following pneumatic retinopexy for macula off retinal detachment.	Gareth D. Mercer, MD PhD FRCS(C) Fellow
11:00	11:11	Morphologic Features and Implications of Regulated versus Dysregulated Rhegmatogenous Retinal Detachment Using Swept-Source Optical Coherence Tomography.	Aurora Pecaku, MD Fellow
11:12	11:23	Co-culture with healthy cells in patient-derived diseased retinal organoids improves photoreceptor outer segment formation.	Kristen Ashworth, MSc Student
11:24	11:35	Pten: a missing piece in the puzzle of retinal degeneration.	Joseph Hanna, MD, MSc Resident
11:36	11:47	In vivo Imaging of an ALS Mouse Model Reveals Progressive and Sex-Dependent Retinal Changes.	Farbod Khorrami, MSc Student
11:48	11:59	Molecular profiles in different stages of primary open angle glaucoma – a prospective study.	Tianwei Ellen Zhou MD CM, PhD Resident
12:00	1:00	Lunch and Poster Session (Odd numbers are judged)	
1:00	1:10	Introduction to Dr. Ula Jurkunas, the 43 <sup>d</sup> Clement McCulloch Lecturer	Matt Schlenker
1:10	2:10	The 43 <sup>nd</sup> Clement McCulloch Lecture  Cell cycle activation in Fuchs Dystrophy: New paradigms in disease pathogenesis and treatments.	Ula Jurkunas, MD
2:10	2:40	COFFEE BREAK + POSTER SESSION (All remaining posters are judged)	

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2:45 – 4:00 PM

Session moderator: Dr. Josh Teichman

8 minute presentation- 3-minute discussion

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2:45	3:05	<b>Researching to make a difference</b>	<b>Matt Schlenker, MD, MSc., FRCS</b> <b>Faculty</b>
3:06	3:17	Analysis of Virtual Immediate Postoperative Visits after Cataract Surgery.	Diana Lucia Martinez, MD Fellow
3:18	3:29	Cataract surgery complications in individuals who previously received intravitreal injections: a population-based cohort analysis.	Winnie, Yu, MSc Student
3:30	3:41	Circadian rhythm disruption in bilateral optic neuropathies.	Jovi Wong, MD, MSc, DPhil Resident
3:42	3:53	Cone Mosaic in Children Undergoing Gene Therapy for RPE65-Associated Leber’s Congenital Amaurosis.	Miguel Cruz Pimentel MD Fellow
3:54	4:05	Evaluation of an Artificial Intelligence System for Automated Hand-Held Fundus Camera Diabetic Retinopathy Grading in a Tele-Retinal Screening Program.	Elizabeth Wei, BMSc, MD(c) Student
4:05	5:00	Poster Judging, Closing Remarks	

The Alumni Award for Best Resident Paper, John Gaby Prize for Best Fellow Paper, The Best Student Paper Award, Dr. Martin J. Steinbach Award for Best VSRP/Masters/PhD student/Research Fellow Paper and The Best Poster Award will be announced at the Ophthalmology Residents’ Graduation Dinner.

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# POSTERS

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

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- 1. Waleed Alsarhani (R)**  
Povidone-iodine in the Treatment of Infectious Keratitis: A Systematic Review
- 2. Kathrine Bhargava (G)**  
Elevated Inflammatory Cytokines in the Aqueous Humor of Glaucoma Patients Undergoing Endothelial Keratoplasty
- 3. Narisa Dhupar (VS)**  
Spatial Transcriptomics of the Human Corneal Endothelium in Fuchs Endothelial Corneal Dystrophy
- 4. Ness Little (G)**  
Adeno-Associated Virus (AAV) Mediated Expression of Bcl-xL Attenuates Apoptosis in Human Corneal Endothelial Cells
- 5. Prem Nichani (R)**  
Bilateral Corneal Perforation Secondary to Immunotherapy for Metastatic Melanoma
- 6. Prem Nichani (R)**  
The Use of Artificial Intelligence Software in Cornea Clinics
- 7. Angelica Hanna (M)**  
Virtual Follow-Ups after Cataract Surgery: A Systematic Review
- 8. Angelica Hanna (M)**  
Socioeconomic Status and Access to Vision Care in Canada
- 9. Angelica Hanna (M)**  
Socioeconomic Status and Visual Impairment and Ocular Disease in Canada
- 10. Ryan Huang (M)**  
Eye Examinations and Sociodemographic Factors: A Retrospective Population-Based Analysis
- 11. Omer Jamal (G)**  
Examining the Influence of Social Determinants on Medical Visit Attendance, Emergency Visits, and Clinical Outcomes Among Children with Eye Cancer: A Retrospective Analysis
- 12. Nikki Roustaf (DF)**  
Visual Impairment and Unmet Ophthalmic Needs of Afghan Refugees in Toronto and the Greater Toronto and Hamilton Area

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- 13. Chijindu Ukagwu (M)**  
Non-Mydriatic Fundus Photography for the Evaluation of Patients with Vision Loss in Canadian Emergency Settings
  - 14. Chris Zajner (M)**  
Disparities in Vision-related Functional Impairments Among Adults in the United States
  - 15. Kiko Zi Yi Huang (G)**  
Eye Care Utilization Trends in Ontario's Public Healthcare System: A 20-Year, Retrospective, Population-based Analysis
  - 16. Kiko Zi Yi Huang (G)**  
Utilization of Eye-Care Providers by Ontario Residents in 2019: A Population-based Study
  - 17. Kiko Zi Yi Huang (G)**  
Prevalence of glaucoma in Canada: Results from the 2016-2019 Canadian Health Measures Survey
  - 18. Tahani Baakdhah (RF)**  
Developing a Retinal Ganglion Cell Organoid Enrichment Protocol for Glaucoma Research and Therapeutics
  - 19. Patrick Xiang Ji (M)**  
Progression of Primary Angle Closure Suspects: A Systematic Review and Meta-Analysis
  - 20. Nishanthini Karuppiah (F)**  
A Comparative Study of Surgical Outcomes of Excisional Goniotomy Using the Kahook Dual Blade (KDB) Combined with Phacoemulsification (KDB-phaco group) in Mild Glaucoma vs Standalone KDB Group in Severe Glaucoma After Failed Glaucoma Surgeries.
  - 21. Taylor Lukasik (R)**  
Effect of 10.0 Nylon Ripcord on Outflow Facility of the PreserFlo® MicroShunt
  - 22. Diego Roccatti-Ortiz (F)**  
Preliminary Results for the PIPS (Peripheral Iridectomy Position Study): A Randomized Controlled Trial Investigating Optimal Laser Peripheral Iridectomy Placement.
  - 23. Babishaa Sauntharajan (G)**  
Mapping the Drainage Pathway from the Suprachoroidal Space: Evidence of Lymphatic Routing and Implications for Therapeutic Delivery in the Eye
  - 24. Runjie (Bill) Shi**  
Glaucoma home monitoring with the Toronto Portable Perimeter (TPP): two-year compliance and repeatability results
  - 25. Li Yan (VS)**  
Using Fused Data from Perimetry and Optical Coherence Tomography to Improve the Detection of Visual Field Progression in Glaucoma

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- 26. Arya Zarrinbakhsh (G)**  
Microgravity and Vision: Investigating Intraocular Pressure Variations and Potential Consequences for Astronauts
- 27. Jenny Zhang (VS)**  
The Early Transcriptomic Landscape of Pressure-Induced Optic Nerve Heads in ex-vivo Organotypic Human Eyes
- 28. Chun Hin Chow (G)**  
Vesicular Dysfunction in Oligodendrocytes Causes Inflammatory Demyelination in the Central Nervous System
- 29. Abdullah El-Sayes (M)**  
Restricted Diffusion in Bilateral Septic Superior Ophthalmic Vein Thrombosis
- 30. Mariam Issa (R)**  
Analysis of diplopia referrals in a tertiary neuro-ophthalmology center
- 31. Irina Sverdlichenko (M)**  
Macular optical coherence tomography findings in patients with syphilitic optic neuropathy – A case series and systematic review
- 32. Kirill Zaslavsky (R)**  
Efficacy of Intra-Arterial or Intravenous Thrombolytic Therapy Versus Conservative Standard Therapy for Central Retinal Artery Occlusion: An Individual Patient Data Meta-Analysis
- 33. Jim Xie (M)**  
Radiological Predictors of Visual Outcome in Myelin Oligodendrocyte Glycoprotein-Related Optic Neuritis
- 34. Jim Xie (M)**  
Sex or Gender Reporting in Ophthalmology Clinical Trials Among United States Food and Drug Administration Approvals Between 1995-2022
- 35. Mojtaba Abrishami (F)**  
Reirradiation with External Beam Stereotactic Radiotherapy for Recurrent Posterior Choroidal Melanoma After Brachytherapy
- 36. Huda Ahmedhussain (F)**  
Correlation of High-Risk Histopathology Features in Magnetic Resonance Imaging in Retinoblastoma
- 37. Benjamin Host (F)**  
Uncertain Heritable Risk in Retinoblastoma Probands: Classification of Genetic Testing Results for Risk Stratification and Screening
- 38. Andrew Yim (G)**  
Elucidating the Underlying Mechanisms of Unique TEAD Interactomes Across Distinct Target-Gene Specificity in YAP Binary Classes

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**39. Withdrew**

**40. Anne Merrylees Dersch (F)**

Social Determinants of Health and Visual Outcomes in Pediatric Cataract

**41. Mohab Eldeeb (R)**

Biofeedback Training for Improving Visual Functions in Children with Nystagmus:  
A Short-and-Long Term Analysis

**42. Bhadra Pandya (M)**

Automated Detection of Retinoblastoma Tumour and Treatment Response Using Optical Coherence Tomography

**43. Bhadra Pandya (M)**

The Association Between Retinal Thickness Fluctuations and Visual Outcomes Following Anti-VEGF Therapy: A Systematic Review and Meta-Analysis

**44. Bhadra Pandya (M)**

Retinal Optical Coherence Tomography Imaging Biomarkers in Retina Epiretinal Membrane: A Systematic Review

**45. Aminat Adama (VS)**

Investigating Early Transcriptional Targets of Neuroprotective LXB4 in Neuronal Injury Models

**46. Layla Ahmed (VS)**

Investigating Missing Heritability in Inherited Retinal Dystrophy

**47. Harracksingh Alicia N. (VS)**

Profiling the Visual System of *Lymnaea stagnalis* as a Novel Model for Investigating Photoreceptive Behaviours and Retinal Processing in Invertebrates

**48. Steven Chen (VS)**

Pathogenic variants of a visual protein constrain mutational pathways in genotype space.

**49. Miguel Cruz Pimentel (F)**

In Vivo Assessment of Cystoid Changes in Rhegmatogenous Retinal Detachment Using Swept-Source Optical Coherence Tomography

**50. Cassandra D'Amata (S)**

A Human Chimeric Retinal Organoid Model for Studying Donor-Host Cell Interactions in Cell Therapies for USH2A-Associated Retinitis Pigmentosa



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**51. Chidalu Edechi (M)**

The Mini-Steamroll: A Modified Abbreviated Variation of the Steamroller Maneuver Following Pneumatic Retinopexy for Rhegmatogenous Retinal Detachment with Large Superior Breaks

**52. Arshia Eshtiaghi (R)**

Artificial Intelligence Chatbot Knowledge on the Diagnosis and Treatment of Common Retinal Disorders

**53. Seyedeh Sara Fooladi (G)**

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

**54. Justin Grad (M)**

Treatments for Retinal Artery Occlusion: A Systematic Review and Meta-Analysis

**55. Peter Hong (VS)**

Interrogation of Rhodopsin Structural Stability and Cytotoxic Chromophore Release

**56. Ryan Huang (M)**

Prediction of Visual Acuity Improvement in Response to Ranibizumab in Age-Related Macular Degeneration Using Artificial Intelligence-Based Analysis of Fluorescein Angiography

**57. Ryan Huang (M)**

Association of Artificial Intelligence-Based Quantitative Fluorescein Angiography Measurements with Clinical Parameters in Patients with Diabetic Macular Edema

**58. Mengjia Huang (VS)**

SNAP-25, but not SNAP-23, is Essential for Photoreceptor Development, Survival, and Function in Mice

**59. Oral presentation**

**60. Brianna Lu (M)**

Assessing Retinal Vascular Leakage with Optical Coherence Tomography Angiography (OCTA) and Deep Convolutional Neural Networks

**61. Isabela Martins Melo (F)**

Assessment and Classification of Proliferative Vitreoretinopathy in Rhegmatogenous Retinal Detachment with Swept-Source Optical Coherence Tomography: A Novel Conceptual Framework

**62. Ryan Mason (R)**

Retinal Displacement Following Rhegmatogenous Retinal Detachment: A Systematic Review and Meta-Analysis

**63. Andrew Mihalache (M)**

Quantitative Assessment of Retinal Vasculature Using Artificial Intelligence-Based Analysis of Fluorescein Angiography in Age-Related Macular Degeneration

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- 64. Andrew Mihalache (M)**  
Interpretation of Clinical Retinal Images Using an Artificial Intelligence Chatbot
- 65. Andrew Mihalache (M)**  
Stretch-Induced Foveal Ectopia (SIFE/Displacement) Following Retinal Detachment Repair: A Novel Assessment Using Spectral-Domain Optical Coherence Tomography
- 66. David Mikhail (M)**  
Comparing the Multimodal Performance of ChatGPT and Gemini Pro in Retinal Image Interpretation
- 67. Yasmin Motekalem (M)**  
Long-Term Re-Detachment Rates of Pneumatic Retinopexy versus Pars Plana Vitrectomy in Retinal Detachment: a PIVOT Post-Hoc Analysis
- 68. Sumana Naidu (R)**  
Morphologic Stages of Full-Thickness Macular Hole Assessed with Spectral Domain Optical Coherence Tomography
- 69. Alexandra Nitoiu (VS)**  
IFT57 May Cause Bardet-Biedl Syndrome with Retinal Dystrophy
- 70. Deepika Parameswarappa (F)**  
Structural and Functional Retinal Phenotype in Mucopolysaccharidosis Type I Hurler and I Hurler-Scheie
- 71. Lauren Pickel (M)**  
Roller coasters and Retinal Detachment
- 72. Aswen Sriranganathan (M)**  
Anti-Vascular Endothelial Growth Factor Treatment Outcomes in Macular Telangiectasia: A Systematic Review
- 73. Michal Syonov (VS)**  
A Dual Role for the HFE2 Protein in Retinal Angiogenesis
- 74. Safwan Tayeb (R)**  
Macular Hole Associated Retinal Detachment in High Myopic Patients: Case series and Overview of a Novel Surgical Technique
- 75. Anna Tran (M)**  
Perspectives on Efficacy and Safety of Anti-Vascular Endothelial Growth Factor (Anti-VEGF) Biosimilars in the Treatment of Neovascular Age-Related Macular Degeneration (nAMD)
- 76. Jessica Wang (G)**  
CRB1 Mutation in Human Retinal Organoids Alters Photoreceptor Development
- 77. Jovi Wong (R)**  
Realistic Generated Images using Latent Diffusion Models to Improve Retinal Disease Classification using Deep Convolutional Neural Networks

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- 78. Michele Zaman (M)**  
Association Between Sociodemographic, Clinical Access, and Regional Factors with Diabetic Retinopathy in the National Health Interview Survey: A Cross-sectional, Population-Based Analysis.
- 79. Michele Zaman (M)**  
Postoperative Aniseikonia in Patients with Unilateral Rhegmatogenous Retinal Detachment: A Systematic Review
- 80. Brendan Tao (M)**  
Evolution of Asymptomatic Pentosan Polysulfate Maculopathy Following Medication Discontinuation: A Case Report
- 81. Brendan Tao (M)**  
Differential Characteristics in Enrollment in Age-Related Macular Degeneration Clinical Trials: A Cross-Sectional Study
- 82. Brendan Tao (M)**  
Comparison of Intravitreal Corticosteroids for Management of Diabetic Macular Edema: A Scoping Review of Long-Term Randomized Trials
- 83. Brendan Tao (M)**  
Intracameral Moxifloxacin Prophylaxis for Postoperative Endophthalmitis: Dose Optimization for Posterior Capsular Rupture and Secondary IOL Cases
- 84. Farheen Khan (G)**  
Evaluation and Adaptation of the FACE-Q Patient-Reported Outcome Measure for Ophthalmology Patients
- 85. Richard Zhang (RF)**  
Effects of relative anterior chamber depth and relative anterior microphthalmos on intraocular lens power calculation accuracy.
- 86. Carmen Balian (S)**  
Preoperative Fasting for Ambulatory Cataract Surgery: A Time-Interrupted Prospective Randomized Study (The PRACTICE Study)
- 87. Carmen Balian (S)**  
Macular Retinal Ganglion Cell Thickness After Ischaemic Stroke, With and Without Visual Pathway Involvement
- 88. Jarryll Uy (G)**  
Modelling the impact of the autism gene SCN2A on retinal development using human stem cell-derived organoid models
- 89. Loukman Ghouti (M)**  
Navigating the Medico-Legal Challenges of Ophthalmology: Insights, Impacts, and Recommendations
- 90. Juan Liyau (G)**  
Advanced Open-Source Machine Learning Tool for Hyperspectral Fluorescence Imaging in Ophthalmology

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**91. Jenny Ma (R)**

Comparison of ChatGPT and Gemini in Surgical Planning for Orbitotomy

**92. Anne Xuan-Lan Nguyen (R)**

Geographic and Sociodemographic Perspectives on Ophthalmic Plastic and Reconstructive Surgery Providers in the United States

**93. Shayaan Kaleem (M)**

Comparative Analysis of Bacterial vs Culture-Negative Endophthalmitis

**94. Danielle Solish (M)**

Sex Disparities in Operating Room Utilization among Cataract Surgeons: A 10-Year Retrospective Population-Based Analysis

**95. Zheng Jing (Jimmy) Hu (G)**

Glaucoma Medication Persistence Rates in Ontario – A Retrospective Population-Based Study.

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**Povidone-Iodine in the Treatment of Infectious Keratitis: A Systematic Review**

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**Purpose:** To evaluate if povidone-iodine is effective and safe in the treatment of infectious keratitis.

**Methods:** A systematic review of Ovid MEDLINE, EMBASE, and Cochrane Library was conducted to find relevant published articles. Outcomes including best corrected visual acuity, infiltrate, ulcer size and colony forming units were collected. All clinical trials and observational studies published in English were included. Descriptive statistics were used to summarize findings.

**Results:** Following database review, 221 articles were identified. Four studies met the inclusion criteria. The studies included 590 cases, with a culture positivity rate of 87.61%. Of the 590 cases, 288 received povidone-iodine treatment, and the rest underwent either standard of care treatment or placebo. When comparing povidone-iodine to standard antibiotic treatment, there was no significant difference in achieving recovery and presumed cure. Moreover, povidone-iodine was shown to be an effective treatment in reducing infiltrate and ulcer size while waiting for culture results. However, in two other studies, povidone-iodine did not significantly reduce CFU and did not improve visual outcomes when added to standard antibiotic treatment. None of the studies reported any safety concerns with topical povidone-iodine.

**Conclusions:** Some studies showed benefit for the use of povidone-iodine in infectious keratitis, while others found no significant differences relative to placebo or when added to topical antibiotic treatment. Further randomized controlled studies with a larger sample size and longer follow up duration are recommended to evaluate the efficacy of povidone-iodine in the treatment of infectious keratitis.

### Elevated Inflammatory Cytokines in the Aqueous Humor of Glaucoma Patients Undergoing Endothelial Keratoplasty

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**Purpose:** Descemet's Membrane Endothelial Keratoplasty (DMEK) is a cornerstone in the treatment of corneal endothelial dysfunction. Long-term graft survival is dependent on a variety of factors including the presence of ocular co-morbidities such as glaucoma. It is well established that patients with glaucoma undergoing keratoplasty have greater risk of graft rejection and failure. Previous studies have demonstrated that glaucoma patients have a distinct aqueous humor (AH) inflammatory cytokine profile. **Purpose:** To further characterize the pro- and anti-inflammatory cytokine levels in patients with glaucoma undergoing keratoplasty and assess its relationship with long-term graft survival.

**Methods:** This was a prospective study including 14 patients with glaucoma undergoing DMEK and 17 patients undergoing cataract surgery alone. AH was extracted from each patient at the beginning of their respective surgeries. A 48-analyte bead assay from Sigma-Aldrich (Milliplex Human Cytokine/Chemokine/Growth Factor Magnetic Bead Panel) was run on each sample to test for a variety of cytokines. Kruskal-Wallis and Dunn's multiple comparison tests were used to determine significance.

**Results:** Twenty cytokines showed statistical significance in the glaucoma group when compared to the control group. CD40L ( $p < 0.001$ ), Eotaxin ( $p = 0.005$ ), FLT-3L ( $p = 0.005$ ), Fractalkine ( $p = 0.02$ ), G-CSF ( $p < 0.001$ ), GRO $\alpha$  ( $p = 0.02$ ), IL-5 ( $p = 0.009$ ), IL-6 ( $p < 0.001$ ), IL-8 ( $p < 0.001$ ), IL-10 ( $p = 0.006$ ), IL-12p40 ( $p = 0.01$ ), IL-15 ( $p = 0.005$ ), IP-10 ( $p = 0.02$ ), MCP-1 ( $p = 0.01$ ), CXCL9 ( $p = 0.01$ ), MIP-1 $\beta$  ( $p = 0.002$ ), and TNF $\alpha$  ( $p < 0.001$ ) were significantly elevated in the glaucoma group. In contrast, GM-CSF ( $p = 0.01$ ), IL-22 ( $p < 0.001$ ), and M-CSF ( $p = 0.007$ ) were all significantly decreased in the glaucoma group.

**Conclusion:** There was a significant increase of many inflammatory cytokines in glaucoma patients compared to cataract controls. These cytokines indicate the potential presence of innate immune cells, such as macrophages, which could affect corneal graft outcomes. Future studies will evaluate DMEK graft survival and its association with cytokine profiles at time of surgery.

**Spatial Transcriptomics of the Human Corneal Endothelium in Fuchs Endothelial Corneal Dystrophy**

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**Introduction:** The corneal endothelium (CE) is composed of a monolayer of corneal endothelial cells (CECs) that rest on a specialized basement membrane called Descemet's membrane. Fuchs endothelial corneal dystrophy (FECD) is the leading cause of CE dysfunction and is characterized by the formation of guttae and progressive CEC loss. There is evidence that the CE is not a homogenous population of CECs, and that spatial differences exist with differential gene expression patterns. However, RNA-based transcriptomic analyses have not been extensively used to characterize cellular differences between central and peripheral spatial domains in healthy and FECD CE. We performed a transcriptomics study to characterize CEC populations isolated from the central and peripheral domains in healthy and FECD donors by bulk RNA sequencing (RNA-seq).

**Methods:** The central 8 mm and peripheral rims from healthy human cadaveric donors (n=3) and FECD cadaveric donors (n=3) were dissected. RNA was isolated and sequenced at 40 million reads/sample. A list of differentially expressed genes (DEGs) was generated for 5 comparisons: normal central and peripheral CE; FECD central and peripheral CE; normal and FECD central CE; normal and FECD peripheral CE; and normal and FECD CE. DEGs were grouped into categories by molecular function and further analyzed by an over-representation test using a PANTHER Go-Slim molecular function annotation dataset. Additional pathway analysis was performed in Cytoscape where enrichment maps were generated for each gene list.

**Results:** A total of 369 DEGs (130 upregulated and 239 downregulated) were found between FECD compared to healthy controls. A total of 167 DEGs (85 upregulated and 82 downregulated) were found between normal central and peripheral CE. Differential expression analysis of transcriptomic profiles and gene ontology analyses demonstrated an enrichment of genes involved in collagen degradation and integrin cell surface interactions between the central and peripheral CE, and collagen formation, crosslinking of collagen fibrils, and extracellular matrix (ECM) organization between healthy and FECD tissues. The dysregulation of ECM-associated pathways suggests a change in the ECM environment in the CE spatially and between healthy and FECD tissues.

**Conclusions:** There are spatial differences in gene expression, particularly in ECM proteins, between central and peripheral CECs, and between healthy and FECD CECs. This supports that the CE is composed of a heterogeneous population of CECs, which become altered in FECD. Future experiments using single cell RNA-seq will further characterize these cellular populations and will provide valuable insight into fundamental corneal biology and FECD pathogenesis.

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**Adeno-Associated Virus (AAV) Mediated Expression of Bcl-xL Attenuates Apoptosis in Human Corneal Endothelial Cells**

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**Introduction:** A significant effort in biomedical research has been to identify mutations responsible for diseases from leukemia to visual degeneration. Yet, even characterizing all possible single mutations underlying a disease is insufficient for understanding its progression. How does pathogenicity arise as mutations accumulate in the soma throughout life or in the germline over generations? This question has remained elusive, even for studies focused on single genes, given the immense space of possible mutational combinations and trajectories that need to be tested. Previous attempts at mapping genotype-phenotype-fitness landscapes have focused primarily on adaptive mutational trajectories inferred from genome sequence data. However, disease-causing mutations are difficult to detect and are not amenable to such approaches, as they are often non-adaptive, transient, and rarely establish at high frequencies in the population.

**Method:** To investigate how disease phenotypes may arise from vast mutational space, we developed a high-throughput platform in yeast capable of assaying two crucial aspects of protein function for the visual protein rhodopsin: light-dependent activation and stability. We achieved this by engineering a fluorescence-based transcriptional reporter for measuring light-dependent rhodopsin activation, and a separate fluorescent protein fusion with distinct absorbance and emission spectra for measuring rhodopsin stability.

**Results:** Anti-apoptotic BclxL2/5 and control ssAAV2/5 were both able to transduce FECD CECs with high efficiency, with transduction rates of 70.47% ± 8.28 and 65.86% ± 3.54, respectively. Infection with BclxL2/5 resulted in significantly lower levels of etoposide-induced apoptosis (23.96% ± 11.54) compared to control ssAAV2/5 (70.43% ± 14.35; p=0.000) and non-transduced FECD CECs (71.68% ± 18.70; p=0.000). In untreated FECD CECs, Bcl-xL2/5 resulted in lower levels of apoptosis (9.98% ± 5.95) compared to control ssAAV2/5 (21.08% ± 16.43; p=0.264), and non-transduced FECD CECs (9.61% ± 7.87; p=0.999). All experiments were done using n = 3.

**Conclusion:** Anti-apoptotic BclxL2/5 can transduce FECD cells with high efficiency and protect against etoposide-induced cell death. Future studies could explore using BclxL2/5 to extend the corneal transplantation window past 14 days following donor death to increase the number of donor corneas available for transplantation.



**Bilateral Corneal Perforation Secondary to Immunotherapy for Metastatic Melanoma**

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**Introduction:** To report an unexpected case of bilateral corneal perforations secondary to bispecific PD-1/IL2v complex immunotherapy for metastatic melanoma, preventative strategies, and methods of treatment.

**Method:** Case report and literature review.

**Results:** A 76-year-old female with a history of severe dry eye and recurrent metastatic melanoma presented with left eye acute atraumatic painless vision loss and was found to have a central corneal perforation; the right eye cornea revealed dry eye changes and no thinning. One day before presentation, the patient had received an infusion of a novel clinical trial bispecific immunotherapeutic agent for her melanoma given disease progression despite forty cycles of a monospecific anti-PD-1 agent. Treatment included intensive lubrication, topical moxifloxacin, oral doxycycline, oral acyclovir, application of a glue patch, and insertion of a bandage contact lens. A month later, one day after her second infusion, her right eye cornea, which had no clinically significant thinning at baseline, was found to be 70% thinned with a concomitant epithelial defect over the area of thinning. She was treated similarly to the left eye and, in collaboration with oncology, her immunotherapy infusions were held. In follow-up two months later, her glue patches have remained stable and her vision has improved significantly bilaterally.

**Conclusion:** Immunotherapeutic agents have revolutionized the treatment of recalcitrant cancer cases, addressing the global burden of cancer management. However, ophthalmologists must be aware of their side effects and take the time to educate patients and collaborate with oncology to ensure both adequate monitoring and prompt initiation of preventative treatment to obviate the necessity for patients to choose between vision-saving and life-preserving care.

## The Use of Artificial Intelligence Software in Cornea Clinics

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**Introduction:** Artificial intelligence (AI), deep learning, and large language models (LLM) have gained significant attention for their potential applications in various domains, including streamlining efficiency, providing education, and advancing research. This study focuses on the use of LLMs in ophthalmology, particularly in managing cornea-related scenarios. Following the success of OpenAI's Chat Generative Pre-Trained Transformer (ChatGPT) and the popularity of other platforms such as Writesonic, Google Gemini, and Bing Chat, this study aims to assess LLMs' ability to respond to prompts related to counseling, management, and advocacy for patients with corneal disease.

**Methodology:** Overarching topics and prompts were generated in collaboration with cornea specialists to identify areas where LLMs, namely ChatGPT, Writesonic, Google Bard, and Bing Chat, could streamline clinic efficiency. Using a rigorous scoring system, three independent cornea specialists, blinded to the LLM used to generate each response, graded the responses on accuracy, comprehension, compassion, professionalism, humanness, comprehensiveness of treatment options, and overall quality. Scores were equally weighted and averaged to generate means which were in turn ranked from highest to lowest score. Subgroup analyses were performed to identify the LLM which responded best to each prompt and based on each rubric criterion.

**Results:** Five categories of prompts were curated (clinic administration, patient counselling, treatment algorithms, surgical management, and research) under which a total of 11 prompts were constructed to produce 66 unique responses across LLMs. ChatGPT consistently outperformed other LLMs across various criteria, achieving an overall response score of approximately 83.8% versus Writesonic scoring 75%, Google Bard 62%, and Bing Chat 55.8%. Subgroup analyses further confirmed ChatGPT's superiority in responding to individual prompts and criteria compared to other LLMs. While ChatGPT's responses were highly scored, Bing Chat's responses included references to scientific literature, potentially enhancing credibility. No LLM-generated response was identified to pose a risk of harm to patients.

**Conclusion:** ChatGPT demonstrated a robust ability to respond to cornea-related prompts, outperforming other LLMs in terms of accuracy and comprehensiveness. The study emphasizes the potential of LLMs, particularly ChatGPT, in streamlining cornea-related clinical, administrative, and research tasks. Future research should involve patient feedback and repeated data collection to assess LLM-generated response improvement longitudinally. While LLMs show promise, caution is advised in their deployment, emphasizing the need for ongoing scrutiny by medical professionals to ensure patient safety while maximizing benefits and minimizing risks.

### Virtual Follow-Ups after Cataract Surgery: A Systematic Review

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**Introduction:** Cataract surgery is routinely performed, and follow-ups are used to monitor complications. It is uncertain whether virtual follow-ups provide a safe and convenient alternative to in-person review. The purpose of this review was to examine the current literature on the association between virtual post-operative follow-up care and patient outcomes after cataract surgery.

**Methodology:** Medline, Embase and CINAHL were searched from inception to October 2023 for relevant articles containing original data. Studies that: 1) included patients that were seen in a virtual follow-up (i.e., telephone or video call) for postoperative appointments after cataract surgery, and 2) reported patient outcomes were included. Risk of bias was assessed using the Newcastle-Ottawa and ROB2 assessment tools. Descriptive statistics were used to summarize findings. The review was registered in PROSPERO (registration number, CRD42023477207).

**Results:** The search yielded 1710 records with seven studies included in this review. The seven studies reported on 2113 cataract surgeries in 1994 patients. The studies ranged between 2004 and 2020. Most of the studies (5/7) included only patients who had uncomplicated cataract surgery. Virtual follow-ups were all conducted by telephone. The follow-up calls were made at varying timepoints including postoperative day 1 (n= 3), postoperative day 7 (n=2) and postoperative day 14 (n=1). Two observational studies directly compared patients who had a telephone follow-up to a control group of patients who had an in-person follow-up. There were no significant differences in complication rates ( $p=0.22$ ) or visual acuity ( $p=0.28$ ) between these follow-up groups. None of the studies reported serious adverse outcomes from replacing in-person follow-ups with telephone follow-ups. One study used virtual follow-ups in conjunction with in-person visits for elderly patients, and having additional telephone follow-ups was associated with decreased surgical recovery time and decreased patient feelings of anxiety and worry. Three studies reported on patient perceptions about the use of telephone follow-ups. A common theme was that patients preferred telephone reviews and found them to be more convenient than in-person follow-ups.

**Conclusion:** For patients with uncomplicated cataract surgery, virtual follow-ups seem to be a safe alternative to in-person visits and were enjoyed by patients. These conclusions are preliminary given the limited literature base, and further study is needed.

**Socioeconomic Status and Access to Vision Care in Canada**

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**Introduction:** Despite a universal healthcare system, access to vision care in Canada is not necessarily equally accessible by all patients. The purpose of this review was to explore the association between socioeconomic status (SES) and access to vision care in Canada.

**Methods:** Medline, Embase, CINAHL and Cochrane were searched from inception to January 2024 for relevant articles containing original data. Studies that explored the association between SES and access to vision care in Canadian patients were included. Risk of bias was assessed using the Newcastle-Ottawa and AXIS assessment tools. Descriptive statistics were used to summarize findings. The review was registered in PROSPERO (registration number, CRD42024502482).

**Results:** The search yielded 908 records with twenty-two studies included in this review. The included studies covered all provinces and territories; however, the studies were most commonly from Ontario (11/22) or nation-wide studies (5/22). The studies ranged in date between 1985 and 2022 and included patients of all ages, including pediatric patients and seniors. The included studies explored the relationship between SES and access to ophthalmic care (1/22), optometric care (2/22), or both (9/22). Overall, 17 of the 22 studies found that patients of lower SES were significantly more likely to have decreased usage of vision care. The remaining five studies found no significant association between SES and access to vision care. Six of the included studies explored rates of diabetic retinopathy screening, five of which found that lower SES was associated with decreased rates of screening. Furthermore, one study noted that pediatric patients from low-medium income neighborhoods had higher clinic visit cancellations and no-shows compared to those from high income neighbourhoods ( $p < 0.001$ ). Patients experiencing homelessness were also significantly less likely to use vision care compared to the general Canadian population ( $p < 0.01$ ).

**Discussion/ Conclusion:** Low socioeconomic status was consistently associated with decreased access to vision care for patients of all ages. Efforts are required to increase accessibility to vision care for low-income individuals and to improve health equity.

**Socioeconomic Status and Visual Impairment and Ocular Disease in Canada**

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**Introduction:** Socioeconomic status is a known social determinant of general health. The purpose of this review was to explore the association between socioeconomic status and visual impairment and ocular disease in Canada.

**Methods:** Medline, Embase, CINAHL and Cochrane were searched from inception to January 2024 for relevant articles containing original data. Studies that explored the association between SES and visual impairment or ocular disease in Canadian patients were included. Risk of bias was assessed using the Newcastle-Ottawa and AXIS assessment tools. Descriptive statistics were used to summarize findings. The review was registered in PROSPERO (registration number, CRD42024502490).

**Results:** The search yielded 908 records with twenty-seven studies included in the review. The included studies covered all provinces and territories, and the majority of studies were nation-wide studies (14/27). The studies ranged in date between 1986 and 2022 and included patients of all ages, including pediatric patients and seniors. Thirteen of the included studies explored the relationship between SES and visual impairment. Nine of the thirteen studies found that patients of lower SES were more likely to have a visual impairment, while four studies found no significant differences. Fourteen studies explored the association between SES and various ocular diseases. Glaucoma, macular diseases, diabetic retinopathy, and idiopathic intracranial hypertension were all noted to be of higher prevalence in patients of lower income levels. Patients of lower SES were at the greatest risk of having cataracts ( $p < 0.05$ ) and were more likely to have more severe cataracts ( $p = 0.001$ ). Among patients with diabetes, those in the lowest SES quintile were at an increased risk of ophthalmological complications compared to higher earners (Hazard Ratio 1.49). Among patients experiencing homelessness, those with an income of more \$1000 per month were significantly less likely to have an ocular pathology compared to those with a monthly income of less than \$1000 (OR 0.36). display differences in growth patterns (lower yield of organoids, slower organoid growth) compared to healthy controls, but share similar molecular localization of Pax6 in early 3D organoids, suggesting that retinogenesis is initiated in both groups. We will further characterize the morphological differences, presence of stage-specific markers, and transcriptomic changes in diseased versus healthy cultures as organoids continue to mature.

**Conclusion:** Income is a determinant of ocular health in Canada. Higher rates of visual impairment and ocular diseases are associated with lower patient socioeconomic status. Efforts are required to mitigate this disparity and to improve health equity.

**Eye Examinations and Sociodemographic Factors: A Retrospective Population-Based Analysis**

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**Introduction:** Regular eye examinations are a key component to improving eye health. However, access to eye care largely remains a work in progress and several factors remain major barriers to eye care services around the globe. This study aims to investigate the associations between sociodemographic factors and whether adults received an eye examination within the past 12 months in the United States.

**Methods:** Data were pooled from the 2022 National Health Interview Survey (NHIS). Participants aged 18 years or older for whom data were available on whether they had an eye examination from an eye specialist were included in our analysis. Univariable and multivariable logistic regression models were used to examine associations between sociodemographic variables and odds of undergoing an eye examination in the past year. An odds ratio (OR) and 95% confidence interval (CI) was reported for each analysis.

**Results:** Across 27,246 adults, 14,812 (53.57%) had an eye examination in the past year and 12,434 (44.97%) did not. In multivariable analysis, the following sociodemographic factors were associated with an increased odds of having undergone an eye examination in the past year: self-identifying as female (OR=1.49, 95%CI=[1.39, 1.61],  $p<0.01$ ), Hispanic (OR=1.25, 95%CI=[1.11, 1.41],  $p<0.01$ ) or Asian (OR=1.30, 95%CI=[1.13, 1.51],  $p<0.01$ ). The following factors were associated with a reduced odds of having undergone an eye examination: being single (OR=0.91, 95%CI=[0.83, 0.99],  $p=0.02$ ) or in a cohabiting relationship (OR=0.72, 95%CI=[0.63, 0.81],  $p<0.01$ ) compared to being married, residing in the West compared to the Northeast (OR=0.87, 95%CI=[0.77, 0.99],  $p=0.04$ ), and lacking citizenship status (OR=0.69, 95%CI=[0.59, 0.81],  $p<0.01$ ), insurance (OR=0.55, 95%CI=[0.47, 0.63],  $p<0.01$ ) or a usual place of care (OR=0.54, 95%CI=[0.48, 0.61],  $p<0.01$ ). Broadly, a lower income ( $p<0.01$  to  $p=0.04$ ) and education level ( $p<0.01$  to  $p=0.05$ ) were associated with a lower odd of undergoing an eye examination.

**Conclusion:** Several sociodemographic factors were associated with whether adults recently underwent an eye examination. Public health efforts dedicated to addressing inequities in vision screening are imperative.

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**Examining the Influence of Social Determinants on Medical Visit Attendance, Emergency Visits, and Clinical Outcomes Among Children with Eye Cancer: A Retrospective Analysis**

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**Purpose:** There is limited evidence on the impact of social determinants of health (SDH) on rare pediatric eye cancer (R-PEC) outcomes in Canada. We examined the association of R-PEC patient SDH with (a) medical visit attendance, (b) age and stage at diagnosis, (c) clinical outcomes, and (d) emergency visits.

**Methods:** This retrospective cohort study between 1-June-2018 and 6-October-2023 included R-PEC patients managed at The Hospital for Sick Children and resided in Ontario. Data collected included: sociodemographic variables, diagnosis details, medical visit attendance and clinical outcomes. Postal code was used to deduce neighborhood income quintile, Ontario marginalization index (OMI), geographic location, distance from hospital, and urbanicity. Pearson Chi-squared analysis and multivariable regression with adjusted odds ratios (aOR) and 95% confidence intervals (CI) were performed (significance was set at  $p < 0.05$ ).

**Results:** There were 324 study subjects with R-PECs affecting the retina (64.2%), optic nerve (28.7%), orbit (5.2%), eyelid (0.9%), and other structures of the eye (0.6%). Rescheduled or no-show medical visits were associated with: highest quintile (most marginalized) of the OMI dimensions material resources ( $p=0.049$ , aOR=1.576, 95% CI=1.003-2.477) and household dwellings ( $p=0.015$ , aOR=1.112, 95% CI=1.021-1.211); living >75 km from the hospital ( $p=0.028$ , aOR=1.109, 95% CI=1.011-1.216); and non-white race ( $p < 0.001$ , aOR=1.758, 95% CI=1.051-2.942). Higher stage at diagnosis was associated with the highest quintile of the OMI dimensions material resources ( $p=0.046$ ), household dwellings ( $p=0.015$ ), age labor force ( $p=0.004$ ), and racialized and newcomer populations ( $p < 0.001$ ); low neighborhood income quintile ( $p=0.038$ ); and non-white race ( $p < 0.001$ ). Older diagnosis age was associated with highest quintile of the OMI dimensions material resources ( $p < 0.001$ ), household dwellings ( $p < 0.001$ ), age labor force ( $p=0.013$ ), and racialized and newcomer populations ( $p=0.002$ ); living >75 km from the hospital ( $p < 0.001$ ); low neighborhood income quintile ( $p=0.017$ ); rural residence ( $p < 0.001$ ), and non-white race ( $p < 0.001$ ). Greater visual impairment was associated with the highest quintile of the OMI dimensions material resources ( $p=0.003$ ), household dwellings ( $p=0.013$ ), and racialized and newcomer populations ( $p=0.042$ ); low neighborhood income quintile ( $p < 0.001$ ); rural residence ( $p < 0.001$ ); and non-white race ( $p < 0.001$ ). Having >1 emergency room visit was associated with low neighborhood income quintile ( $p=0.022$ ); highest quintile of the OMI dimension racialized and newcomer populations ( $p=0.002$ ), and non-white race ( $p=0.041$ ).

**Conclusion:** Addressing unfavorable SDH could serve to improve clinic attendance, age and stage at diagnosis, final visual outcome and reduce emergency room visits among patients with R-PECs.

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### Visual Impairment and Unmet Ophthalmic Needs of Afghan Refugees in Toronto and the Greater Toronto and Hamilton Area

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**Introduction:** To assess the prevalence of visual impairment and access to eye care among recently arrived Afghan adult and children refugees in the Greater Toronto and Hamilton Area (GTHA).

**Methods:** 100 subjects with angle-closure glaucoma scheduled for LPI will be randomly assigned to one of two groups:

Group 1: LPI in superior position on the right eye and temporal position on the left eye.

Group 2: LPI in temporal position on the right eye and superior position on the left eye.

Preoperatively, all subjects will undergo a ophthalmic examination and complete a visual symptom questionnaire. Postoperatively, subjects will be assessed at 1 hour, 2 week, and 3 months for pain intensity and visual symptoms using the same questionnaire. Additionally, any adverse events will be monitored and recorded.

Primary outcome measures:

Visual symptoms: Presence of reported visual symptoms (e.g., glare, Horizontal, vertical and crescent shaped lines, halos, ghost images, diplopias, shadows and blurry vision) at each follow-up visit at 1 hour, 2 weeks, and 3 months postoperatively.

Pain: Mean difference in pain scores between groups"

**Results:** "84 patients completed the study and were included in the present analysis. Mean age in the full sample was 64.54 years (SD 10.8 years). A preponderance of female subjects was observed (66.7 vs 33.3%), most patients were Caucasian (64.3%). There were no statistically significant differences between groups 1 and 2 in regard to age, gender, or ethnicity.

When examining the association between patients' group and the perceived symptoms after iridotomies, there were no statistically significant associations in any category.

Finally, when examining perceived pain after iridotomies, higher mean pain scores were detected on the temporal iridotomies for left eye basal, right eye 2 weeks and left eye two weeks (Table 4), with statistical significance. No other timepoints had statistically significant differences in the pain score.

**Conclusion:** These are the preliminary results for the PIPS which is designed for a sample size of 200 subjects. At the time of writing there is no statistical difference in visual symptoms between groups for superior and temporal locations. A larger sample size could provide a better insight into the best possible position for LPI.



## Non-mydriatic fundus Photography for the Evaluation of Patients with Vision Loss in Canadian Emergency Settings

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**Introduction:** Fundoscopy is an essential component of the initial evaluation of patients with vision loss but is challenging for non-ophthalmologists. For emergency medicine physicians, non-mydriatic ocular fundus photography is superior to other forms of ophthalmoscopy in sensitivity, specificity, and inter-examination agreement. Our study evaluates the use of non-mydriatic photography as a triage and telemedicine tool for the evaluation of patients with vision loss in a Canadian emergency setting. The study design is a prospective cross-sectional study of patients presenting to emergency ophthalmology clinics at the Trillium Health Partners-affiliated sites between August and October 2023 with a chief complaint of vision loss.

**Methods:** Non-mydriatic fundus images of both eyes were obtained by a non-ophthalmologist using a handheld, non-mydriatic fundus camera prior to pupil dilation. The images were shared with a single fellowship-trained ophthalmologist without patient context. The reviewer was asked to (1) select the best photo obtained for each eye and rate image quality on a Likert scale of 1 (critical features of the posterior pole can not be distinguished) to 5 (all details of critical features visible), (2) comment on the presence or absence of fundus abnormalities and (3) provide an opinion on whether the fundus image would have changed patient disposition if available at the time of the initial ED exam. In the second phase of the study, the same fundus images will be shared with the referring ED physician, who will be asked the same three questions.

**Results:** Of 36 patients thus far evaluated in the ED for vision loss, only 5 (13.9%) had a documented fundus examination. All 36 patients had fundus photos obtained at the time of next-day Ophthalmology consultation, and 86.1% (62/72) of images were deemed to have acceptable quality (Likert scale  $\geq 2$ ). Factors limiting image quality included media opacity (i.e. vitreous hemorrhage, cataract), pupillary miosis, photosensitivity, and eyelid/periorbital abnormalities (i.e. edema). 16.7% (6/36) of patients had a visible fundus abnormality noted on photography that was not seen at the time of the initial ED exam. In each case, ED consultation with Ophthalmology was not sought, and outpatient consultation with Ophthalmology was arranged. Fundus abnormalities included macula-off retinal detachment, optic disc pallor, macular scarring, macular hemorrhage, and dot-blot hemorrhage.

**Conclusions:** Fundoscopy is infrequently performed in the emergency setting for patients presenting with vision loss. Our interim results indicate that non-mydriatic ocular fundus photography is a cost-effective, reproducible method of fundus examination, even for non-expert examiners. Further analysis is needed to determine if In-person or remote viewing of fundus images can inform more accurate triage decisions, either by indicating the need for expedited care or by providing reassurance that Ophthalmology consultation can occur less urgently.

**Disparities in Vision-related Functional Impairments Among Adults in the United States**

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**Purpose:** The relationships between vision-related functional impairment and sociodemographic factors at a population level remain unknown. In this study we investigate the relationships between vision-related functional impairment (VFI) with sociodemographic and healthcare access factors in a large, nationally representative sample of the United States population.

**Methods:** Data from the 2017 National Health Interview Survey (NHIS) were used. The NHIS involves responses from the United States civilian, non-institutionalized population 18 years or older. It provides self-reported data on demographic characteristics, socioeconomic factors, health status, and health care access. NHIS participants who responded to at least one of our target questions about vision-related functional impairment were included in the study. VFI was defined for participants based on if they responded 'yes' to one of the target questions about experiencing a VFI. Data analysis was performed through univariable and multivariable logistic regression.

**Results:** Overall, 26,711 participants were included. Multivariable analysis, controlling for relevant confounding factors, uncovered greater odds of VFI amongst females (OR = 1.16, 95% CI = 1.07-1.26,  $p < 0.001$ ), and LGBTQ+ individuals (OR = 1.46, 95% CI = 1.20-1.78,  $p < 0.001$ ). There were lower odds of VFI amongst Non-Hispanic Asian compared to White participants (OR = 0.69, 95% CI = 0.56-0.84,  $p < 0.001$ ). Participants with less than a high school degree had higher odds of VFI (OR = 1.17, 95% CI = 1.02-1.33,  $p = 0.02$ ). Amongst economic and healthcare access factors, a greater odds of VFI was associated with public health insurance versus private coverage (OR = 1.19, 95% CI = 1.07-1.32,  $p = 0.001$ ), having delayed medical care due to costs (OR = 1.86, 95% CI = 1.65-2.10,  $p < 0.001$ ), and being unemployed (OR = 1.39, 95% CI = 1.26-1.53,  $p < 0.001$ ). Participants whose incomes were lower than the poverty threshold (OR = 1.54, 95% CI = 1.32-1.80,  $p < 0.001$ ) had higher odds of VFI than those with income  $> 5x$  poverty threshold.

**Conclusion:** Several demographic and economic factors are associated with VFI in a representative sample of the U.S. population. Odds of VFI were related to sex, race, education, as well as several factors related to income and income-related access to healthcare. These results highlight the importance of addressing social and economic factors that are associated with the development of VFI when formulating and implementing health policies.

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**Eye Care Utilization Trends in Ontario's Public Healthcare System: A 20-Year, Retrospective, Population-based Analysis**

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**Introduction:** Eye-care utilization trends reflect a population's eye-care seeking behaviours, which is influenced by disease occurrence, health-insurance coverage, vision health-policy shifts, demographic changes, and other potential barriers. We investigated eye-care utilization trends among Ontarians to assess potential influencing factors.

**Methods:** Ontario population-based physician billing data from 1997-2019 were analyzed. Utilizing eye-related diagnostic codes, the annual number of eye-related visits (including revisits) and distinct eye patients (excluding revisits) per 100 population were determined. Stratified analyses were performed based on urban/rural residency, patient age, physician specialty, and visit-type (emergency/non-emergency, which was classified by if the visit occurred in an emergency-room).

**Results:** Between 1997-2019, the annual number of eye-related visits made per 100 Ontarians increased 29% (59.4 to 76.9) for non-emergency visits but decreased 21% (1.17 to 0.93) for emergency visits. The average annual number of visits per patient increased 63% (1.9 to 3.1) for non-emergency cases and remained unchanged (1.2) for emergency cases.

Excluding revisits, the annual number of individuals with an eye diagnosis per 100 population decreased 22% (from 32.0 to 25.1) for non-emergency cases and 20% (from 0.99 to 0.79) for emergency cases.

From 1997-2019, rural residents had lower non-emergency visit rates than urban residents (average 90.6 vs 94.9 per 100 population, respectively). However, emergency visit-rates were more than double for rural (2.3) compared to urban residents (1.0) in all study years, excluding 1997.

Both urban and rural residents in the 20-39 and 40-64 age-groups showed a large decline in non-emergency public-funded visits to optometrists after 2004 (60.3% in 2003 to 25.1% in 2019 in urban residents aged 20-39), but a substantial increase in public-funded visits to ophthalmologists (17.9% in 2003 to 44.9% in 2019 in urban residents aged 20-39), likely due to delisting of routine eye-exams in 2004. Trends in other age-groups for ophthalmology and optometry visits remained stable or slightly increased.

From 1997-2019, yearly top diagnoses varied by age-groups, but remained consistent overall for non-emergency visits (myopia, glaucoma, cataract) and emergency visits (corneal foreign body, conjunctivitis).

**Conclusions:** Between 1997-2019, there was a 29% rise in non-emergency eye visits but a 21% drop in emergency eye visits per 100 population in Ontario. The annual number of eye-related patients per 100 people decreased for both non-emergency and emergency visits. Per patient, yearly repeat non-emergency eye-visits increased 63% over 22 years, likely contributing to the overall 29% increase in non-emergency visits. Urban residents had more frequent non-emergency visits, but fewer emergency visits than rural residents.

**Utilization of Eye-Care Providers by Ontario Residents in 2019: A Population-based Study**

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**Introduction:** Eye-care services in Canada are provided by ophthalmologists, optometrists, primary care providers (PCPs, including family physicians, pediatricians, and nurse-practitioners), and emergency-physicians. For ophthalmic conditions, the utilization of each eye-care provider remains unclear. This study utilizes population-based billing data to address this gap.

**Methods:** Using 2019 physician billing data from the Ontario Health Insurance Plan (OHIP) and eye-related diagnostic codes, we calculated the annual number of eye-visits (including revisits) and distinct eye-related patients (excluding revisits) per 100 population. Results were stratified by urban/rural residency, age, physician-specialty, and visit-type (emergency/non-emergency, determined by whether the visit occurred in an emergency room).

**Results:** "In 2019, there were 11.5 million provincially funded non-emergency visits and 139,023 emergency visits in Ontario. The annual number of eye-visits per 100 population was 76.9 for non-emergency cases and 0.9 for emergency cases. Excluding revisits, the number of distinct eye-related patients per 100 population was 25.1 for non-emergency and 0.8 for emergency cases. On average, each patient had 3.1 visits for non-emergency cases and 1.2 visits for emergency cases.

Among non-emergency OHIP visits, 57% of eye-care was provided by ophthalmologists (6.6 million visits or 14,133 visits per ophthalmologist), 35% by optometrists (4.0 million visits or 1,525 visits per optometrist) and 8% by PCPs. Emergency care was mainly provided by PCPs (with training in emergency medicine, 74.7%), emergency-physicians (16.6%), and ophthalmologists (7.7%).

In non-emergency cases, rural patients (55.3%) received slightly fewer ophthalmologist services than urban patients (57.4%). For emergency cases, ophthalmologist care received by rural patients (4.7%) was nearly half of urban patients (8.3%).

For children aged 0-4 and 5-19, optometrists were the primary providers for non-emergency OHIP visits (48% and 80%, respectively), with the top diagnoses being refractive error and conjunctivitis. In adults, ophthalmologists were the primary provider (45%-74% for age groups 40-64, 65-79 and 80+), with glaucoma and retinal disease being most prevalently diagnosed. Corneal foreign body and conjunctivitis were among the top 3 emergency diagnoses in all age-groups.

**Conclusions:** In 2019, about 1 in 4 individuals received non-emergency eye-care in Ontario's public healthcare system, while 1 in 100 obtained emergency eye-care. In general, over half of non-emergency care was provided by ophthalmologists and about 1/3 by optometrists. Emergency eye-care was predominantly provided by PCPs and emergency-physicians, particularly in rural areas. Ophthalmologist utilization for emergency cases was nearly half in rural vs urban patients. Common diagnoses were refractive errors and conjunctivitis for Ontarians under 20, and glaucoma and retinal diseases for adults.

**Prevalence of glaucoma in Canada: Results from the 2016-2019 Canadian Health Measures Survey**

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**Introduction:** Canada lacks population-based eye-exam data on glaucoma, hindering our understanding of disease burden, distribution, risk factors, and policy development on disease management. Utilizing eye-exam data from the Canadian Health Measures Survey (CHMS), we estimated the prevalence of glaucoma in Canada to fill this knowledge gap.

**Methods:** Results from self-reports and valid eye-exams for glaucoma from 2,612 participants aged 40-79 in the CHMS 2016-2019 were analyzed using survey weights provided by Statistics Canada to represent the target survey population. Participants who failed Frequency Doubling Technology Perimetry (FDT) and had an optic-nerve vertical cup-to-disc ratio (CDR) $\geq$ 0.7 were considered to have definite glaucoma. Those with only a failed FDT, or only a CDR $\geq$ 0.7, or only intraocular pressure (IOP) $>$ 21 mmHg, or those with 'normal' values of FDT, CDR, and IOP but used glaucoma medications, were considered glaucoma suspects. Participants passing FDT, having CDR $<$ 0.7, IOP $\leq$ 21 mmHg, and not using glaucoma medications were deemed as not having glaucoma.

**Results:** An estimated 421,800 Canadians aged 40-79 self-reported having glaucoma, representing a prevalence of 2.5% (95% confidence interval [CI] 1.7%-3.3%). Prevalence was higher in those aged 65-79 (5.0%) vs. 40-64 (1.6%), in individuals with less than secondary-school graduation (5.0%) compared to secondary-school graduates (2.0%) or higher (2.3%) and amongst those who visited an ophthalmologist in the last 12 months (10.0%) vs. those who visited an optometrist (1.4%). Less than half (44.0%) of self-reported glaucoma individuals used glaucoma medications. The mean age at first glaucoma diagnosis was 52.6 (95% CI 48.6-56.7) years. The mean duration of glaucoma was 12.0 (95% CI 8.2-15.9) years.

From eye-exams, an estimated 71,000 Canadians had definite glaucoma and an additional 1.7 million Canadians were labeled as glaucoma suspects. Corresponding prevalence was 0.7% (95% CI 0.3%-1.1%) and 16.3% (95% CI 13.2%-19.4%), respectively.

Among glaucoma suspects, 44.3% had ocular hypertension (OHT, mean IOP 22.8 mmHg). Only 6.8% of individuals with OHT used glaucoma medications. IOP $\geq$ 28 mmHg was found in 2.4% of OHT individuals and none used glaucoma medications.

About 40% (37.5% or 26,625 individuals) of Canadians with exam-determined definite glaucoma were unaware they had glaucoma.

**Conclusions:** 2.5% of Canadians aged 40-79, self-reported having glaucoma. 0.7% were identified as having glaucoma based on clinical examination. Eye-exams identified 1/6 of Canadians as glaucoma suspects, necessitating further investigation. Few Canadians with OHT used glaucoma medications, including those with IOP $\geq$ 28 mmHg. Nearly 40% of Canadians with exam-determined definite glaucoma were unaware they had glaucoma.

**Developing a retinal ganglion cell organoid enrichment protocol for glaucoma research and therapeutics**Tahani, Baakdhah<sup>1</sup>, MD, MSc, PhD, Jeremy, Sivak<sup>1</sup>, PhD<sup>1</sup>Donald K Johnson, Eye Institute, University of Toronto

**Purpose:** Glaucoma is a neurodegenerative eye disease that involves damage to the optic nerve, which is formed of fibers projected from retinal ganglion cells (RGCs) to transmit electrical signals to the brain. Glaucoma is the second leading cause of blindness in North America and the leading cause of permanent blindness worldwide. Unfortunately, RGCs lost in glaucoma cannot be generated or replaced within the eye due to a lack of proliferative capabilities in adult tissues. There is a lot of interest in the field to study and replace lost RGCs by growing them in vitro using 2D cultures of pluripotent stem cells (PSCs). Yet, the development of a differentiation protocol with an efficient yield has been faced with many challenges, such as relatively small numbers and a particular vulnerability to injury. In this project, we are taking advantage of recent advances in culture techniques to establish and refine a novel differentiation protocol to generate RGC-enriched organoids from human PSCs.

**Method:** The protocol is being optimized and adapted from currently established whole-retina organoid methods, with several improvements to increase the proportion of RGCs and associated inner retinal cell types. Whole retinal organoids provide an excellent starting place because they recapitulate the developmental timing and spatial organization of the human retina. Because of their three dimensional organization, organoids allow direct cell-cell and cell-matrix interactions, producing cells with relevant physiological and pathological responses.

**Results:** Preliminary data using our modified protocol show substantially higher expression RGC markers (Atoh7 and Brn3b) compared to control organoids.

**Conclusion:** Ongoing studies are profiling the function, abundance, and subtype of RGCs produced by this novel method. This technique will be a powerful platform for studying RGC function and glaucoma pathogenesis, testing of therapeutics, and cell replacement.

**Progression of Primary Angle Closure Suspects: A Systematic Review and Meta-Analysis**

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**Introduction:** Primary angle closure suspects (PACS) are individuals with ocular anatomical configurations predisposing them to angle closure attacks, and progression to primary angle closure (PAC), potentially leading to glaucoma and blindness. Understanding the progression rate from PACS to PAC and/or acute angle closure (AAC) is crucial for early intervention and preventing vision-threatening outcomes. This review aims to elucidate the rate of angle closure attacks among PACS and evaluate the impact of prophylactic interventions.

**Method:** A systematic search was performed on OVID MEDLINE and EMBASE for studies published until November 2023 that reported on the progression rate from PACS to PAC in at least five patients. Using random-effects modelling, risk ratios (RR) and 95% confidence intervals (CI) were used to estimate the frequency of PAC and AAC progression between patients who received laser peripheral iridotomy (LPI) versus those who did not.

**Results:** Three RCTs and two observational studies were included, encompassing a total of 1,997 PACS patients from Southeast Asia. The weighted average age of the participant pool was 59.1 years old, with 80.7% females and an average follow-up period of 6.2 years (range: 2 to 14 years). Overall, 264 patients (13.2%) progressed to PACS (77.9% females, n=4/5 studies) and 9 (0.5%) experienced AAC. Among the studies included, two out of five provided comparative data on the progression from PACS to PAC and AAC in the context of LPI versus no LPI intervention, encompassing 1,366 out of the 1,997 patients analyzed (average follow-up of 9.5 years). Patients not receiving LPI displayed a 2.49-fold increase in the risk of progression to PAC (RR: 2.49; 95% CI: [1.49, 4.18]; p-value < 0.001), suggesting that lack of LPI treatment is associated with a higher risk of disease progression. However, for the progression to AAC, statistical significance was not reached with an RR of 3.33 (95% CI [0.67, 16.45]; p-value = 0.14).

**Discussion/Conclusion:** This review highlights a significant rate of progression from PACS to PAC, underscoring the important role of early diagnosis and the potential benefit of prophylactic LPI in mitigating the risk of progression to PAC. Although the increased risk of progression to AAC without LPI was not statistically significant, the trend suggests a potential protective effect of LPI against severe outcomes. These findings emphasize the importance of monitoring and managing PACS to prevent vision-threatening complications, advocating for a proactive approach in the management of individuals at risk of angle closure disease.

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**A comparative study of surgical outcomes of excisional goniotomy using the Kahook Dual Blade (KDB) combined with phacoemulsification (KDB-phaco group) in mild glaucoma vs standalone KDB group in severe glaucoma after failed glaucoma surgeries.**

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**Method:** In this study, a retrospective chart review was performed involving 10 eyes in KDB- phaco vs 10 eyes in KDB group. The outcome measures included mean IOP reduction, mean reduction in IOP lowering medications and adverse effects. Surgical success was defined as IOP reduction of at least 20% from baseline at 6 months, and /or reduction of at least 1 glaucoma medication.

**Results:** Statistically significant mean IOP and mean number of IOP medication reductions from baseline were achieved at all points in both groups. At 3 months, mean IOP decreased significantly from  $29.5 \pm 3.5$  to  $15.1 \pm 2.5$  ( $p < 0.001$ ) and from  $21.8 \pm 2.9$  to  $11.5 \pm 2.2$  ( $p < 0.001$ ) in the KDB and phaco-KDB groups, respectively. The number of IOP lowering agents decreased from a baseline of  $3.9 \pm 1.2$  to  $0.62 \pm 0.39$  ( $p < 0.001$ ) at 1 month followed by a slight increase to  $0.87 \pm 1.2$  at 3 months in the KDB group whereas in the phaco-KDB group, medications reduced from  $1.6 \pm 1.1$  to  $0.23 \pm 0.4$  ( $p < 0.001$ ) at 1 month and remained unchanged at 3 months. The common complications on day 1 were corneal edema, which was significantly greater in the KDB group at 72.7% vs 37.5% in phaco-KDB group ( $p < 0.001$ ) and hyphema which was 54.5% in KDB group vs 37.5% in phaco-KDB group. All the complications resolved spontaneously in 1-2 weeks with no adverse effects. Surgical success is yet to be calculated after a follow up of 6 months.

**Conclusion:** KDB achieved a statistically significant IOP and medication burden reduction in both groups. The most common complication reported in both groups was corneal edema which was significantly greater in the KDB group. No severe complications were reported. Although its efficacy decreases over time, its cost effectiveness and favorable safety profile makes this procedure a potentially useful primary adjunctive in high risk eyes.



**Effect of 10.0 Nylon Ripcord on Outflow Facility of the PreserFlo® MicroShunt**Taylor Lukasik<sup>1</sup>, MD, David Yan<sup>1</sup> MD,<sup>1</sup>Department of Ophthalmology and Vision Sciences, University of Toronto

**Introduction:** The PreserFlo® MicroShunt gained Health Canada approval in 2021 and is currently approved for the treatment of primary open angle glaucoma in patients on maximally tolerated medical therapy. Despite a more desirable safety profile than traditional bleb forming glaucoma intervention, hypotony remains a common complication. Inserting a 10-0 Nylon ripcord suture into the Microshunt has been hypothesised to reduce outflow reduce postoperative hypotony.

**Methods:** The PreserFlo® MicroShunt was inserted into a 26G cannula and sealed with cyanoacrylate gel glue. The cannula was then attached to iv tubing and attached to a fluid reservoir at fixed perfusion heights equivalent to 10 and 20 mmHg, perfusing ~1000 ul for multiple timed runs. The perfusion time and volume were then measured to determine outflow facility. A 10.0 nylon suture (Ethilon® CS160-6) was then inserted into the MicroShunt spanning the full length of the MicroShunt and at half length. The outflow facility was again measured at 10 mmHg and 20 mmHg.

**Results:** The outflow facility of the MicroShunt without a ripcord was  $0.87 \pm 0.03$  ul/min/mmHg at 10 mmHg and  $0.78 \pm 0.12$  ul/min/mmHg at 20 mmHg perfusion pressure. With the 10.0 nylon ripcord in place at full length, the outflow facility was significantly reduced to  $0.30 \pm 0.03$  ul/min/mmHg ( $p < 0.001$ ) at 10 mmHg and  $0.29 \pm 0.02$  ul/min/mmHg ( $p < 0.001$ ) at 20 mmHg perfusion pressure. With the ripcord at half length the outflow facility was measured at  $0.43$  ul/min/mmHg ( $p < 0.001$ ) at 10mmhg and  $0.41$  ul/min/mmHg ( $p < 0.001$ ) at 20mmhg. There was no significant difference in outflow facility between 10 and 20 mmHg perfusion pressure ( $p = 0.51$ ). Clinically observed IOP and early hypotony rates of the MicroShunt with ripcord placement will be presented.

**Conclusion(s):** The PreserFlo® Microshunt is an incisional glaucoma procedure developed with the intent of providing substantial IOP-lowering efficacy while reducing many of the adverse events and postoperative management requirements associated with trabeculectomy and tube shunt implantation. The introduction of a 10.0 nylon ripcord can reduce the outflow facility by a factor of ~3.0. As the designed outflow facility of the MicroShunt will produce ~1.5-2.0 mmHg of pressure drop along the device at human physiologic aqueous flowrates of ~2.4 ul/min, the placement of a removable 10.0 nylon ripcord during surgery could raise the pressure drop along the device to ~4.5-6.0 mmHg. This procedural modification could mitigate the risk of early hypotony, the most commonly observed adverse event associated with the MicroShunt.

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**Preliminary results for the PIPS (Peripheral Iridectomy Position Study): A Randomized Controlled Trial Investigating Optimal Laser Peripheral Iridectomy Placement**

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**Introduction:** Laser peripheral iridectomy (LPI) is a common procedure for managing angle-closure. However, the optimal placement of LPI to minimize postoperative pain and visual symptoms remains unclear. This study, the Peripheral Iridectomy Position Study (PIPS), aims to investigate the effect of LPI position on pain and visual discomfort through a randomized controlled trial.

**Methods:** "100 subjects with angle-closure glaucoma scheduled for LPI will be randomly assigned to one of two groups: Group 1: LPI in superior position on the right eye and temporal position on the left eye. Group 2: LPI in temporal position on the right eye and superior position on the left eye. Preoperatively, all subjects will undergo a ophthalmic examination and complete a visual symptom questionnaire. Postoperatively, subjects will be assessed at 1 hour, 2 week, and 3 months for pain intensity and visual symptoms using the same questionnaire. Additionally, any adverse events will be monitored and recorded.

Primary outcome measures:

Visual symptoms: Presence of reported visual symptoms (e.g., glare, Horizontal, vertical and crescent shaped lines, halos, ghost images, diplopias, shadows and blurry vision) at each follow-up visit at 1 hour, 2 weeks, and 3 months postoperatively.

Pain: Mean difference in pain scores between groups"

**Results:** "84 patients completed the study and were included in the present analysis. Mean age in the full sample was 64.54 years (SD 10.8 years). A preponderance of female subjects was observed (66.7 vs 33.3%), most patients were caucasian (64.3%). There were no statistically significant differences between groups 1 and 2 in regard to age, gender, or ethnicity.

When examining the association between patients' group and the perceived symptoms after iridotomies, there were no statistically significant associations in any category.

Finally, when examining perceived pain after iridotomies, higher mean pain scores were detected on the temporal iridotomies for left eye basal, right eye 2 weeks and left eye two weeks (Table 4), with statistical significance. No other timepoints had statistically significant differences in the pain score.

**Conclusion:** These are the preliminary results for the PIPS which is designed for a sample size of 200 subjects. At the time of writing there is no statistical difference in visual symptoms between groups for superior and temporal locations. A larger sample size could provide a better insight into the best possible position for LPI.

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**Mapping the Drainage Pathway from the Suprachoroidal Space: Evidence of Lymphatic Routing and Implications for Therapeutic Delivery in the Eye**

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**Introduction:** The suprachoroidal space serves as a compartment for delivering biologics, nanoparticles, and genes to the posterior segment of the eye. However, the routes of drainage of solutes and fluid from this space remains elusive. The present study aims to map and characterize the drainage pathway from the suprachoroidal space by injecting a near-infrared fluorescent nanoparticle tracer injection.

**Methods:** A near-infrared fluorescent nanoparticle tracer, CF770 conjugated with bovine serum albumin (MW:70kDa, 0.5 $\mu$ L), was injected into the suprachoroidal space (10nl/s) of the right eye in adult mice (C57BL/6J; n=8). Sham-injected left eyes were utilized as controls. In vivo and ex vivo fluorescence images of the eye and neck lymph nodes were captured using a scanning laser ophthalmoscope at 10-, 15-, and 20-minute intervals post-injection. Mice were euthanized 20 minutes after injection, and their tissues were processed for histological validation. Sagittal sections of the orbit, 20 $\mu$ m thick, were double labeled with podoplanin and podocalyxin, marking lymphatic vessels and blood vessels' endothelial cells, respectively. Tissue sections without primary antibodies served as negative controls. Immunofluorescence-stained sections were imaged using a confocal scanning laser microscope and a near-infrared epifluorescence microscope at 20x and 63x magnifications.

**Results:** In vivo fluorescent imaging depicted the presence of a lymphatic network with a tendency for the nasal region in the orbit. Near-infrared epifluorescence microscopy revealed that the tracer drains through the sclera and orbit. Immunofluorescence analysis identified podoplanin-positive lymphatic vessels in the choroid with a central lumen, distinct from blood vessels. Furthermore, a near-infrared tracer was detected in the lumen of podoplanin-positive lymphatic channels in the conjunctiva. Ex vivo imaging demonstrated that the tracer injected into the right suprachoroidal space drains into the right accessory submandibular neck lymph node.

**Conclusions:** This study provides the first evidence that fluid and nanoparticles exit the eye through a nasal route into the sclera and orbit from the suprachoroidal space and subsequently, drain into the ipsilateral accessory submandibular lymph node. It presents evidence of lymphatic vessels in the choroid and demonstrates tracer draining into conjunctival lymphatic channels. A better understanding of this intricate pathway originating from the suprachoroidal space holds significant implications for designing new therapeutic modalities for glaucoma such as novel drainage devices or drug delivery strategies targeting the suprachoroidal space.

**Glaucoma home monitoring with the Toronto Portable Perimeter (TPP):  
two-year compliance and repeatability results**

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Yvonne Buys<sup>3</sup>, MD, Graham Trope<sup>3</sup>, MD, Willy Wong<sup>2</sup>, PhD, Moshe Eizenman,

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**Introduction:** Visual field tests are indispensable in monitoring patients with glaucoma. Theoretical simulations suggest that frequent (fortnightly vs standard six-monthly) testing allows for earlier progression detection. (Anderson 2017) Virtual reality perimeters can make this a reality by allowing frequent testing at home in a relaxed, convenient environment. This study aims to evaluate the compliance and repeatability of home visual field monitoring using the Toronto Portable Perimeter (TPP) by glaucoma patients.

**Methods:** Patients with field defects on the Humphrey Field Analyzer (HFA) were recruited from Toronto Western Hospital. Each participant was instructed during a 20-minute session on how to use the TPP before taking the device home to perform TPP-Standard 24-2 visual field tests. Participants' preferences between TPP and HFA were evaluated through a questionnaire administered at the first follow-up. The repeatability of TPP and HFA (SITA) tests was assessed by examining the differences between consecutive test-retests with both modalities.

**Results:** Among the 25 participants (mean age: 67.4 years, range: 48–80 years, female: 48%, mean MD: -5.2 dB, range: -14.8–+1.7 dB), 72% (18/25) successfully conducted unsupervised tests at home. The mean test frequency over 2 years was 1.5 tests per month. 61% (11/18) completed  $\geq 1$  tests per month; 33% (6/18) participants completed  $\geq 2$  tests per month. Unfamiliarity with technology and time constraints were the most cited reasons for non-compliance in retired and working participants, respectively. Participants reported that TPP tests produced less anxiety ( $p=0.02$ ) and preferred testing with the TPP at home ( $p<0.01$ ). The TPP's MD and VFI were strongly correlated with the SITA-Standard 24-2 (Pearson  $r=0.86$ ,  $0.91$  for MD and VFI;  $p<0.01$ ) and SITA-Faster 24-2C ( $r=0.80$ ,  $0.91$ ;  $p<0.01$ ). The test-retest repeatability for MD was similar among TPP, SITA-Standard and SITA-Faster tests (SD of test-retest differences: 1.4, 1.5, 1.5 dB, respectively; lower SD indicates more repeatable results). TPP's VFI test results were more repeatable than those obtained by SITA-Standard and SITA-Faster (SD: 3.7%, 4.3%, 4.2%, respectively). The test duration for TPP-Standard was on average 16 seconds shorter than SITA-Standard (5 min 24 sec vs 5 min 40 sec;  $p=0.004$ ), but longer than SITA-Faster (3 min;  $p<0.01$ ).

**Conclusion:** Participants who used TPP at home achieved similar MD repeatability and better VFI repeatability compared to clinical HFA tests. While about half of all recruited participants performed the test at least once a month, others cited complexity of technology and finding time to conduct home visual field tests as impediments to taking up frequent home testing.

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## Using Fused Data from Perimetry and Optical Coherence Tomography to Improve the Detection of Visual Field Progression in Glaucoma

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**Introduction:** Visual field (VF) testing and optical coherence tomography (OCT) are both used to monitor glaucoma progression. However, combining these modalities can be challenging due to differences in data types. This study aims to develop a machine learning-based data fusion model to combine data from VF testing and OCT for improved detection of VF progression detection.

**Methods:** "We developed an autoencoder (AE) model to fuse differential light sensitivity from VF testing and retinal nerve fiber layer thickness profiles from OCT. The AE model was designed to discover a compact encoding of the input VF and RNFLT profile data, with the encoding serving as the AE-fused data. During model training, a novel encoding loss was introduced to ensure the similarity of AE-fused data to VF tests while capturing key features from OCT measurements. Therefore, the resulting AE-fused data can be interpreted in the same way that a VF test is interpreted. For model evaluation, we labeled eyes as progressing if the linear regression slope of mean deviation was worse than  $-0.5$  dB/year, calculated from all measured VF data for each eye. Then, we used data from only the first two years to detect VF progression. The detection sensitivity and specificity obtained from the AE-fused data were compared to those from the measured VF data and a state-of-the-art Bayesian linear regression (BLR) model that integrates structural and functional changes. "

**Results:** A total of 2504 VF-OCT test pairs from 253 eyes of 140 glaucoma patients were included for model training and evaluation. In the initial 2-year follow-up, the specificity of detecting VF progression using AE-fused data was 0.70 (95% CI: 0.68 to 0.71), representing a 94% improvement ( $P < 0.001$ ) over the detection specificity with the measured VF data (0.36, 95% CI: 0.35 to 0.38) and a 27% improvement ( $P < 0.001$ ) over the detection specificity when using data from the BLR model (0.55, 95% CI: 0.54 to 0.57). In the same period (i.e., the initial 2 years), the sensitivity of detecting VF progression with the AE-fused data was 0.53 (95% CI: 0.47 to 0.58), outperforming that of the BLR model (0.35, 95% CI: 0.31 to 0.38,  $P < 0.001$ ) and insignificantly lower than that of using measured VF data (0.54, 95% CI: 0.51 to 0.58,  $P = 0.291$ ).

**Conclusions:** The capacity of the autoencoder data fusion model to generate clinician-interpretable AE-fused data can improve VF progression detection, making it a promising data integration approach in glaucoma management.

### Microgravity and Vision: Investigating Intraocular Pressure Variations and Potential Consequences for Astronauts

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**Introduction:** Spaceflight-Associated Neuro-ocular Syndrome (SANS) is a newly identified eye and optic nerve pathology with an unclear cause, posing risks to astronauts' health and long-duration space missions. Although microgravity impacts intraocular pressure (IOP), which could significantly influence SANS, its changes have not been thoroughly explored in this context. A longitudinal study using NASA's hindlimb unloading (HU) model, an affordable and accessible mouse analog for microgravity, was conducted to examine microgravity's effects on IOP dynamics. This approach aims to better understand microgravity's role in SANS and potentially guide future astronaut health strategies.

**Methods:** A HU protocol was developed, suspending mice by their tails at an approximate 30-degree angle for 21 days, followed by a 14-day recovery period. Twenty male B6(Cg)-Tyrc-2J/J albino mice were randomly assigned to either the control (n=10) or HU (n=10) group. Serial in vivo tonometry was conducted on both eyes at baseline (day 0), during suspension (days 8, 14, and 21), and post-recovery (days 22, 28, and 35) to assess IOP. Concurrent body weight measurements were taken. The control group was not subjected to suspension but followed an identical assessment schedule. Linear mixed-effects models were employed to analyze longitudinal changes in IOP between the HU and control groups comprehensively.

**Results:** Significant increases in IOP were observed in the HU group on day 14 compared to baseline (day 0) in both the right and left eyes ( $p < 0.05$  for each). Consequently, a splined mixed-effects model was utilized to further examine the IOP changes before and after day 14 in both groups. In the HU group, IOP significantly rose from day 0 to day 14 in the right eye ( $p < 0.05$ ), followed by a notable decrease from day 14 to day 35 in both eyes ( $p < 0.05$  for each). Conversely, the control group exhibited no significant IOP changes at any time point (all  $p > 0.05$ ).

**Conclusions:** The study demonstrated that IOP increases from baseline to day 14, then decreases to near baseline levels, underlining the potential of HU as a valuable model for investigating the ocular changes experienced by astronauts. This finding suggests that HU could be an effective method for studying the mechanisms behind astronaut eye changes, offering insights into preventive and therapeutic strategies for SANS.

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**The Early Transcriptomic Landscape of Pressure-Induced Optic Nerve Heads in ex-vivo Organotypic Human Eyes**

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**Introduction:** 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. Following perfusion the ONH was rapidly isolated from four pairs of eyes and prepared for total mRNA sequencing. Results were analyzed by paired differential expression analysis and pathways/geneset analyses. In parallel, four pairs of fixed perfused eyes were used for spatial transcriptomics of the ONH region using the Visium platform (10x Genomics). Data processing and visualization were performed on SpaceRanger and Loupe Browser. Differential analyses of ONH and LC identified by barcodes were performed within and between samples.

**Methods:** All eyes maintained physiological or elevated IOP for 6 hours. Differential expression, Gene Ontology and Gene Set Enrichment analyses revealed significantly altered genes and pathways associated with astrocyte and microglial reactivity, and mechanosensing. K-mean clustering of spatial profiling results identified a distinct ONH expression profile. A panel of astrocyte and cell-adhesion genes highlights the LC region relative to the rest of ONH. Preliminary differential analysis revealed altered genes related to cellular stress responses and oxidative phosphorylation in the LC.

**Results:** Total mRNA and spatial transcriptomic profiling of the perfused human ONH reveals significant neuroinflammatory changes in response to elevated IOP. These changes provide insight into molecular events relevant to early human ocular hypertension, and are consistent with patterns found early in animal models.

**Conclusions:** N/A

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## Vesicular Dysfunction in Oligodendrocytes Causes Inflammatory Demyelination in the Central Nervous System

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**Introduction:** Myelin is an insulation surrounding axons permitting rapid conduction of electrical signals. Demyelination is evident in neurological disorders such as Multiple Sclerosis and Alzheimer's Disease, impacting motor, sensory, and cognitive functions. Optic neuritis, an inflammatory demyelination in the optic nerves, remains a major optic neuropathy causing visual loss. Oligodendrocytes are cells forming myelin in the central nervous system. However, the molecular machinery underlying the maintenance of myelin in adults remains elusive. We hypothesize that SNARE-dependent vesicular fusion is necessary for sustaining myelin integrity and hence, removing a critical SNARE protein will lead to demyelination with neuroinflammation.

**Methods:** To investigate the role of vesicular trafficking in oligodendrocytes, we generated oligodendrocyte-specific conditional knockout of SNAP-23, a SNARE protein expressed in oligodendrocytes, in young adult mice to analyze the behavioural, structural, and functional impairments associated with demyelination.

**Results:** 5-to-10 weeks after induction of SNAP-23 conditional knockout (SNAP-23 icKO), mice developed tremors, hindlimb weakness, and limp tail. Accelerating rotarod test indicated impaired motor performance and learning in SNAP-23 icKO mice. Further, SNAP-23 conditional knockout mice demonstrated demyelination across the central nervous system with axonal conduction deficits. Compound action potential conductance in the optic nerves was significantly reduced in SNAP-23 icKO. In vivo, SNAP-23 icKO had a delayed flash visual evoked potential response, suggesting impaired visual processing. Neuroinflammation with infiltration of peripheral immune T cells, mainly CD8+ cytotoxic T cells, into the central nervous system was also observed. Mechanistically, SNAP-23 removal in oligodendrocytes caused abnormal axon-myelin structures and impaired myelin protein trafficking underlying autoimmunity and demyelination.

**Conclusion:** SNAP-23-dependent vesicular trafficking is necessary for oligodendrocytes to maintain healthy myelin in adults. Impaired vesicular fusion in oligodendrocytes causes inflammation and demyelination in the optic nerves, ultimately affecting visual information conduction. Understanding a novel mechanism of demyelination induced by oligodendrocytes will provide potential therapeutic targets for neurological disorders with myelin abnormalities and restore vision in optic neuritis.



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**Restricted Diffusion in Bilateral Septic Superior Ophthalmic Vein Thrombosis**Abdullah El-Sayes,<sup>1</sup> H.BSc, James J.B. Armstrong<sup>2</sup>, MD, Rahul Sharma, MD<sup>1</sup>UGME McMaster University<sup>2</sup>Schulich School of Medicine and Dentistry, Department of Ophthalmology, Western University<sup>3</sup>Department of Ophthalmology and Vision Sciences, University of Toronto

**Introduction:** Superior ophthalmic vein thrombosis (SOVT) is a rare vascular disorder impacting a critical venous conduit from the orbit and adjacent tissues. Impaired SOV drainage causes venous congestion and may disturb orbital perfusion. It typically presents with ophthalmalgia, proptosis, periorbital swelling, and conjunctival congestion. Prompt diagnosis and management of SOVT is essential for vision preservation. However, early diagnosis can be difficult, particularly with subtle clinical signs. This case study presents a rare presentation of bilateral SOVT due to septic thrombi of odontogenic cause detected using diffusion weighted imaging (DWI), a specialized form of MRI elucidating the diffusion of water in physiologic tissue.

**Methods:** N/A (case report submitted)

**Results:** "A 49-year-old male presented with a two-day history of severe left periorbital edema, conjunctival injection, and chemosis with a three-week history of ipsilateral odontogenic pain. The right eye began demonstrating signs of conjunctival chemosis, hyperemia, and periorbital edema two days later. IOP was within normal range OU, and disk edema and retinal vein dilation were absent on fundus examination. Blood cultures returned positive for *Streptococcus constellatus*, raising suspicion of a bacteremia from odontogenic source.

**Findings:** MRI revealed irregular enlargement of the SOV OU (OS>OD). Left SOV demonstrated dilation, intraluminal filling defect and wall enhancement. DWI revealed a spontaneous intense hypersignal within the left SOV exhibiting restricted diffusion, without involvement of the cavernous sinuses. There was a corresponding area of hypointensity on apparent diffusion coefficient maps, confirming the DWI signal reflected true restriction in diffusion.

**Management:** These findings suggested a bacteremia from odontogenic source and an associated septic SOVT. Triple regimen antibiotics were administered alongside low weight molecular heparin. Symptoms reduced the following day and resolved to baseline within eight days."

**Conclusion:** SOVT is a rare but sight-threatening condition. Initial presentation may be subtle, but prompt diagnosis is necessary for preservation of vision. This study is among few that demonstrate the impact of DWI in elucidating SOVT and potentially an underlying etiology, providing critical insight for effective management.

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**Analysis of Diplopia Referrals in a Tertiary Neuro-Ophthalmology Center**

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**Introduction:** Diplopia is a common presenting symptom in patients with neuro-ophthalmic disorders. While 16% of patients presenting with diplopia in the emergency department have a life-threatening condition, little is known about the morbidity and mortality associated with neuro-ophthalmology consultations for patients referred for diplopia. This paper describes the potential for loss of vision, progression of symptoms, or systemic morbidity and mortality in patients referred to a tertiary neuro-ophthalmology practice for diplopia.

**Methods:** A retrospective chart review of all patients seen by two neuro-ophthalmologists in a tertiary neuro-ophthalmology practice between December 2, 2021 and May 21, 2022 was performed. All patients who were referred for diplopia were included. Our primary outcome was to describe the potential for vision loss, progression of symptoms or systemic morbidity or mortality if patients were not referred for a neuro-ophthalmic consult.

**Results:** 196 patients were referred for diplopia. The mean age at presentation was  $61.3 \pm 17.0$  years and 48.5% were women. The most common final diagnosis reached following neuro-ophthalmology consultation were cranial nerve palsies (38.3%, 75/196), convergence insufficiency and decompensated phoria (22.4%, 44/196), non-neuro-ophthalmic causes (19.9%, 39/196), thyroid eye disease (4.5%, 9/196), myasthenia gravis (3.5%, 7/196), and multiple sclerosis (6/196, 3.1%). 15.3% of patients referred to neuro-ophthalmology for diplopia had potential of morbidity or mortality. Specifically, 1% (2/196) had potential of vision loss due severe papilledema in context of untreated IIH, and 3.0% (6/196) had potential for systemic morbidity or mortality due to brain aneurysms (2/196), pituitary apoplexy (1/196), anaplastic glioma (1/196) and other malignancy (2/196). In addition, 11.2% (22/196) had potential for progression of symptoms due thyroid eye disease (9/196), myasthenia gravis (7/196), and multiple sclerosis (6/196). Of the patients who had a pre-referral neuro-imaging study, 30.1% required additional neuroimaging after neuro-ophthalmic consultation.

**Conclusion:** Overall, 15.3% (30/196) of patients with diplopia had potential for morbidity without neuro-ophthalmology consult. This study emphasizes the importance of urgent neuro-ophthalmologic referral for patients with diplopia to allow for appropriate evaluation and investigation to reduce morbidity and mortality.

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**Macular Optical Coherence Tomography Findings in Patients with Syphilitic Optic Neuropathy – A Case Series and Systematic Review**

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**Introduction:** Syphilis is a sexually or congenitally acquired infectious disease that can affect multiple organs systems, including the eye. When left undiagnosed and untreated, it can lead to significant morbidity and mortality. Syphilitic optic neuropathy can be difficult to diagnose as it can mimic many other non-syphilitic causes of optic-nerve involvement, leading to delay in treatment. Diagnosing ocular syphilis may be facilitated by assessing for specific outer retina abnormalities on macular optical coherence tomography (OCT).

**Methods:** This was a case series and case-based systematic review. For the case series, a retrospective chart review was conducted of all patients who presented to a tertiary university-affiliated neuro-ophthalmology practice over 6 months with undifferentiated optic neuropathy and were eventually diagnosed with syphilitic optic neuropathy. For the systematic review, OVID MEDLINE, EMBASE and COCHRANE CENTRAL databases were searched to identify all cases of syphilitic optic neuropathy with macular OCT. The primary research outcome was the prevalence of cases with outer retinal abnormalities on OCT.

**Results:** Four cases were identified that were eligible for inclusion. The ages ranged from 27 to 62 years old, and two of the patients were female. On examination, vision ranged from Snellen 20/50 to hand motion; all patients had optic neuropathy and macular OCT revealed chorioretinitis characterized by retinal pigment epithelium excrescences. The patients subsequently underwent uveitis work-up and were diagnosed with syphilis. They were treated with intravenous penicillin and showed improvement in outer retina appearance on follow-up. The systematic review consisted of 24 cases and 35 eyes with syphilitic optic neuropathy and reported macular OCT findings. Eighty-three percent (20/24) were males, and the mean age was 47.7 (SD: 49.2). The mean visual acuity at presentation was Snellen 20/57. On fundoscopy, 25.7% (9/35) of eyes had vitritis, while 22.8% (8/35) had placoid chorioretinal lesions. On OCT, 45.7% (16/35) of eyes had abnormal outer retina findings, most commonly disruption of the ellipsoid zone and/or retinal pigment epithelium excrescences. All patients were treated with penicillin or ceftriaxone, and final mean visual acuity was Snellen 20/29.

**Conclusions:** Two patients identified in the case series and nearly half of patients in the literature with syphilitic optic neuropathy had concurrent specific outer retina abnormalities (disruption of ellipsoid zone and/or placoid chorioretinitis in the form of RPE excrescences) seen on macular OCT. Thus, we recommend clinicians obtain macular OCT for all patients presenting with undifferentiated optic neuropathy to facilitate earlier diagnosis of syphilis.

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**Efficacy of Intra-Arterial or Intravenous Thrombolytic Therapy Versus Conservative Standard Therapy for Central Retinal Artery Occlusion: an Individual Patient Data Meta-Analysis**

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**Introduction:** There is a lack of high-quality data supporting thrombolytic treatment for non-arteritic central retinal artery occlusion (naCRAO). We performed an individual participant data meta-analysis to compare the efficacy of intra-arterial thrombolysis (IAT) and intravenous thrombolysis (IVT) with conservative standard therapy (CST).

**Methods** Embase, Medline, and CENTRAL were searched from inception to June 2023 and IPD were solicited from original investigations that reported treatment modality, time from onset of symptoms to treatment, and visual acuity (VA) data. Analysis was limited to studies with N=5, and eyes presenting with severe vision loss (SVL, VA < 20/200) that were treated within 24 hours. The percentage of eyes with moderate vision loss or worse (MVL, VA < 20/50) and change in logMAR visual acuity post-treatment was compared between the IAT, IVT, and CST groups. Chi-squared tests and Student's t-tests were used to compare categorical or continuous variables, respectively.

**Results:** Of 143 studies reporting 2956 patients with naCRAO, 65 studies provided IPD for 1104 eyes (37.3% capture rate). There were 808 eyes meeting inclusion criteria: 359/759 IAT, 191/367 IVT, and 258/1830 CST. The mean age of patients was 65.1 years (standard deviation [SD] 13.1), and 365 (33.1%) were female. At presentation, the logMAR visual acuity was 2.3 (SD 0.5) with slightly better VA in the CST group (2.2, p = 0.01). Among eyes that received treatment ≤6 hours from symptom onset, the likelihood of MVL was lower with IAT (76.8% vs. 90.2%, P=0.017, number needed to treat (NNT)=7.5) and IVT (78.5% vs. 90.2%, P=0.027, NNT=8.6) compared to CST. Similarly, greater improvements in mean logMAR VA were achieved with IAT (-0.788 vs. -0.453, P < 0.01) and IVT (-0.728 vs. -0.453, P < 0.01) compared to CST. There were no differences in rate of MVL or logMAR changes between the IAT and IVT groups if administered within 6 hours of symptom onset. When administered between 6-24 hours, IAT improved the rate of MVL (84.2% vs. 92.8%, P=0.015) and logMAR change relative to CST (-0.576 vs. -0.301, P<0.01).

**Conclusions:** Compared to CST for naCRAO, early administration of IAT or IVT is associated with increased likelihood of favorable visual outcome. IVT appears to be non-inferior to IAT when administered within 6 hours. IAT has a small statistically significant benefit compared to CST when administered between 6 and 24 hours. These results should be confirmed in a randomized, placebo-controlled clinical trial.

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**Radiological Predictors of Visual Outcome in Myelin Oligodendrocyte Glycoprotein-Related Optic Neuritis**

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**Introduction:** A subset of patients with myelin oligodendrocyte glycoprotein-related optic neuritis (MOG-ON) experiences a poor visual outcome, but no prognostic factors have been identified. This study aimed to determine whether magnetic resonance imaging (MRI) biomarkers are associated with visual prognosis in MOG-ON.

**Methods:** Design, Setting, and Participants: A cross-sectional analysis of patients seen for first episodes of MOG-ON at three tertiary neuro-ophthalmology practices between January 2012 and July 2023 was conducted. Adult patients were included if they had positive anti-MOG antibody titers obtained through cell-based assay, met the 2023 diagnostic criteria for MOG antibody-associated disease, and demonstrated optic nerve enhancement on MRI brain and orbits within one month of symptom onset. Patients were excluded if they met McDonald criteria for multiple sclerosis or had positive aquaporin-4 antibody titers.

Exposures: Degree of orbital, canalicular, and intracranial or chiasmal enhancement (none, mild, moderate, or severe compared to the lacrimal gland) on orbital T1-weighted, contrast-enhanced, fat-suppressed sequences.

Main Outcomes and Measures: Visual acuity (VA) and visual field mean deviation (VFMD) at 3 months or more of follow-up. Poor visual outcome was defined as VA or VFMD worse than 20/40 or -5.0 dB, respectively.

**Results:** A total of 129 eyes of 92 patients (median [IQR] age 37.0 [20.8-51.3], 65.2% female) were included. Poor VA outcome was seen in 6.2% of cases and poor VFMD outcome in 16.9%. Compared to eyes with moderate-severe enhancement, eyes with mild orbital optic nerve enhancement (30.8% vs. 9.1%,  $P=.02$ ) and mild canalicular optic nerve enhancement (32.3% vs. 7.1%,  $P=.02$ ) had a higher proportion of poor VFMD outcome. These associations remained consistent in subgroup analysis of MRIs performed before initiation of treatment but were not seen in analysis of MRIs performed after treatment. No radiologic characteristic was associated with poor VA outcome.

**Conclusion:** In eyes with first MOG-ON episodes, milder optic nerve enhancement in the canalicular and orbital segments is associated with poorer VF recovery. Prospective and mechanistic studies are needed to confirm the prognostic utility of MRI in MOG-ON.

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### Sex or Gender Reporting in Ophthalmology Clinical Trials Among United States Food and Drug Administration Approvals Between 1995-2022

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**Introduction:** As critical determinants of scientific rigor, reproducibility, and equity, sex and gender should be considered in clinical trial design and reporting. This study aimed to evaluate the accuracy of sex and gender reporting and extent of sex- and gender-based analysis in clinical trials associated with United States Food and Drug Administration (FDA) drug approvals between January 1, 1995 and December 31, 2022.

**Methods:** Design, Setting, and Participants: In this cross-sectional study, the following trial documents were reviewed by pairs of independent reviewers in decreasing order of priority: peer-reviewed publication, ClinicalTrials.gov report, and FDA medical and statistical reviews. Trial protocols and supplementary materials were also reviewed.

**Main Outcome Measures:** The proportion of trials that correctly applied sex and gender terminology, reported the method of assessing sex or gender, and conducted sex- or gender-based data analysis. Incorrect application of sex and gender terminology was defined as interchangeable use of sex- and gender-related terms without a clear justification.

**Results:** Between 1995-2022, 34 ophthalmic drugs corresponding to 85 trials received FDA approval, of which 16 drugs (47.1%) corresponding to 32 trials (37.6%) were associated with peer-reviewed publications. Sixteen (19.5%) trials used sex and gender terminology correctly. No trial reported how sex and gender were collected nor enrolled participants from sexual orientation and gender identity minority populations. Most trials (96.5%) reported sex- and gender-disaggregated demographic data, but few conducted sex- or gender-based analysis for data on dropout (1.2%), primary outcomes (28.2%), secondary outcomes (2.4%), and adverse events (9.4%). Erroneous sex and gender reporting was associated with later publication year (2008.5 vs. 2001.0; median difference, 7.5; 95% CI, -6.0 to 11.0;  $P < .001$ ) and higher journal influence metrics, including 2022 journal impact factor (13.7 vs. 5.9; median difference, 7.8; 95% CI, -1.4 to 152.4,  $P < .001$ ) and 2022 journal citation indicator (4.9 vs. 2.1; median difference, 2.9; 95% CI, 0 to 20.0,  $P < .001$ ).

**Conclusion:** Over three-quarters of ophthalmology trials associated with FDA drug approvals conflate sex and gender and over two-thirds lack sex- and gender-based analyses. More rigorous integration of sex and gender appears warranted for FDA and presumably other trials to improve their validity, reproducibility, and equity.

**Reirradiation with External Beam Stereotactic Radiotherapy for Recurrent  
Posterior Choroidal Melanoma After Brachytherapy**

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**Introduction:** This study aims to evaluate the effectiveness and long-term safety of external beam stereotactic radiotherapy (SRT) as a non-invasive alternative to enucleation for managing recurrent choroidal melanoma following Iodine-125 brachytherapy.

**Methods:** A retrospective review of patients with recurrent choroidal melanoma following Iodine-125 brachytherapy treated with SRT at Princess Margaret Cancer Center from June 2013 to December 2020 was conducted. Actuarial rates of tumor control, globe salvage, and treatment complications were assessed.

**Results:** Forty-four consecutive patients experiencing recurrent choroidal melanoma after prior Iodine-125 brachytherapy with a median follow-up period of 35 months (range 17-55 months) post-SRT were included. A 97.7% tumor recurrence control rate and an 81.8% globe salvage rate were observed. Enucleation was required in seven (15.9%) of patients due to a painful blind eye after reirradiation, and one (2.3%) patient was wee enucleated due to tumor recurrence, with a median enucleation-free survival time of 80.5 months. SRT-related complications included radiation retinopathy (43.2%), radiation papillopathy (54.5%), neovascular glaucoma (38.6%), radiation-induced cataract (43.2%), and vitreous hemorrhage (27.3%).

**Conclusions:** External beam stereotactic radiotherapy emerges as a non-invasive alternative to enucleation for recurrent choroidal melanoma after brachytherapy with robust rates of tumor recurrence control and globe salvage.

**Correlation of High-Risk Histopathology Features in Magnetic Resonance Imaging in Retinoblastoma**

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**Introduction:** Enucleation is the treatment of choice for advanced intraocular retinoblastoma, especially when the risks of attempted eye and vision salvage are greater than the benefits. MRI plays a crucial role in the pre-operative evaluation of this risk by providing a non-invasive evaluation of the tumor's relationship with crucial ocular structures. However, the signs of tumor invasion into the choroid, optic nerve or in the extraocular space are not always captured on imaging, leading to a false negative result. To address this, our study aims to study the morphological characteristics of high-risk histopathological features (HRPF), such as massive choroidal invasion and retro-laminar optic nerve invasion and compare it with pre-operative MRI images of the eye with retinoblastoma.

**Methods:** We retrospectively reviewed the medical records and staging MRI images of all patients undergoing primary enucleation for retinoblastoma at our institute from January 2000 to October 2023. We collected data regarding staging, treatment, and histopathological features. A neuroradiologist reviewed all radiological images that correlated with eyes that demonstrated features of high-risk pathology. All situations determined to be false negatives were further scrutinized by a second neuroradiologist. Further review of all radiological images associated with eyes without HRPF is pending.

**Results:** Twenty eyes of 20 patients were eligible for the study. The mean age at diagnosis was 28.4 + 2.3 months. AJCC pTNM were pT3a with massive choroidal invasion in 9 (45%), followed by pT3b with retrolaminar invasion of the optic nerve head in 8 (40%) and pT3d in 1 (5%) and pT4 in 2 (10%) patients. We found the sensitivity of MRI in detecting post-laminar optic nerve invasion to be 50%, massive choroidal invasion to be 82%, and scleral and extra-scleral extension to be 67% and 50%, respectively. Positive predictive value, specificity and accuracy will be determined after evaluating all MRI scans associated with eyes that underwent primary enucleation.

**Conclusions:** Our study underscores the importance of diagnostic imaging in evaluating retinoblastoma patients and detecting high-risk histopathological features. Identification of high-risk features of retinoblastoma on MRI imaging allows for better selection of eyes considered to be safe for eye salvage. False negative MRIs were mostly associated with concerns related to issues arising from image acquisition. Some eyes showed pathological features that were smaller than the spatial resolution achievable in the machine. This information allows us to improve the quality and protocol of MRI to achieve a higher sensitivity to detect HRPF.



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**Uncertain Heritable Risk in Retinoblastoma Probands: Classification of Genetic Testing Results for Risk Stratification and Screening**

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**Introduction:** Early diagnosis and prompt intervention is crucial to outcomes in retinoblastoma. Genetic testing for RB1 pathogenic variants is essential for the determination of germline mutations (heritable retinoblastoma) that places probands and relatives at risk for bilateral/multifocal disease and second cancers. All probands should undergo high-sensitivity genetic testing for RB1 variants in blood and, when available, tumour samples. Despite testing, there remain cohorts of retinoblastoma probands and/or relatives in which heritable risk remains uncertain and potentially leads to unnecessary screening. This study documented the number of retinoblastoma probands with uncertain heritable risk presenting to The Hospital for Sick Children (SickKids), and subclassified them on the basis of the nature of their uncertainty, with a view to the refinement of screening protocols for these probands and their first-degree relatives.

**Methods:** A 10-year retrospective observational case series with review of medical records and genetic testing results of all retinoblastoma probands that were seen as a new patient at SickKids during the study period (1st January 2014 – 31st December 2023). Variables collected included patient demographics, disease laterality and severity, type and results of genetic testing, pathogenic variants detected and family history.

**Results:** "There were 173 retinoblastoma probands identified (bilateral 45% (n=78), unilateral 55% (n=95)). Of these, 27.2% (n=47) were found to have uncertain heritable risk.

Of these probands with unilateral disease, 59.6% (n=28) were cases where tumour tissue was not tested and no RB1 pathogenic variant was detected in blood samples, 8.5% (n=4) had tumour tested with no mutation found, and no blood germline pathogenic variant detected, 8.5% (n=4) had only one tumour mutation detected, and no blood germline pathogenic variant detected, 4.3% (n=2) had a germline variant of uncertain significance, and 2.1% (n=1) had not had genetic testing performed.

Of the probands with bilateral disease and uncertain heritable risk (ie uncertain potential risk of disease in siblings/offspring), 12.8% (n=6) were diagnosed and/or tested outside of the province with no available genetic testing information, and 4.3% (n=2) had bilateral retinoblastoma with no germline mutation detected (low level somatic mosaicism).

**Conclusion:** These results provide a new descriptive subclassification system for probands with uncertain heritable risk. Further study to describe the long term follow up of unilateral probands, and relatives of all probands, to describe the risk of development of further primary retinoblastoma or second cancers is planned. This can inform the development of specific screening guidelines for probands and relatives with uncertain heritable risk.

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## Elucidating the Underlying Mechanisms of Unique TEAD Interactomes Across Distinct Target-Gene Specificity in YAP Binary Classes

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**Introduction:** The corneal endothelium (CE) is composed of a monolayer of corneal endothelial cells (CECs) that rest on a specialized basement membrane called Descemet's membrane. Fuchs endothelial corneal dystrophy (FECD) is the leading cause of CE dysfunction and is characterized by the formation of guttae and progressive CEC loss. There is evidence that the CE is not a homogenous population of CECs, and that spatial differences exist with differential gene expression patterns. However, RNA-based transcriptomic analyses have not been extensively used to characterize cellular differences between central and peripheral spatial domains in healthy and FECD CE. We performed a transcriptomics study to characterize CEC populations isolated from the central and peripheral domains in healthy and FECD donors by bulk RNA sequencing (RNA-seq).

**METHODS:** The central 8 mm and peripheral rims from healthy human cadaveric donors (n=3) and FECD cadaveric donors (n=3) were dissected. RNA was isolated and sequenced at 40 million reads/sample. A list of differentially expressed genes (DEGs) was generated for 5 comparisons: normal central and peripheral CE; FECD central and peripheral CE; normal and FECD central CE; normal and FECD peripheral CE; and normal and FECD CE. DEGs were grouped in categories by molecular function and further analyzed by an over-representation test using a PANTHER Go-Slim molecular function annotation dataset. Additional pathway analysis was performed in Cytoscape where enrichment maps were generated for each gene list. Classification Random Convolutional Kernel Transform (ROCKET) [1] is applied to the collected full-field ERG data. The ROCKET transformer is a one-layer convolutional neural network, which computes 10,000 feature maps, which are then aggregated and passed to linear classifier. The novelty of the ROCKET algorithm is the number of descriptive features, generated for each waveform.

**RESULTS:** A total of 369 DEGs (130 upregulated and 239 downregulated) were found between FECD compared to healthy controls. A total 167 DEGs (85 upregulated and 82 downregulated) were found between normal central and peripheral CE. Differential expression analysis of transcriptomic profiles and gene ontology analyses demonstrated an enrichment of genes involved in collagen degradation and integrin cell surface interactions between the central and peripheral CE, and collagen formation, crosslinking of collagen fibrils, and extracellular matrix (ECM) organization between healthy and FECD tissues. The dysregulation of ECM-associated pathways suggests a change in the ECM environment in the CE spatially and between healthy and FECD tissues.

**Conclusion:** There are spatial differences in gene expression, particularly in ECM proteins, between central and peripheral CECs, and between healthy and FECD CECs. This supports that the CE is composed of a heterogeneous population of CECs, which become altered in FECD. Future experiments using single cell RNA-seq will further characterize these cellular populations and will provide valuable insight into fundamental corneal biology and FECD pathogenesis.

**Social Determinants of Health and Visual Outcomes in Pediatric Cataract**

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**Introduction:** This study investigated the association of social determinants of health with visual outcomes after pediatric cataract surgery.

**Methods:** We retrospectively reviewed children who underwent pediatric cataract surgery between 2018 and 2022. Exclusion criteria were residence outside of Ontario, non-quantifiable vision, secondary cataracts (e.g., traumatic, uveitic), and unilateral cataract surgery performed under 7 months of age. Social determinants of health included sex, ethnicity, preferred language, and need for interpreter. Using 2016 census data and postal code, we deduced patients' neighborhood income quintile, geographic region of residence, and urbanicity. Best-corrected visual acuity was collected from the most recent clinic visit. T-tests and chi-square tests were used to analyze social determinants and vision outcome.

**Results:** Sex, postal code, geographic region, and urbanicity were available for all 61 patients included. Income quintile was available for 59 (97%) and preferred language for 52 (85%). None had ethnic group or need for interpreter recorded. There was no significant difference in visual acuity by sex, preferred language, urbanicity, or region (Females 0.38 logMAR, males 0.56 logMAR,  $p=0.08$ ; English 0.41 logMAR, non-English 0.53 logMAR,  $p=0.48$ ; urban 0.45 logMAR, rural 0.77 logMAR,  $p=0.11$ ; region  $p=0.8$ ). 29% of low-income patients, 33% of medium-income patients, and 54% of high-income patients achieved better than logMAR 0.3 vision ( $p=0.25$ ).

**Conclusions:** Trends were present between social determinants of health and vision outcomes, but no significant associations were found. This study highlights current gaps in available data on our patients' social determinants of health with low documentation of ethnicity, preferred language, and interpreter need.

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**Biofeedback Training for improving visual functions in children with nystagmus:  
a short-and-long term analysis**

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**Introduction:** Idiopathic Infantile Nystagmus Syndrome (IINS) is responsible for about 10% of all infantile nystagmus cases. While visual acuity is usually not markedly decreased in IINS, other visual functions, such as near vision, contrast sensitivity, and fixation stability, can be affected. When IINS patients are asymptomatic, no treatment is required. However, if visual functions are affected or an abnormal head posture develops, interventions are warranted. There are multiple surgical, medical, and optical medical treatment options available to help improve the visual functions of patient with low-vision due to IINS. Microperimetric biofeedback training has been employed in other conditions associated with low vision to promote eccentric visual fixation and improving visual functions. In a recent pilot study conducted by our group, we have demonstrated improved short-term visual outcomes and quality of life in IINS patients. We aim to report on the long-term visual outcomes of audio-visual biofeedback training (BT) in IINS patients.

**Methods:** Prospective case series that included 25 patients with IINS and decreased visual functions treated with audio-visual biofeedback training. Inclusion criteria were IINS patients, 5 - 17 years old, ability to follow the visual and auditory stimuli and training instructions. Patients were excluded if they had co-existing ocular conditions (i.e., retinal diseases, media opacity, etc.) and inability to perform training and testing. Children treated with audio-visual BT on the MAIA microperimeter were analyzed pre-BT, 1-week post-BT (short term), and at least 1-month post-BT (long term). Outcomes: binocular best corrected visual acuity (BBCVA) for distance and near, fixation stability (FS), reading speed (RS), contrast sensitivity (CS), stereopsis, and Children's Visual Function Questionnaire. BBCVA for distance and near, and FS were measured in the long term. One-way repeated ANOVA and paired t-tests were used for statistics.

**Results:** "At the 1-week follow-up visit, there was a significant improvement in contrast sensitivity (from  $0.19 \pm 0.18$  to  $0.06 \pm 0.09$ ;  $p < 0.001$ ), reading speed (from  $78.4 \pm 30.5$  to  $108.2 \pm 36.1$ ;  $p < 0.001$ ), and QoL questionnaire scores (from  $26.0 \pm 2.7$  to  $27.3 \pm 2.7$ ;  $p = 0.002$ ). However, while there was a pattern of improvement in stereopsis (from  $231.9 \pm 265.4$  to  $106.5 \pm 125.7$ ), the change was not statistically significant ( $p = 0.163$ ). BBCVA logMAR VA improved from  $0.38 \pm 0.18$  to  $0.29 \pm 0.19$  and  $0.26 \pm 0.18$  in the 1-week ( $p < 0.001$ ) and final follow-up ( $p < 0.001$ ) visits, respectively. Twenty-two (88.0%) patients had an improvement at the final follow-up visit. Similarly, there was a significant improvement in near BCVA from baseline ( $0.19 \pm 0.13$ ) to the 1-week ( $0.05 \pm 0.09$ ;  $p < 0.001$ ) and final follow-up ( $0.04 \pm 0.07$ ;  $p < 0.001$ ) visits with 68.0% of patients experiencing improvement at the final visit. Fixation stability improved from  $15.4 \pm 18.0$  at baseline to  $7.2 \pm 8.5$  ( $p = 0.037$ ) at 1-week and  $5.3 \pm 7.8$  ( $p = 0.006$ ). At the final visit, 22 (88.0%) patients had an improvement compared to baseline.

**Conclusions:** Biofeedback training delivered significant improvement in a relatively short time period (80 minutes total) in BBCVA for distance and near, fixation stability, contrast sensitivity, reading speed, and subjective visual functioning in patients with nystagmus. As a safe and cost-efficient rehabilitation technique and following validation with larger studies, this study brings strong evidence that BT could provide a novel and relevant visual rehabilitation for patients with nystagmus.

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### Automated Detection of Retinoblastoma Tumour and Treatment Response Using Optical Coherence Tomography Analysis

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**Introduction:** Retinoblastoma (RB) is the most common ocular malignancy affecting pediatric populations. Optical coherence tomography (OCT) enables in vivo imaging of the retina and plays an instrumental role in the diagnosis and management of ocular diseases. There are several treatment options for RB, including enucleation and laser- or cryo-ablation. OCT is used to aid in the diagnosis of RB, guide treatment decisions, and assess treatment response. Extensive evaluation of multiple OCT scans over several visits is required to ensure adequate identification and treatment of RB tumors with focal ablation. This process is susceptible to human error, and automation is warranted to optimize patient outcomes. Therefore, the purpose of this study was to manually segment OCT scans of a patient with RB to develop automated methods for segmenting and co-registering sequential OCT scans.

**Methods:** OCT B-scans from an RB patient were manually annotated using 3D Slicer. Specifically, RB tumor margins, scar boundaries, and additional retinal landmarks (e.g., sclera, inner nuclear layer-outer plexiform layer junction, internal limiting membrane) were annotated to serve as a reference for quantitative and qualitative validation of an automated segmentation algorithm. A convolutional neural network (i.e., U-Net) was trained for each class for 50 epochs with a learning rate of  $1e-4$ . The training dataset was composed of 75% of segmented images, and the model was subsequently evaluated on a test dataset consisting of 25% of segmented images. Jaccard index (JI) was computed for each segmentation class to evaluate the segmentation performance of the automated segmentation model.

**Results:** Performance of the automated segmentation model was variable across segmentation classes. Specifically, automated segmentation of RB tumour demonstrated the highest degree of similarity ( $n = 400$ ;  $JI = 0.80$ ), followed by scar ( $n = 223$ ;  $JI = 0.63$ ). RPE segmentation was moderately similar ( $n = 1553$ ;  $JI = 0.50$ ), followed by ILM ( $n = 1461$ ;  $JI = 0.45$ ) and INL ( $n = 1346$ ;  $JI = 0.45$ ). Segmentation of the sclera demonstrated the lowest segmentation similarity ( $n = 1430$ ;  $JI = 0.38$ ) when compared to all other classes.

**Conclusion:** The present study demonstrates the potential for an automated segmentation model in the detection and monitoring of RB tumours. Further refinement of the segmentation algorithm may improve the ability to automate detection of RB tumours with a higher degree of accuracy and capture temporal changes in tumour progression.

**The Association Between Retinal Thickness Fluctuations and Visual Outcomes Following Anti-VEGF Therapy: A Systematic Review and Meta-Analysis**

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**Introduction:** To examine the association between retinal thickness (RT) fluctuations and best-corrected visual acuity (BCVA) in eyes with neovascular AMD, macular edema secondary to RVO, and DME treated with anti-VEGF therapy.

**Methods:** A systematic search of Ovid MEDLINE, EMBASE, and the Cochrane Library was performed from January 2006 to December 2022. Studies comparing visual or anatomic outcomes of patients treated with anti-VEGF therapy, stratified by magnitudes of RT fluctuation, were included. ROBINS-I and Cochrane RoB 2 tools were used to assess risk of bias, and certainty of evidence was evaluated with GRADE criteria. Meta-analysis was performed with a random effects model. Primary outcomes were final BCVA and change in BCVA relative to baseline.

**Results:** 13900 articles were screened; 14 studies were identified in the systematic review and 4 studies were included in the meta-analysis. Final ETDRS VA was significantly worse in eyes with the highest level of RT fluctuation (weighted mean difference (WMD) = 6.83 letters; 95% CI, 4.41, 9.24;  $p < 0.00001$ ;  $I^2 = 76%$ ; 2995 eyes). RT at last observation was significantly greater in eyes with high RT fluctuations (WMD = 27.35  $\mu\text{m}$ ; 95% CI, -0.04, 54.75;  $p = 0.05$ ;  $I^2 = 88%$ ; 962 eyes).

**Conclusion:** Final visual outcome is associated with magnitude of RT fluctuation over the course of therapy. Minimizing RT fluctuations is essential to optimizing visual outcomes in patients treated with anti-VEGF therapy. These findings are limited by a small set of studies, risk of bias, and considerable heterogeneity.

**Retinal Optical Coherence Tomography Imaging Biomarkers in 1 Epiretinal Membrane: A Systematic Review**

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**Introduction:** To identify and review the most novel optical coherence tomography (OCT) nomenclature and their clinical applications in retina.

**Methods:** A review of the literature was conducted to identify novel OCT nomenclature reported to date. A descriptive summary of all terms was completed, and representative illustrations were developed to highlight the most relevant features.

**Results:** A total of 37 OCT terminologies were identified. Nine terminologies were included in the vitreomacular interface disorders group, including the 4 stages of epiretinal membrane, macular pseudohole, tractional lamellar hole, degenerative lamellar hole, cotton ball sign, and foveal crack sign. Eight terminologies were included in the AMD group, including outer retinal tubulation, multi-layered pigment epithelial detachment, onion sign, double-layer sign, reticular pseudodrusen, complete outer retinal atrophy, complete RPE and outer retinal atrophy, and pre-choroidal cleft. Seven terminologies were included in the vascular disorders group, including pearl necklace sign, diffuse retinal thickening, disorganization of retinal inner layers, INL microcysts, hyperreflective retinal spots, paracentral acute middle maculopathy, and acute macular neuroretinopathy. The uveitic disorders group consisted of four terminologies, including bacillary layer detachment, syphilis placoid, rain cloud sign, and pitchfork sign. Two terminologies were identified in the disorders relating to toxicity group, including flying saucer sign and MEK inhibitor-associated retinopathy. Moreover, two terminologies were included in the disorders associated with systemic conditions group, including choroidal nodules and needle sign. There were two terminologies in the pachychoroid spectrum group, including pachychoroid and brush border pattern. Within the miscellaneous group, three terminologies were identified, including omega sign, macular telangiectasia, and omega sign (II).

**Discussion/Conclusion:** The pertinent features of 37 OCT terminologies were summarized and detailed illustrations consolidating the relevant features of each biomarker were included. Novel OCT biomarkers continue to be described in the literature, and a nuanced understanding of these biomarkers is essential for ophthalmologists due to their prognostic and predictive value.

### Investigating Early Transcriptional Targets of Neuroprotective LXB4 in Neuronal Injury Models

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**Introduction:** Glaucoma is an incurable group of optic neuropathies that lead patients down a road of worsening tunnel vision to eventual total blindness. The degeneration of retinal ganglion cells (RGCs) and their axons in the optic nerve is an ever present characteristic noted as a major factor to the pathology. We have identified neuroprotective activity of the endogenous lipid mediator Lipoxin B4 (LXB4) in acute and chronic models of glaucomatous injury. LXB4 was found to be significantly more potent than similar lipid mediators, with its activity mediated through a separate unknown mechanism than its well-studied isomer, LXA4. LXB4's signaling and associated targets have yet to be identified, yet in injury models is most potent as a 1 hour pretreatment to injury. This requirement points to transcriptional regulation as the driving factor in neuroprotective activity. We have previously performed bulk RNA sequencing and now aim to refine an approach with single cell RNA sequencing, coupled with our existing injury model to recapitulate and possibly extend these findings in primary neurons.

**Methods:** "Bulk RNA Sequencing: HT22 neuronal cells were seeded at 1x10<sup>6</sup> cells/well in DMEM media overnight. 4 groups; LXA4, LXB4, 15-HETE (inactive LXB4 precursor) and Vehicle were treated at 1 $\mu$ M for 1 hour. Total RNA was isolated, purified and sequenced on an Illumina platform. Data was then bioinformatically analyzed with differential gene expression to identify lipoxin-specific transcripts. Top Hit Validation: TERT and telomerase activity was studied through TERT agonists in neuronal injury models. This was coupled with further in-vivo validation of previously identified functions of TERT in neurodegenerative disease models. Single cell RNA sequencing: C57BL/6 mice were intravitreally injected with 10 $\mu$ M LXB4 and Vehicle 1-hour before 10mM kainic acid (KA) insult. Retinas were dissected after defined timepoints and RGCs positively selected using CD90.2 microbeads following neural dissociation.

**Results:** Compared to Vehicle, 242 LXB4-specific genes, 539-LXA4, and 440 15-HETE-specific genes were identified ( $p < 0.01$ ). 10 LXB4-specific genes passed the statistical test of  $p_{adj} < 0.05$  and  $\log_2FC > 3$  to be used in subsequent analyses. Of those TERT was the most high differentiated gene unique to the LXB4 group.

**Discussion/Conclusion:** LXB4 is a potent neuroprotective lipid with ambiguous activity. The current work seeks to capture early transcriptional responses in relation to glaucoma models. Next steps include validation of signature genes to further define their relation to LXB4 neuroprotective activity.



**Investigating Missing Heritability in Inherited Retinal Dystrophy**

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**Introduction:** Inherited Retinal Dystrophy (IRD) is a heterogeneous group of degenerative disorders leading to vision loss. Around 300 genes have been associated with IRDs. Despite genetic testing, 15-50% of IRD cases remain undiagnosed and are classified as "gene-elusive".

**Methods:** Five pedigrees with presumed autosomal/X-linked recessive IRD and inconclusive/negative clinical panel tests underwent ocular examinations, and genome sequencing (GS) was performed on probands. Variants were annotated and validated using filtration pipelines developed at The Center for Applied Genomics, and in the lab. Phenotype driven panel filtering was performed to identify candidate variants, followed by segregation analysis and functional validation. GS analysis was performed as necessary.

**Results:** Case 1, a 59-year-old male diagnosed with fundus albipunctatus, had 7 variants identified on panel filtering. However, no variants of interest were identified.

Case 2, a 14-month-old male diagnosed with Leber's congenital amaurosis, had 24 variants identified in panel-based filtering, with RPGRIP1 being the only gene with multiple variants. Segregation analysis of RPGRIP1 verified that 3 were maternally inherited (c.3100-229\_3238+234dup, c.1468-2A>G and c.491-112G>A), and variant c.906+26T>C is paternal. Functional validation of the paternal variant is being conducted.

Case 3, an 11-year-old male diagnosed with early onset retinal dystrophy. Two heterozygous variants in the gene CRB1, one exonic (c.906+26T>C) and another intronic (c.849-26A>G) were prioritized. Segregation analysis confirmed them to have been inherited in trans. Minigene confirmed that the intronic variant would result in a splice acceptor loss leading to exon 4 skipping and a premature stop codon (p.[Arg284fs6\*]).

Case 4, a 33-year-old male diagnosed with X-linked retinitis pigmentosa, was found to have a large deletion at the 3' untranslated region (UTR) for the gene RPGR. Functional validation is being conducted.

Case 5, a 22-year-old female diagnosed with multifocal vitelliform dystrophy, had 8 variants identified in panel-based filtering, with IMPG1 being the only gene with variants that were inherited in trans (c.563-174T>G, c.2045-7421C>T, c.1291+13335C>T). Functional validation of variants are being conducted.

**Conclusions:** The findings of the current study support the notion that gene-elusive cases may be partially explained by non-coding variants and highlight the importance of leveraging comprehensive genome analysis for accurate diagnosis. Studies are being conducted to understand the functional impact of these variants and develop therapeutic strategies.

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**Profiling the Visual System of *Lymnaea stagnalis* as a Novel Model for Investigating Photoreceptive Behaviours and Retinal Processing in Invertebrates**

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**Introduction:** To navigate the external world, animals perceive and react to light using complex visual system machinery. To date, diverse animal models have been employed to explore visual system function and potential mechanisms in both physiological and pathophysiological states. While invertebrate models have been instrumental in elucidating visual properties, few have been established to investigate photoreceptive behaviors and retinal processing. As well, our current understanding of the cellular and molecular mechanisms that underlie photoreception across the animal kingdom is limited, highlighting the need to establish new animal models for studying the fundamentals of vision.

**Method:** In this study, we capitalized on valuable features of *L. stagnalis*, along with recent transcriptomic work, to establish a platform for assessing visual system function through anatomical and histological evaluations of the *L. stagnalis* eye, functional analysis of phototaxis behaviors, and phylogenetic assessments of core molecules involved in phototransduction.

**Results:** First, to understand the laminar retinal organization in the *L. stagnalis* eye and determine whether rhodopsin-positive cells were present and distributed throughout discrete retinal layers, we employed TEM and histological screens to uncover for the first time the presence of rhodopsin-positive sensory photoreceptor cells that may be associated with light sensitivity. Next, to characterize the functional outputs of photosensation, we created a novel neurobehavioral test to assess snail phototaxis *in vivo* using DeepLabCut software. By extrapolating locomotory features such as trajectory length, speed, acceleration, and tortuosity, neurobehavioral assessments revealed that most animals in a cohort exhibit positive phototaxis behaviors. Lastly, to elucidate the molecular basis of phototransduction in *L. stagnalis*, we conducted transcriptomic mining of the *L. stagnalis* CNS transcriptome, identifying three novel putative rhodopsin-like genes. Using phylogenetic assessments and AlphaFold2 structural predictions, we revealed the evolutionary conservation and structural similarity of *L. stagnalis* rhodopsin-like proteins to higher-order animal rhodopsins. Our transcriptome mining further uncovered a rich repertoire of genes for both vertebrate Gt-coupled and invertebrate Gq-coupled phototransduction signaling pathways in the CNS. This allowed us to predict the signaling pathways underlying photosensation in *L. stagnalis*.

**Conclusion:** Taken together, this study offers valuable insights into the conservation of photoreception processes and distinctive visual mechanisms in *L. stagnalis*, setting the stage for additional exploration of this model organism in vision research. The importance of this study lies in establishing *L. stagnalis* as a crucial model for understanding vision sciences, laying the groundwork for future investigations into the molecular and evolutionary facets of photosensitivity and phototaxis behaviors.

**Pathogenic Variants of a Visual Protein Constrain Mutational Pathways in Genotype Space**

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**Introduction:** A significant effort in biomedical research has been to identify mutations responsible for diseases from leukemia to visual degeneration. Yet, even characterizing all possible single mutations underlying a disease is insufficient for understanding its progression. How does pathogenicity arise as mutations accumulate in the soma throughout life or in the germline over generations? This question has remained elusive, even for studies focused on single genes, given the immense space of possible mutational combinations and trajectories that need to be tested. Previous attempts at mapping genotype-phenotype-fitness landscapes have focused primarily on adaptive mutational trajectories inferred from genome sequence data. However, disease-causing mutations are difficult to detect and are not amenable to such approaches, as they are often non-adaptive, transient, and rarely establish at high frequencies in the population.

**Methods:** To investigate how disease phenotypes may arise from vast mutational space, we developed a high-throughput platform in yeast capable of assaying two crucial aspects of protein function for the visual protein rhodopsin: light-dependent activation and stability. We achieved this by engineering a fluorescence-based transcriptional reporter for measuring light-dependent rhodopsin activation, and a separate fluorescent protein fusion with distinct absorbance and emission spectra for measuring rhodopsin stability.

**Results:** Using this platform, together with fluorescence-activated cell sorting and ultradeep sequencing, we screened a combinatorial mutation library encoding all possible combinations of amino acid substitutions at four sites in rhodopsin representing 160,000 protein variants and discovered hundreds that neither compromise rhodopsin stability nor light activatability. With such a large volume of data, we applied systems-level analyses to generate a map of protein variant effects, revealing that ~4.6 percent of variants are functional with the remaining variants compromising at least one aspect of function.

**Conclusion:** This result suggests that although genotype space is dominated by non-functional pathogenic variants, a small but substantial proportion of variants are functionally permissive and likely constitute viable mutational pathways. Together our platform enables the high-throughput discovery of protein variant effects for visual proteins and is demonstrated to be capable of identifying non-functional, and potentially pathogenic, variants that constrain viable mutational pathways in genotype space.

**In Vivo Assessment of Cystoid Changes in Rhegmatogenous Retinal Detachment Using Swept-Source Optical Coherence Tomography**

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**Introduction:** Objective: What is the sequence of morphological features leading to cystoid changes in rhegmatogenous retinal detachment?

**Methods:** Methods: Prospective cohort study. Primary RRDs referred to St. Michael's Hospital, Toronto, Canada, from 2020 to 2023 were included. All patients underwent SS-OCT (PLEX Elite 9000; Carl Zeiss Meditec, Inc.). Patients with poor imaging or without consistent follow up were excluded.

**Results:** Results: A total of 461 patients were included in this study. The initial morphological change in RRD is a hydration of photoreceptors outer segments. With increasing duration of RRD, there is hydration of the Henle Fiber Layer and the outer nuclear layer. The osmotic and hydraulic forces in the subretinal space then lead to the formation of a honeycomb pattern in the Henle Fiber Layer and outer nuclear and lastly the inner nuclear layer (INL) is hydrated with microcystic changes being evident.

**Conclusions:** "Conclusions: The morphological sequence of events leading to cystoid changes in RRD starts in the outer retina and ends in the inner retina. Müller cell dysfunction may play a role in the accumulation of fluid in the INL in RRD.

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### A Human Chimeric Retinal Organoid Model for Studying Donor-Host Cell Interactions in Cell Therapies for USH2A-Associated Retinitis Pigmentosa

Cassandra D'Amata

**Introduction:** There are currently no human models of retinal cell engraftment that enable the study of allogenic donor-host cell interactions between healthy and disease cells in a degenerating retina. Our lab has generated chimeric retinal organoids (“chimeroids”) from a mixture of pluripotent stem cell lineages. We hypothesize that our chimeroids represent a novel in vitro human model of retinal cell engraftment in a common USH2A mutant causing autosomal recessive retinitis pigmentosa, and will provide a new way to study cell-cell interactions between healthy and diseased human retinal cells.

**Methods:** Chimeroids were generated using patient-derived USH2A mutant iPSCs, which we edited with CRISPR/Cas9 to express nuclear H2B promoter-driven GFP (USH2A-GFP), and H9 ESCs that are lentiviral-transduced to express nuclear H2B promoter-driven RFP (H9-RFP). We combined cultures of undifferentiated H9-RFP and USH2A-GFP cells in various ratios in 2D, alongside single lineage controls. We then differentiated 3D retinal organoids following established protocols. USH2A has a role in photoreceptor (PR) outer segment (OS) maintenance, which is critical to PR cell survival. Chimeroids and control organoids were evaluated for markers of retinal cell fate specification, gene expression, and PR morphology at different stages of organoid development.

**Results:** USH2A diseased organoids show markedly shorter presumptive OS, lower Rhodopsin (Rho) expression, and lower Arrestin-3 (Arr3) expression in mature organoids (Week 24) compared with healthy H9 controls. Decreased Rho and Arr3 gene expression in USH2A organoids was confirmed by qRT-PCR. In contrast, chimeroids display longer presumptive OS as well as improved Rho and Arr3 protein expression compared to diseased controls. Restored Rho- and Arr3-expressing USH2A-derived cells within chimeroids can be observed by immunohistochemistry in regions of high mosaicism as well as USH2A-GFP dominated regions.

**Conclusion:** We have generated retinal chimeroids using a patient-derived diseased iPSC line. Ongoing small molecule testing and FAC sorting will allow us to examine the modified properties of healthy and diseased cells in our chimeroids. This may reveal new therapeutic targets. Our modular chimeroid platform may, in principle, be applied to any inherited retinal disease genotype for which human iPSCs and an organoid phenotype exist.

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The Mini-Steamroll: A Modified Abbreviated Variation of the Steamroller Maneuver Following Pneumatic Retinopexy for Rhegmatogenous Retinal Detachment with Large Superior Breaks

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**Introduction:** Proper patient positioning is crucial for the success of pneumatic retinopexy (PnR), a minimally invasive procedure which uses intravitreal gas injection to treat rhegmatogenous retinal detachment (RRD). This prospective case series describes the mini-steamroll, a novel positioning maneuver for patients with large superior breaks in rhegmatogenous retinal detachment (RRD) following pneumatic retinopexy (PnR).

**Methods:** "A total of six patients who presented with RRD to St. Michael's Hospital, Toronto, were included in this case series. All patients had RRD and underwent PnR. After obtaining a full ocular history and detailed depressed scleral exam at presentation (Best corrected visual acuity (BCVA), duration of vision loss or visual field defect, foveal status, extension of retinal detachment, and presence of retinal breaks or lattice degeneration), all patients underwent ultra-widefield retinal imaging at baseline and repeat imaging 10 minutes after the gas injection.

Patients were injected with sulfur hexafluoride (SF<sub>6</sub>), and they were required to maintain a face-down position immediately after the procedure.

After the gas injection, patients were instructed to perform the mini-steamroll maneuver which consists of a face-down position for ten minutes followed by positioning to the retinal break.

The mini-steam roll maneuver was considered successful if we observed a significant reduction in the amount of subretinal fluid after 10 min face-down. In case of failure (no substantial reduction in subretinal fluid volume), the patient would switch to the full steamroller maneuver.

**Results:** In each case, the mini-steamroll maneuver resulted in a significant reduction in subretinal fluid, aiding in reattachment. The technique was effective for patients with large superior breaks or multiple smaller superior breaks, allowing subretinal fluid to escape into the vitreous cavity during face-down positioning. This approach was well-tolerated and encouraged patient compliance with treatment.

**Conclusions:** "This case series demonstrates that the mini-steamroll maneuver may be considered an alternative for patient positioning following PnR in certain cases. Mini steamroll has the potential to carry the benefits of both direct-to-the-break and the steamroller maneuver techniques that are currently in use.

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**Artificial Intelligence Chatbot Knowledge on the Diagnosis and Treatment of Common Retinal Disorders**

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**Introduction:** ChatGPT is a large language model that operates by predicting and generating text based on patterns learned from a diverse range of internet resources during its development. We aim to evaluate ChatGPT's responses to diagnostic and therapeutic questions on common retinal disorders.

**Methods:** In this cross-sectional study, we prompted ChatGPT with questions regarding diabetic retinopathy (DR), retinopathy of prematurity (ROP), age-related macular degeneration (AMD), epiretinal membrane (ERM), macular hole (MH), posterior vitreous detachment (PVD), rhegmatogenous retinal detachment (RRD), retinoschisis (RS), retinitis pigmentosa (RP), retinal artery occlusion (RAO), and retinal vein occlusion (RVO). Two retina specialists independently graded responses using a Likert scale ranging from 1 (unacceptable inaccuracies) to 5 (no inaccuracies). Our primary endpoint was the median grade given to ChatGPT-3.5 and ChatGPT-4's responses. Our secondary endpoints were differences between the two chatbot models in mean response time, length in characters and readability scores.

**Results:** ChatGPT-3.5 performed worst (median grade=3/5) on questions pertaining ROP, RS, or RVO and best (median grade=4/5) on questions pertaining to DR, AMD, ERM, PVD, RP, or RRD. ChatGPT-4 performed worst (median grade=4/5) on questions pertaining to ROP, MH, RS, RP, or RVO and best (median grade=4.5/5) on questions pertaining to DR, AMD, ERM, PVD, RRD, or RAO. ChatGPT-4 (81.8%) achieved a greater proportion of responses with a grade of at least 4/5 than ChatGPT-3.5 (54.5%;  $p<0.01$ ). ChatGPT-4 took significantly longer to generate responses compared to ChatGPT-3.5 ( $p<0.01$ ) and produced significantly longer responses ( $p<0.01$ ). Evaluation using readability indices indicated that the responses of ChatGPT-4 tended to be more challenging to read than the responses of ChatGPT-3.5.

**Conclusions:** ChatGPT provides valuable responses on retinal disorders, although may sometimes lack nuance and have important omissions. Patients should appreciate the educational potential of chatbots in ophthalmology while approaching them with caution.

## Harnessing the Potential of Mammalian Retinal Müller Glia to Regenerate Cone Photoreceptors

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**Introduction:** Cones are photoreceptors, crucial for visual acuity. Their loss leads to blindness in diseases such as Retinitis Pigmentosa (RP). Zebrafish can regenerate their retina and restore their vision upon injury. More specifically, Müller glia (MG) undergo dedifferentiation into a progenitor-like state, then divide and differentiate to replace the missing cells. Contrary to Zebrafish, Mammals cannot fully regenerate their retina. Mammalian MG can regenerate certain inner retinal neurons but to date, no study has reported high-yield regeneration of mature cones. Unlike murine cones, human cones have high levels of MYCN oncoprotein. However, the reason behind this high expression in post-mitotic neurons is unknown. Murine cones arise in the embryonic stage and post-natal progenitors cannot differentiate into cones. Our preliminary data suggests that overexpression of MYCN in postnatal murine retinal progenitors can induce cone lineage. Progenitors and MG are transcriptionally similar therefore, I will investigate whether induced expression of MYCN can facilitate the conversion of MG into cones. Additionally, as MG convert into cones, their population declines thus I will investigate whether MG division can be achieved by removing cell cycle inhibitors such as RB or p53. I hypothesize that manipulating the expression of MYCN and various cell cycle inhibitors will facilitate a full cone regenerative program.

**Methods:** To target MYCN to MG we will use Glast-CreERT2 transgenic mice, with tamoxifen-inducible, MG-specific Cre. At birth, these mice are electroporated with a Cre-dependent plasmid containing MYCN-GFP. Tamoxifen treatment leads to MG-specific expression of MYCN and GFP in adult mice. To mimic the loss of photoreceptors in humans, we will use rd1 mice which display severe retinal degeneration. To facilitate MG cell cycle entry, we will use Glast-Cre and Rb/p53 floxed alleles to conditionally delete Rb or p53 in MG. Changes in retinal development and cell cycle will be assessed by immunostaining, RNAscope and Single cell RNA sequencing (scRNA-Seq). We'd also perform CRISPR screens to study the underlying genetic circuitry and identify clinically relevant targets.

**Results:** We have been deciphering the mechanism driving the MYCN-dependent fate switch using cutting edge techniques such as scRNA-Seq. We have already identified several promising candidates that we'd like to explore in our regeneration project.

**Conclusions:** This study explores MYCN's potential in driving cone genesis. Achieving MG division and cone genesis would offer a clinically applicable solution to retinal regeneration thus revolutionizing available treatments for vision loss.



## Treatments for Retinal Artery Occlusion: A Systematic Review and Meta-Analysis

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**Introduction:** Retinal artery occlusions (RAOs) lead to rapid-onset vision loss that is usually irreversible unless retinal circulation is recovered prior to ischemic damage. A 2020 scientific statement by the American Heart Association acknowledged that thrombolysis may be beneficial for RAO, although the literature remains inconclusive with considerable inconsistency across management approaches. The purpose of this systematic review and meta-analysis is to provide a comprehensive overview of the safety and efficacy of thrombolysis for RAO.

**Methods:** We performed a systematic literature search from January 2005 to July 2023 on Ovid MEDLINE, Embase, and the Cochrane Library to elicit relevant literature. We included comparative studies reporting on the efficacy and safety of thrombolysis versus conservative modalities for non-arteritic RAO. Outcomes were the change in best-corrected visual acuity (BCVA) from baseline and the incidence of adverse events. We conducted a meta-analysis using random effects models. Continuous and dichotomous outcomes were reported using weighted mean differences (WMDs) and risk ratios (RRs), respectively.

**Results:** Nine studies reporting on 641 eyes at baseline were included in our review, of which 314 received thrombolysis and 327 received conservative treatment. Six studies were observational and three were randomized trials. The mean duration from symptom onset to treatment varied across study arms, ranging from 3.4 to 36 hours. Five studies conducted intra-arterial thrombolysis and four studies used intravenous thrombolysis. Across four studies reporting on 275 eyes, the change in BCVA at last study observation was similar between the thrombolysis and conservative treatment groups (WMD=-0.05 logMAR, 95%CI=[-0.19, 0.09], p=0.47). The incidence of headache (p=0.20), tinnitus (p=0.80), hyperesthesia (p=0.41), intracranial hemorrhage (p=0.14) and intraocular pressure-related adverse events (p=0.29) were also similar between groups. Consistent findings were observed in subgroups of central RAO and studies that administered tissue plasminogen activator. Five included studies with outcomes not compatible with the meta-analysis were narratively reviewed, of which four found greater visual improvement in the thrombolysis group. All five studies reported similarly low rates of adverse events across groups. Of note, two studies each reported one case of symptomatic ischemic stroke in their thrombolysis groups.

**Conclusion:** Our investigation did not find significant evidence to support the routine use of thrombolysis for improving BCVA in patients with RAO; however, there remains some evidence in favour of the practice. Notably, most studies had an average duration from symptom onset to treatment that surpassed the recommended 4.5-hour window. Additional research into thrombolysis for RAO is warranted.

**Interrogation of Rhodopsin Structural Stability and Cytotoxic Chromophore Release**

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**Introduction:** Degenerative retinal diseases, like retinitis pigmentosa (RP), affect 1 in 4000 people worldwide. RP is most often caused by non-synonymous mutations in RHO, the gene encoding rhodopsin, the light-sensing receptor of rod cells in the retina. Since rods are critical to conferring dim-light and peripheral vision, changes to rhodopsin function can have significant impacts on quality of life. Previous investigations have attempted to classify various RHO disease mutations based on in vitro rhodopsin surface expression and misfolding. These investigations have been useful for classifying many variants that were of severe pathogenicity but do not explain how changes in protein function may be associated with milder disease progression. Recent studies of rhodopsin biochemistry suggest that light-activated rhodopsin stability plays a critical role in preventing cytotoxic effects associated with the dissociated all-trans-retinal (ATR) chromophore. Since changes to rhodopsin structure can impact the stability of the active state, we hypothesized that cytotoxic effects associated with accelerated rates of ATR release may be related to some cases of mild RP.

Specifically, we predicted that rhodopsin mutants nearby the Activation Switch 1 domain may be associated with mild RP. Activation Switch 1 is centred around a critical E122-H211-W126 interaction, which is known to maintain the stability of the dark-state and light-activated structures of rhodopsin. Additionally, there are a number of mutation sites in rhodopsin associated with degenerative visual disease in humans that are proximal to Activation Switch 1. "

**Methods:** Thus, we have investigated variants associated with mild disease in the Activation Switch 1 region that do not cause significant protein misfolding, as well as other natural variants in humans. Proteins have been heterologously expressed and purified to be assayed in the laboratory using spectroscopic approaches that measure the stability of light-activated rhodopsin. Light-activated stability was monitored through fluorescence spectroscopy, to observe the rates of chromophore release associated with the active state decay.

**Results:** Our preliminary results have shown that some of these variants, including M163T, have significantly accelerated retinal release which is believed to be associated with higher cytotoxicity. Homology modeling of these variants has suggested that the variants with accelerated retinal release have a widened chromophore exit pore, which may explain the observed changes in kinetics.

**Conclusion:** As the results of these variants are being interpreted in light of the known clinical phenotype, this study will expand our understanding of the molecular basis of retinal degeneration and human visual disease associated with mutations in the rhodopsin gene.

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**Prediction of Visual Acuity Improvement in Response to Ranibizumab in Age-Related Macular Degeneration Using Artificial Intelligence-Based Analysis of Fluorescein Angiography**

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**Introduction:** To elicit whether baseline quantitative vascular parameters derived from intravenous fluorescein angiography can predict improvement in best-corrected visual acuity (BCVA) in response to ranibizumab in patients with neovascular age-related macular degeneration (nAMD).

**Methods:** A prospective cohort study was conducted at a single center in Toronto, Canada from 2017 to 2023, involving patients over 50 years with a diagnosis of active choroidal neovascularization secondary to AMD. At baseline, patients were imaged with fluorescein angiography using an ultra-widefield scanning laser ophthalmoscope. Images were processed using the artificial intelligence RETICAD system to extract quantitative retinal vascular parameters, including blood-retinal-barrier (BRB) permeability, perfusion, and blood flow. All nAMD patients were treated using a pro re nata regimen of ranibizumab and final outcomes were measured at 12 months of follow up. Associations between quantitative retinal vascular parameters with functional and anatomical outcomes were examined using univariable and multivariable regression models. Receiver-operating characteristic (ROC) curves and area-under-the-curve (AUC) values were used to determine the predictive value of fluorescein angiography parameters for BCVA improvement following treatment.

**Results:** The study population included 60 eyes from 60 patients with confirmed nAMD. Among patients with nAMD, most were female (n=37, 61.7%), Caucasian (n=44, 73.3%), and had a mean age of  $80.8 \pm 8.0$  years. On multivariable analysis, baseline central BRB permeability was associated with the change in BCVA from baseline to 12 months ( $p=0.034$ ), and the number of ranibizumab injections over 12 months ( $p=0.003$ ). Patients with improved BCVA had significantly lower baseline values of central ( $p=0.003$ ) and peripheral ( $p=0.007$ ) BRB permeability compared to those with no improvement. ROC analysis revealed central and peripheral BRB permeability were strong predictors of BCVA improvement (AUC=0.85).

**Conclusion:** Baseline quantitative fluorescein angiography parameters, particularly BRB permeability, were predictive of BCVA improvement following ranibizumab treatment. Future work should explore associations between quantitative fluorescein angiography parameters and functional and anatomical outcomes in diverse nAMD patient populations.

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**Association of Artificial Intelligence-Based Quantitative Fluorescein Angiography Measurements with Clinical Parameters in Patients with Diabetic Macular Edema**

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**Introduction:** To investigate the association between baseline clinical characteristics of patients with diabetic macular edema (DME) and quantitative intravenous fluorescein angiography parameters, including blood-retinal barrier (BRB) permeability, retinal perfusion, and blood flow.

**Methods:** In this prospective, single-centre study in Toronto, Canada, we recruited consecutive patients with DME presenting with a central macular thickness (CMT) > 310 µm from 2017-2023. Patients with DME underwent fluorescein angiography using an ultra-widefield scanning laser ophthalmoscope. Fluorescein angiography images were processed using the artificial intelligence RETICAD FA assist system to extract quantitative BRB permeability, retinal perfusion, and blood flow measurements. Univariable and multivariable regression models were used to investigate associations between quantitative fluorescein angiography parameters and baseline characteristics, including best-corrected visual acuity (BCVA), CMT, and macular volume. This study was performed with approval from a local institutional review board and written informed consent was required for participation by eligible patients.

**Results:** The study population consisted of 56 eyes with DME and seven eyes from healthy controls. Among eyes with DME, 44 (78.6%) were male and 24 (42.9%) were Caucasian. The mean age of DME patients was 61.6 ± 11.6 years old. Central and peripheral BRB permeabilities were significantly higher in DME patients relative to healthy controls ( $p < 0.001$ ), whereas central and peripheral retinal perfusion was significantly lower in DME eyes ( $p < 0.001$  and 0.002, respectively). In our multivariable analysis, BRB permeability measured in the central and peripheral retina was significantly associated with BCVA ( $p = 0.003$  and 0.002, respectively) and macular volume ( $p = 0.025$  and 0.045, respectively). Blood flow measured centrally was also significantly associated with macular volume ( $p = 0.048$ ).

**Conclusion:** An increased BRB permeability in DME eyes was associated with a greater baseline macular volume and worse BCVA. Furthermore, DME eyes had a greater BRB permeability and lower retinal perfusion compared to control eyes. Future research should explore the clinical utility of quantitative fluorescein angiography measurements in diverse patient populations.

**SNAP-25, but not SNAP-23, is Essential for Photoreceptor Development, Survival, and Function in Mice**Mengjia Huang<sup>1</sup>, Shuzo Sugita<sup>1</sup>, PhD<sup>1</sup>Department of Physiology, University of Toronto

**Introduction:** Vision requires the effective communication of light information by photoreceptors onto their second-order cells. Photopigments in the outer segments of photoreceptors transform photons of light into an electric signal. This signal is then passed on from photoreceptors through the release of the neurotransmitter glutamate. SNARE-mediated vesicular transport is thought to play roles in photoreceptor glutamate exocytosis and photopigment delivery. However, the functions of Synaptosomal-associated protein (SNAP) isoforms in photoreceptors are unknown.

**Methods:** We revisit the expression of SNAP-23 and SNAP-25 using a combination of in situ hybridization and immunohistology. Following, we generate photoreceptor-specific knockout mice to investigate the roles of SNAP-23 and SNAP-25. We look at retinal morphology, light response, and visual acuity in these conditional knockout mice. Using immunohistology and electron micrographs, we examine photoreceptor morphology and ultrastructure.

**Results:** Although we found that SNAP-23 shows weak mRNA expression in photoreceptors, SNAP-23 removal did not affect retinal morphology or vision. SNAP-25 mRNA was developmentally regulated and underwent mRNA trafficking to photoreceptor inner segments at postnatal day 9 (P9). SNAP-25 knockout photoreceptors developed normally until P9 but degenerated by P14 resulting in severe retinal thinning. Photoreceptor loss in SNAP-25 knockout mice was associated with abolished electroretinograms and vision loss. We found mistrafficked photopigments, enlarged synaptic vesicles, and abnormal synaptic ribbons which potentially underlie the observed photoreceptor degeneration.

**Conclusion:** Our results conclude that SNAP-25, but not SNAP-23, mediates photopigment delivery and synaptic functioning required for photoreceptor development, survival, and function. Using this study, we uncover that the other target plasma membrane SNARE protein required for vesicle fusion in photoreceptors is SNAP-25.

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### Assessing Retinal Vascular Leakage with Optical Coherence Tomography Angiography (OCTA) and Deep Convolutional Neural Networks

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**Introduction:** Fluorescein angiogram (FA) is an invaluable tool to map out retinal vasculature and assess for vascular leakage. However, it remains an invasive test associated with potential adverse effects. Another imaging modality, optical coherence tomography angiography (OCTA), also can be used to map out the retinal vasculature without the introduction of a foreign dye. Although safer, unlike the FA, OCTA cannot directly assess for vascular leakage. However, a clinical question of whether OCTA can indirectly detect vascular leakage still remains. The objective of this study is to evaluate the feasibility of predicting vascular leakage from OCTA images using deep learning, specifically with convolutional neural networks (CNNs). We hypothesize that there are sufficient OCTA characteristics that may predict vascular leakage.

**Methods:** We performed a retrospective chart review between August 2018 and August 2023 of patients visiting the Department of Ophthalmology at St. Michael's Hospital (Toronto, Canada) who had at least one FA collected from at least one eye and a corresponding OCTA scan. Institution research ethics approval was obtained. Patient data was anonymized and categorized into either having vascular leakage or no leakage based on the FA test. We trained an ensemble of five deep CNNs based on the InceptionV3 architecture, using depth-encoded 2D OCTA fundus images as inputs and the FA leakage status as labels. We measured the accuracy and area under the receiver operating characteristic (AUROC) curve on a test set of patient images.

**Results:** FA and OCTA data from 130 patients was retrieved, resulting in a total of 258 OCTA images. We split the data into 104 patients for training and 26 patients for testing (80/20% split). After training for 50 epochs, we achieved a mean accuracy of 78% and mean AUROC of 0.805 on the test set.

**Discussion/Conclusion:** This feasibility study showed that an ensemble of five deep convolutional neural networks was able to predict presence of retinal vascular leakage from OCT angiography data alone with a high mean accuracy. Development of these technologies could eventually augment or even replace the need for FA testing to determine whether there is retinal vascular leakage.

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**Assessment and Classification of Proliferative Vitreoretinopathy in Rhegmatogenous Retinal Detachment with Swept-Source Optical Coherence Tomography: A Novel Conceptual Framework**

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**Introduction:** To describe the morphologic features of proliferative vitreoretinopathy (PVR) detected with swept-source OCT (SS-OCT) in rhegmatogenous retinal detachment (RRD).

**Methods:** "Primary RRDs presenting to St. Michael's Hospital from January 2020-July 2023 were retrospectively assessed at baseline for signs of PVR. Posterior pole and/or ultra-widefield SS-OCT was assessed for the predominant type of PVR (pre, intra or subretinal), and the associated retinal abnormalities were characterized.

**Results:** "Forty-one patients had signs of PVR on baseline SS-OCT, of which 66%(27/41) were male, mean age of 53.5(±18.5) years old, and 78%(32/41) were phakic. Mean baseline logMAR visual acuity was 1.4(±0.7), with a duration of fovea-off of 46.1(±135) days and RRD extent of 7.3(±3.08) clock hours. 44%(18/41) presented with subretinal PVR, of which 17%(3/18) had coexisting pre-retinal PVR. 56%(23/41) presented with intra-retinal PVR, of which 83%(19/23) presented with concurrent pre-retinal PVR. Sub-retinal PVR appears on SS-OCT as a hyperreflective line in contact with the neurosensory retina or as an amorphous band over the RPE. The former may cause folding of the outer retina if photoreceptor segments are still intact. Subretinal PVR was associated with shallow regulated RRDs on clinical examination ( $p<0.001$ ). In contrast, intra-retinal PVR was associated with bullous dysregulated RRDs, and was always present with concurrent outer retinal corrugations (ORCs). Intra-retinal PVR is observed as a thickening of the inner retina with disorganized and indistinguishable retinal layers ( $p<0.001$ ). Intra-retinal PVR is also characterized by fused ORCs which appear to form irregular protrusion of the outer retina. Initial signs of intra-retinal PVR were noticed in areas of RRD morphologic stage 3b and 4, where ORCs were fused together. On the contrary, subretinal PVR was associated with RRD morphologic stage 5.

**Conclusions:** In order to better characterize the intrinsic retinal changes in PVR in humans in vivo, we assessed baseline SS-OCT. The type of PVR observed was significantly associated with baseline RRD clinical status (regulated versus dysregulated). PVR formation seems to be associated with a proliferative pathway (when intra-retinal), which occurs primarily in dysregulated cases, versus an apoptotic/atrophic pathway (when subretinal), which occurs primarily in regulated cases. Intraretinal PVR seems to occur at RRD morphologic stage 3b and 4, when ORCs seem to fuse together. This fusion of ORCs appears to be an early and important sign of intraretinal PVR. Recognizing the spectrum of morphologic changes on OCT may assist with early and accurate diagnosis and classification of PVR, particularly intra-retinal PVR, which is most challenging to address surgically.

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**Retinal Displacement Following Rhegmatogenous Retinal Detachment:  
A Systematic Review and Meta-Analysis**

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**Introduction:** Rhegmatogenous retinal detachment (RRD) is one of the most common sight-threatening ophthalmic surgical emergencies. Refinements in pars plana vitrectomy (PPV), scleral buckle (SB) and pneumatic retinopexy (PnR) have given excellent anatomic reattachment rates. Nevertheless, many patients report unsatisfactory functional outcomes including metamorphopsia. Suboptimal functional outcomes may be the result of retinal displacement. In this study we assessed quantitatively the proportion of patients who develop retinal displacement following RRD repair.

**Methods:** Using inclusion criteria of English-language articles investigating retinal displacement following RRD repair with fundus autofluorescence, we identified 21 studies encompassing 1258 eyes. Study and evidence quality was assessed using ROBINS-I, Cochrane risk of bias, and GRADE frameworks. Outcome measures included frequency of retinal displacement, visual acuity, metamorphopsia, and displacement direction. A meta-analysis was performed using a Mantel-Haenszel method to report risk ratios (RR) for categorical variables, and a fixed-effects model was applied. Weighted mean difference (WMD) and 95% confidence interval was computed for continuous variables using the inverse variance method and a random-effects model.

**Results:** Retinal displacement was found in 35±20% of RRD repairs. SB without tamponade had the lowest rate of retinal displacement (RR=9.60 [2.01-45.95], p=0.005), followed by PnR and finally PPV. Macula-off RRDs were more likely to have retinal displacement (2.66 [1.82-3.90], p<0.001), but there was no clear relationship between the presence of displacement and extent of initial RRD. Silicone oil tamponade may reduce risk of displacement following PPV compared to gas (2.16 [1.22-3.83], p<0.009), as may immediate face-down positioning for 2 hours. Retinal displacement following PPV occurred in the downward direction in 92±14% of cases and with gas tamponade. Interestingly, when silicone oil tamponade is used or when PnR is performed, superior retinal shift is more frequent. Retinal displacement does not appear to significantly impact visual acuity (0.05 [-0.21-0.31, p=0.70), although it may increase distortion.

**Conclusions:** Functional outcomes are of paramount importance to patients, and there is increasing evidence that a high-integrity anatomic attachment may lead to superior functional outcomes. SB and PnR are likely associated with less retinal displacement compared to PPV with a full gas fill, and PPV with silicone oil also has a comparatively low rate of retinal displacement. When performing PPV with gas, immediate face-down positioning for at least 2 hours may reduce retinal displacement. Larger prospective studies may provide the conclusive evidence that allows the surgeon to adopt techniques that minimize displacement and provide high-integrity retinal attachment and superior functional outcomes.



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**Quantitative Assessment of Retinal Vasculature Using Artificial Intelligence-Based Analysis of Fluorescein Angiography in Age-Related Macular Degeneration**

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**Introduction:** This study seeks to investigate associations between quantitative vascular measurements derived from ultra-widfield fluorescein angiography (FA) and baseline characteristics on optical coherence tomography (OCT) in patients with neovascular age-related macular degeneration (nAMD).

**Methods:** We prospectively recruited patients over the age of 50 years old with a diagnosis of active choroidal neovascularization in the context of nAMD, presenting to a single centre in Toronto, Canada from 2017-2023. Patients were imaged with FA using an ultra-widfield scanning laser ophthalmoscope and images were processed using the artificial intelligence-based RETICAD FAassist system to extract quantitative data pertaining to blood flow, perfusion, and blood-retinal barrier (BRB) permeability. Associations between blood flow, perfusion and BRB permeability with best-corrected visual acuity, central macular thickness (CMT) and macular volume (MV) were examined using univariable and multivariable regression models. Research ethics board approval was obtained for our study.

**Results:** A total of 81 eyes from 81 nAMD patients and seven eyes from seven healthy controls were included. Among patients with nAMD, most were female (n=50, 61.7%) and Caucasian (n=61, 75.3%), with a mean age of  $79.8 \pm 7.9$  years old. In eyes with nAMD, central BRB permeability and perfusion were significantly higher than peripheral retinal values ( $p < 0.001$  and  $p = 0.009$ , respectively). Compared to healthy controls, BRB permeability in the central and peripheral retina was significantly higher in nAMD patients ( $p < 0.001$  and  $p < 0.001$ , respectively). Nonetheless, there was no significant difference observed in both perfusion and blood flow in nAMD eyes compared with healthy control eyes. On univariable analysis, BRB permeability measured centrally was significantly associated with CMT ( $p = 0.035$ ), while perfusion and blood flow measured centrally were significantly associated with MV ( $p = 0.043$  and  $p = 0.037$ , respectively). BRB permeability remained significantly associated with CMT upon adjustment for demographic variables ( $p = 0.026$ ). No significant associations were observed between BCVA and FA quantitative vascular parameters derived from ultra-widfield FA.

**Conclusions:** Quantitative vascular biomarkers on ultra-widfield FA, particularly BRB permeability, were associated with baseline OCT characteristics in nAMD patients. Future works should explore longitudinal associations between quantitative FA parameters and clinical characteristics in diverse nAMD patient populations.

### Interpretation of Clinical Retinal Images Using an Artificial Intelligence Chatbot

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**Introduction:** The subspecialty of retina is dependent on nuanced interpretations of multimodal imaging to ensure high diagnostic accuracy. This investigation aims to assess the performance of ChatGPT-4 in providing accurate diagnoses to multimodal retina cases from OCTCases, a medical education platform from the Department of Ophthalmology and Vision Sciences at the University of Toronto.

**Methods:** We prompted a custom chatbot with 69 retina teaching cases containing multimodal ophthalmic images, asking it to provide the most likely diagnosis. In a sensitivity analysis, we inputted increasing amounts of clinical information pertaining to each case until the chatbot achieved a correct diagnosis. Our primary outcome was the proportion of cases for which the chatbot was able to provide a correct diagnosis. Our secondary outcome was the chatbot's performance in relation to the amount of text-based information accompanying ophthalmic images. We performed multivariable logistic regressions on Stata v17.0 (StataCorp LLC, College Station, Texas) to investigate associations between the amount of text-based information inputted per prompt and the odds of the chatbot achieving a correct diagnosis, adjusting for the eye laterality of cases, number of ophthalmic images inputted, and imaging modalities.

**Results:** Across 69 retina cases collectively containing 139 ophthalmic images, the chatbot was able to provide a definitive, correct diagnosis for 35 (50.7%) cases. The chatbot needed variable amounts of clinical information to achieve a correct diagnosis, where the entire patient description as presented by OCTCases was required for a majority of correctly diagnosed cases (23/35 cases, 65.7%). Relative to when the chatbot was only prompted with a patient's age and sex, the chatbot achieved a higher odds of a correct diagnosis when prompted with an entire patient description (OR=10.1, 95%CI=[3.3, 30.3], p<0.01). Despite providing an incorrect diagnosis for 34 (49.3%) cases, the chatbot listed the correct diagnosis within its differential diagnosis for 7 (20.6%) of these incorrectly answered cases.

**Conclusions:** This custom chatbot was able to accurately diagnose approximately half of the retina cases requiring multimodal input, albeit relying heavily on text-based contextual information that accompanied ophthalmic images. The diagnostic ability of the chatbot in interpretation of multimodal imaging without text-based information is currently limited. The appropriate use of the chatbot in this setting is of utmost importance, given bioethical concerns.

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**Stretch-Induced Foveal Ectopia (SIFE/Displacement) Following Retinal Detachment Repair:  
A Novel Assessment Using Spectral-Domain Optical Coherence Tomography**

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**Introduction:** Retinal displacement is a common occurrence following rhegmatogenous retinal detachment (RRD) repair which has been linked to impaired functional outcomes, particularly postoperative aniseikonia. Fundus autofluorescence is commonly used to identify retinal displacement; however, concerns regarding detection accuracy persist. This investigation aims to elicit a novel methodology using spectral-domain optical coherence tomography (SD-OCT) to quantify foveal displacement post-RRD repair.

**Methods:** This retrospective case series conducted at St. Michael's Hospital in Toronto, Canada included consecutive patients undergoing surgical repair for fovea-involving RRD with SD-OCT (Carl Zeiss Meditec, Jena, Germany) images available before RRD development and 1-2 months post-RRD repair. Fellow eyes without RRD at corresponding time points were included to validate the methodology. Using 6 mm x 6 mm infrared cube scans, two independent graders (A.M., M.B.) computed vertical, horizontal, and overall distances between foveal centers and optic nerve head (ONH) centers on ImageJ. An unpaired t-test was used to compare baseline distances between study and fellow eyes, whereas paired t-tests were used to compare baseline and follow-up distances in each group.

**Results:** A total of 76 eyes (n=38 RRD eyes and n=38 fellow eyes) from 38 participants undergoing RRD repair were included in our analysis. 24 (63%) patients were male and 14 (37%) as female, for which the mean age was  $57 \pm 11$  years old. The intraclass correlation coefficient for line segment lengths was 0.99, indicating nearly perfect agreement and reliability for measurements of fovea-to-ONH distances across all participants. At the baseline visit, there were no significant differences between RRD and fellow eyes with respect to overall ( $p=0.13$ ), horizontal ( $p=0.10$ ), and vertical ( $p=0.20$ ) fovea-to-ONH distances. Compared to baseline, there was a significantly increased overall ( $p=0.02$ ) and vertical ( $p=0.03$ ) fovea-to-ONH displacement in study eyes at 1-2 months post-RRD repair. However, these findings were not observed in fellow eyes at the same time points ( $p=0.06$  and  $p=0.19$ , respectively). Across 18 patients treated with pars plana vitrectomy, overall ( $p=0.01$ ) and vertical ( $p=0.04$ ) displacement in study eyes was significantly greater at 1-2 months post RRD-repair compared to baseline. These findings did not hold across 17 patients who underwent successful pneumatic retinopexy ( $p=0.24$  and  $p=0.54$ , respectively).

**Conclusions:** Considerable differences in foveal location were observed when comparing pre-RRD and post-RRD repair SD-OCT scans, which were not observed in fellow eyes without RRD. Furthermore, greater vertical displacements were observed in study eyes, particularly in those undergoing pars plana vitrectomy, complementing previous literature on retinal displacement.

## Comparing the Multimodal Performance of ChatGPT and Gemini Pro in Retinal Image Interpretation

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**Introduction:** This paper aims to assess the performance of two new large language models (LLMs), ChatGPT-4 and Google's Gemini Pro, on retinal multimodal imaging interpretation. Specifically, this study compares the LLMs' diagnostic accuracy on a public dataset of retinal cases containing ophthalmic images and clinical data.

**Methods:** We systematically prompted ChatGPT-4 and Gemini Pro with a public dataset of 73 retinal cases, of which 64 cases were included, from the ophthalmology education website OCTCases.com from December 22, 2023 to December 24, 2023. Using the entire clinical case and ophthalmic images, we asked the LLMs: "What is the most likely diagnosis?" We developed a prompting algorithm to compare the factor(s) implicated in the LLMs' correct and incorrect diagnoses. We recorded the case characteristics, LLMs' responses to initial and follow-up prompting, response length, and the factors contributing to their responses. We reported the diagnostic accuracy of ChatGPT-4 and Gemini Pro in each case by comparing the LLMs' outputs with the answer key on OCTCases. Accuracy was the primary outcome and was measured as the proportion of correctly diagnosed cases from the total number of cases. The clinical characteristics that were contributory to decision-making of the LLMs was considered a secondary endpoint. Proportions of accuracies and contributory factors were compared between LLM models using a chi-squared ( $\chi^2$ ) test. Differences in performance were considered statistically significant at a p value of  $< 0.05$ .

**Results:** ChatGPT-4 achieved 39.0% diagnostic accuracy, while Gemini Pro achieved 20.3% diagnostic accuracy ( $\chi^2$ ,  $p < 0.05$ ). In correctly answered cases, imaging findings were the primary factor identified as most contributory to the decision-making of both ChatGPT-4 (40%) and Bard (53.8%) ( $p > 0.05$ ). In incorrectly answered cases, patients' age (39.2%) and imaging findings (43.6%) were most commonly implicated in decision-making by Gemini Pro and ChatGPT-4, respectively. ChatGPT-4 and Gemini Pro self-identified a mean of 5.2 and 3.8 factors contributing to their decision per case (Mann-Whitney U,  $p > 0.05$ ).

**Conclusions:** While the performance of both LLMs was overall poor, ChatGPT-4 outperformed Gemini Pro on multimodal analysis of clinical retinal cases. After further prompting, ophthalmic images were most frequently cited as the key factor in achieving correct diagnoses. Future research may consider testing LLMs on larger datasets to improve generalizability of results, and to compare LLMs with traditional ML models on image analysis and predictions of treatment outcomes.

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**Long-Term Re-Detachment Rates of Pneumatic Retinopexy versus Pars Plana Vitrectomy in Retinal Detachment: a PIVOT Post-Hoc Analysis**

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**Introduction:** The purpose of our study was to assess long-term re-detachment rates following pneumatic retinopexy (PnR) versus pars plana vitrectomy (PPV) in rhegmatogenous retinal detachments (RRD).

**Methods:** "Conducted post-hoc analysis of the "PnR versus PPV for the Management of Primary RRD Outcomes Randomized Trial" (PIVOT) trial. PIVOT participants were ineligible if any re-intervention to reattach the retina was performed within one year of the initial procedure. Re-detachment was determined by medical chart review or telephone interview. The latter was the only accepted method for those with less than two years of follow-up (otherwise marked as unreachable and excluded).

**Results:** After exclusion of ineligible and unreachable participants from the PIVOT trial, 61 (72.6%) PPV participants and 62 (80.5%) PnR participants were analyzed by either chart review or phone call. Long term re-detachment rate was 0% and 1.61% (1/62) in the PPV and PnR groups respectively ( $p=0.32$ ). The mean follow-up duration in years was  $4.34\pm 2.80$  versus  $4.26\pm 2.81$  in the PPV and PnR groups, respectively.

**Conclusion:** There was no statistically significant difference in long-term re-detachment rates for PnR vs PPV. Both procedures are durable treatment options for RRD over an extended period, rarely requiring additional intervention for re-detachment.

## Morphologic Stages of Full-Thickness Macular Hole Assessed with Spectral Domain Optical Coherence Tomography

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**Introduction:** The sequential stages of full-thickness macular hole has never been described in vivo in humans using imaging. The purpose of this study is to describe the sequential morphological changes following full-thickness macular hole (FTMH) formation, utilizing a novel, objective staging system based on optical coherence tomography (OCT), and to determine its association with baseline visual acuity (VA) and duration of symptoms.

**Methods:** Retrospective multicenter study. Primary FTMH referred to St. Michael's Hospital, Toronto Canada, and Retina Consultants of Texas, Texas, Houston, USA, from 2009 to 2022 were included. Multimodal imaging of 1000 patients were initially assessed. To be eligible for this study patients had to have at least two preoperative SD-OCT scans and no other retinal pathology. The electronic medical charts were reviewed. The staging was based on the assessment of outer retinal morphology on successive SD-OCT central foveal scans. Univariable and multivariable logistic and linear regression analyses were conducted to evaluate the association between baseline MH stage and baseline VA and duration of symptoms. Results were considered statistically significant if the P value < 0.05.

**Results:** 52 eyes were included. The mean age(SD) was 65.4 ( 8.4) years. 67.3% (35/52) were female. The mean presenting logMAR (SD) VA was 1.03 ( 0.41). Outer retinal changes following FTMH occurred in 4 stages: 1) separation of the neurosensory retina from the RPE with well-defined interdigitation zone (IDZ), ellipsoid zone (EZ), and external limiting membrane (ELM) (4/52, 7.7%); 2) Hydration: thickening of photoreceptor inner (IS) and outer segments (OS) (27 /52;51.9 % ) ; 3) patchy (moth-eaten)photoreceptor loss (16/52;30.8 %); 4) severe or complete loss of ISs and OSs and /or bare ELM (5/52, 9.6%).When assessing follow-up preoperative OCT, none of the Stage 1 FTMHs remained at the same stage. 28.9 %(15/52) of eyes were in Stage 2; 34.6 % (18 /52) in Stage 3 and 36.5% (19 /52 ) were in Stage 4.

The progression time (days, SD) from Stage 1 to Stage 2 was 21(0), Stage 2 to Stage 3 was 284 (216.7), and Stage 3 to 4, was 482 (543.4). There was a statistically significant association between increasing stage and longer duration of symptoms (p=0.032) and, most importantly, between increasing stage and worse VA at baseline (p<0.001), $\beta$ = 0.22 (95%CI = 0.11-0.33) after adjusting for sex, age and lens status.

**Conclusions:** This novel staging system describes the sequential morphologic changes in FTMH with SD-OCT over time. The baseline morphological stage of FTMH was associated with the duration of symptoms and baseline visual acuity. This objective staging system provides a potential novel imaging biomarker for FTMH.

**IFT57 May Cause Bardet-Biedl Syndrome with Retinal Dystrophy**

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**Introduction:** Primary cilia are critical organelles found on the surface of most cells, and play an important role in cell signalling. When this process goes wrong, patients develop ciliopathies, which are a genetically and clinically heterogeneous group of diseases that cause a wide range of comorbidities. The connecting cilium of the photoreceptor is a homologous structure of the primary cilia, allowing transfer of proteins from the inner segment to the outer segment of the photoreceptor.

**Methods:** A 29-year old male has rod-cone degeneration which led to legal blindness. He also has features including polydactyly, mild cognitive impairment, and a fatty liver, which are suggestive of a Bardet-Biedl Syndrome (BBS) ciliopathy. Following negative clinical genetic testing, genome sequencing identified biallelic variants in IFT57 in trans, which were predicted to be highly conserved by in silico tools. The variants included a deletion in exon 6 that caused a frameshift and loss of function, and a c.1190T>A; p.(Val397Glu) missense variant in exon 11 that is predicted to be damaging by in silico algorithms. Due to their rarity, these variants were labelled of unknown significance according to the ACMG criteria. IFT57 is part of complex B of the intraflagellar transport IFT proteins. The IFT machinery is a bidirectional transport system of proteins from the cilia base to the tip and back. This plays an important role in the maintenance of cilia. IFT57 variants have not yet been associated with BBS or a human retinal dystrophy.

**Results:** Using patient-derived fibroblasts (PDF), immunofluorescence revealed lower cilia count/percentage and cilia that are abnormal in length and shape. We also show that Val397Glu variant IFT57 and other IFT-B complex proteins like IFT88 exhibit impaired anterograde transport in PDF cilia. Transfection of IFT57 knockout IMCD3 cells with WT IFT57 rescues the abnormal cilia phenotype, while transfection with Val397Glu only partially rescues the cilia phenotype. In RPE1 IFT57 knockout cell lines, transfection with Val397Glu does not rescue cilia, indicating that the role of IFT57 may be cell autonomous.

**Conclusion:** Taken together, these results suggest that the Val397Glu missense variant in IFT57 destabilises the IFT-B complex, affecting cilia formation and anterograde transport. Elucidating the link between IFT57 and BBS is important to clarify the genetic nature of BBS and inherited retinal dystrophies, opening new research avenues.

### Structural and Functional Retinal Phenotype in Mucopolysaccharidosis Type I Hurler and I Hurler-Scheie

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**Introduction:** Visual prognosis in mucopolysaccharidosis (MPS) type I may be guarded despite timely management of corneal cloudiness and glaucoma in the presence of retinal degeneration. Systemic hematopoietic stem cell transplantation and enzyme replacement therapy have largely been considered to have no effects on retinal degeneration. We aim to define the structural and functional retinal phenotype in MPS I subjects by analyzing spectral-domain optical coherence tomography (SD-OCT) and full-field electroretinogram (ERG) features.

**Methods:** Eighteen children (55% males) with MPS I Hurler (I-H, n=15) and Hurler-Scheie (I-H/S, n=3) who had SD-OCT and ERG from 2005 to 2023 were included in this retrospective review. The diagnosis of MPS was confirmed by the presence of biallelic variants in IDUA and/or  $\alpha$ -L-Iduronidase enzymatic deficiency. Descriptive and qualitative analysis of the SD-OCT parameters were performed. Age-wise Pearson's correlation of the a-wave amplitude and b/a ratio of the dark-adapted (DA)3 and DA10 ERGs was performed.

**Results:** The median age of presentation was 5 years (range 2 to 9) with a mean visual acuity of  $0.6 \pm 0.3 \log \text{MAR}$ . All children had diffuse ground glass-like stromal opacities with 21/36 eyes requiring deep anterior lamellar keratoplasty. Fifteen patients (83%, 15/18) had bilateral normal fundus appearance whilst three had peripapillary subretinal yellowish deposits in one eye. Maculopathy defined as parafoveal loss of the ellipsoid zone on SD-OCT was noted in four patients (mean age  $13.5 \pm 2$  years). SD-OCT demonstrated foveal external limiting membrane (ELM) thickening in 17/18 patients with a median thickness of 36 $\mu\text{m}$  (range 26 to 43 $\mu\text{m}$ ). Foveal ELM thickening was observed in the absence of clinically apparent retinal changes in all patients. One patient without ELM thickening was the youngest (2 years) and had normal retinal exam. Baseline ERGs at the mean age of 11 years (range 2 to 18) showed a reduced average b/a ratio of 0.9 (range: 0.3 to 1.6) and 0.8 (range 0.2 to 1.2) to the DA 3 and DA10 ERGs, respectively. 11 and 14 patients had an electronegative ERG to DA 3 and DA10 ERGs respectively. Significant correlation was noted between age - b:a ratio ( $p = 0.0075$ , DA 3;  $p = 0.0094$ , DA 10) and age - visual acuity ( $p = 0.0272$ ).

**Conclusions:** ELM thickening is the most consistent finding in MPS 1 eyes noted in 94% of individuals within our study group. SD-OCT is an important investigative tool for MPS 1 patients, despite unremarkable retinal examination. The changes in b/a amplitude ratio in DA 3 and DA 10 ERGs appear to be a good biomarker of the progression of retinal degeneration.



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**Roller Coasters and Retinal Detachment**

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**Methods:** A literature search was performed with terms 'retinal detachment' and 'traumatic' or 'roller coaster' or 'bungee jumping'. Articles involving direct traumatic injury (coup, or contrecoup type 2) were excluded. All citing articles of relevant existing reports were scanned for additional reports of acceleration associated retinal detachment. Two original cases are additionally reported.

**Results:** We report two cases of retinal detachment following roller coaster riding. A literature search reveals two previous such cases, and an additional three cases following bungee jumping. In all cases the affected individual had known risk factors for retinal detachment, with the most common being myopia.

**Conclusion:** Rapid acceleration/deceleration forces such as those experienced on roller coasters may lead to retinal detachment in predisposed individuals, particularly those with high myopia.

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**Anti-Vascular Endothelial Growth Factor Treatment Outcomes in Macular Telangiectasia: A Systematic Review**

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**Introduction:** Effective treatment for type 2 macular telangiectasia (MacTel) remains unknown. In this study, we assessed clinical outcomes of anti-vascular endothelial growth factor agents (anti-VEGF) for patients with MacTel.

**Methods:** We conducted a systematic literature search on Ovid MEDLINE, Embase, and Cochrane Library from inception to January 2023 for peer-reviewed articles reporting on different treatment regimens of anti-VEGF agents in MacTel. Our primary outcomes were the final best-corrected visual acuity (BCVA) and the change in BCVA from baseline. Secondary outcomes were central macular thickness (CMT), central choroidal thickness (CCT), and fluorescein angiography (FA) leakage.

**Results:** A total of 1,107 studies were screened, and 10 studies reporting on 377 eyes of 239 patients were included. Seven studies reported positive outcomes and recommended the use of anti-VEGF agents for MacTel, while 3 studies concluded that there was no functional benefit of treatment. Mean best-corrected visual acuity (BCVA) changed from  $0.42 \pm 0.39$ , or 20/52 to  $0.35 \pm 0.18$ , or 20/45 over  $23.4 \pm 8.3$  months of follow up in non-proliferative MacTel. Mean BCVA changed from  $0.66 \pm 0.43$ , or 20/92 to  $0.52 \pm 0.34$ , or 20/66 at final follow-up in eyes with subretinal neovascular membrane (SRNVM). In non-proliferative MacTel, mean central macular thickness (CMT) changed from  $201 \pm 32$   $\mu\text{m}$  to  $199 \pm 29$   $\mu\text{m}$ . CMT in participants with SRNVM or MNV changed from  $328.23 \pm 161.16$   $\mu\text{m}$  to  $267.44 \pm 118.56$   $\mu\text{m}$  at final follow up. Central choroidal thickness (CCT) was reported only in proliferative MacTel, with initial and final CCT of  $272.37 \pm 52.65$   $\mu\text{m}$  and  $247.40 \pm 48.80$   $\mu\text{m}$ , respectively. Overall, FA leakage outcomes were improved on ranibizumab therapy. No serious adverse events were reported in association with anti-VEGF treatment. Given that most studies were nonrandomized and had small associated sample sizes, there was heterogeneity and limited generalizability of findings.

**Conclusion:** There remains a lack of evidence evaluating the efficacy of anti-VEGF treatment in MacTel. The findings of our study, albeit limited, suggests that anti-VEGF agents may be associated with favourable anatomical and functional outcomes, particularly in proliferative MacTel, however, future large-scale clinical trials are warranted.

### A Dual Role for the HFE2 Protein in Retinal Angiogenesis

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**Introduction:** Angiogenesis, the formation of new vessel sprouts from pre-existing vasculature, plays a crucial role in vascularization and specialized structure generation for the developing retina. Manipulating angiogenic mechanisms holds promise for treating retinal diseases including diabetic retinopathy, age related macular degeneration, and retinal vein occlusions. Our study focuses on the role of Hemojuvelin (HFE2), a protein produced and secreted by the liver and muscle tissue, revealing its dual role in angiogenic activity. We found that liver-secreted HFE2 acts as a pro-angiogenic factor, while muscle-derived HFE2 suppresses angiogenesis in the developing retina. Differential modifications of liver- and muscle-derived HFE2 likely contribute to these distinct effects. Our aim is to establish that these modifications may lead to preferential binding to HFE2's receptors, Neogenin (NEO1), and Bone Morphogenic Protein (BMP), providing insights into the underlying mechanisms modulating angiogenesis.

**Methods:** Using mouse models with liver and muscle HFE2 knockouts (HFE2<sup>fl/fl</sup>- $\Delta$ Alb-Cre and HFE2<sup>fl/fl</sup>- $\Delta$ Acta-Cre), we studied the in vivo function of these proteins in the developing retina (P6-P11) with whole mount staining protocols for angiogenic markers (ESM1, ERG, PH3, CD31). The tube formation assay was used to assess if these effects can be replicated in vitro. Reporter assays, Western blots, ELISA binding assays, and RT-qPCR were done to understand the underlying mechanism behind this observed phenomenon.

**Results:** Assessment of the retinal vascular layers at critical stages of development showed a decrease in angiogenic activity in HFE2<sup>fl/fl</sup>- $\Delta$ Alb-Cre mice while HFE2<sup>fl/fl</sup>- $\Delta$ Acta-Cre exhibited the opposite effect. These findings were replicated in our in vitro tube formation assay, where human brain endothelial cells treated with muscle or liver derived HFE2 protein displayed a decrease or increase in vascular formation and growth, respectively. Through western blot analysis, we discovered that muscle derived HFE2 lacks the ability to undergo cleavage at its autocatalytic site, crucial for the binding to receptor Neogenin. Furthermore, ELISA binding assays revealed that liver derived HFE2 preferentially binds to Neogenin. Reporter assays and RT-qPCR analysis revealed that treatment with muscle-derived HFE2, but not liver-derived HFE2, increases Notch activity through a BMP-mediated pathway.

**Conclusion:** This research uncovers a novel role for HFE2 on regulating retinal vascularization. We will investigate HFE2 expression levels throughout mouse development using BioOrthogonal Non-Canonical Amino Acid Tagging. This research deepens the understanding of angiogenic processes, providing insights into underlying mechanisms and potential therapeutic options for retinal diseases. Moreover, this research reveals how distinct organ systems influence retinal angiogenesis, laying a broader foundation for clinical intervention.

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**Macular Hole Associated Retinal Detachment in High Myopic Patients: Case series and Overview of a Novel Surgical Technique**

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**Introduction:** Macular hole retinal detachment (MHRD) occurs in highly myopic eyes and is presumed to happen due to anteroposterior vitreoretinal traction and reduced retinal adherence to the choroid. Treatment usually involves pars plana vitrectomy (PPV) with internal limiting membrane (ILM) peel and gas or oil tamponade. However, this can be technically challenging, not always successful and carries risk of indocyanine green toxicity. The present study aims to describe two cases of MHRD and discusses a novel surgical technique in the management of these cases.

**Methods:** Complete ophthalmologic work-up was done including visual acuity, fundus examination and optical coherence tomography (OCT).

**Results:** Case 1 was a 57-year-old female with past ocular history of high myopia and amblyopia OD was seen in retina service for decreased vision in the right eye (OD). At presentation her visual acuity (VA) was counting fingers OD, and 20/60 left eye (OS). OCT demonstrated myopic foveoschisis, grade 3 full thickness macular hole and MHRD OD and foveoschisis with intraretinal fluid OS. Pneumatic retinopexy was performed to reattach the retina prior to PPV with ILM peel, air fluid exchange and amniotic membrane plug. At one year follow up, VA improved to 20/200 OD with reattachment of the retina, closure of the macular hole but with persistent small defect.

Case 2 was a 54-year-old female with past ocular history of bilateral LASIK for high myopia, presenting with sudden loss of vision OS due to MHRD OS. Her visual acuity was 20/200 OS. Pneumatic retinopexy was performed to reattach the macula preoperatively. Subsequently, the patient underwent PPV, ILM peel and gas tamponade. At one month follow up, VA improved to 20/60 OS with reattachment of the retina and full closure of the macular hole on OCT.

**Conclusions:** Treatment of MHRD has traditionally been with PPV, ILM peel and gas tamponade, sometimes resulting in failure of MH closure and recurrent detachment. Our cases demonstrate the use of pneumatic retinopexy to reattach the retina prior to PPV. This technique avoids challenges and risks associated with ILM peeling of the detached retina and may improve the outcomes of the surgery.

**Perspectives on Efficacy and Safety of Anti-Vascular Endothelial Growth Factor (Anti-VEGF) Biosimilars in the Treatment of Neovascular Age-Related Macular Degeneration (nAMD)**

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**Introduction:** With expiry of originator anti-vascular endothelial growth factor (anti-VEGF) patents, policies are transitioning to the use of biosimilars. It remains unclear as to how this transition will impact patient outcomes and provider practices. This study aimed to explore the perspectives of Canadian ophthalmologists and patients with neovascular age-related macular degeneration (nAMD) on anti-VEGF biosimilar safety and efficacy, as well as current knowledge on rollout policy.

**Methods:** Ophthalmologists performing anti-VEGF injections were invited from August to October 2023 to participate in a physician survey. nAMD patients were invited in-person in August 2023 to participate in a patient survey. Both surveys included ranking questions and visual analogue scales (VAS) (1-10) to measure agreement with given statements. A priori, "agreement" with these statements was defined as a VAS response of between 7 and 10. All survey participants were invited to a semi-structured interview to supplement survey responses. Analysis of interview data was performed in Dedoose, a specialized software for qualitative analysis, where responses were analyzed using Thorne's interpretive description approach.

**Results:** There were 38 ophthalmologists across 9 provinces who participated in the survey and 3 who subsequently completed an interview. 47% of ophthalmologists in our sample were unaware of their province's anti-VEGF biosimilar rollout policy and 68% were uncomfortable with using biosimilars, with interviews suggesting preference to be late- rather than early-adopters of biosimilars. 79% of ophthalmologists felt that the switch to biosimilars should not be mandatory. Safety and efficacy of biosimilars were most commonly ranked by ophthalmologists to be the most important factors in choice of treatment. 50 nAMD patients participated in the survey and 11 subsequently completed an interview. 88% of patients in our sample were not comfortable being switched to a biosimilar, with 94% indicating that they believe their doctor should have the choice to decide which drug is best for them. Interviews revealed that patients assumed biosimilars were of lower safety and efficacy compared to originators but had great trust in their physicians' treatment decisions.

**Conclusion:** Hesitancy with the use of anti-VEGF biosimilars was seen both among Canadian ophthalmologists and patients with nAMD, most commonly in relation to safety and efficacy. Most physicians and patients believed that a switch to biosimilars should not be mandatory.

### CRB1 Mutation in Human Retinal Organoids Alters Photoreceptor Development

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**Introduction:** Inherited retinal diseases (IRDs) cause progressive and irreversible blindness in approximately two to five million people globally. Crumbs cell polarity complex component 1 (CRB1) mutations account for around 10% of all genotypes associated with two common IRDs, causing severe early vision loss in children and young adults with no treatment. This vision loss is caused by a decrease in the number of photoreceptors, and some animal studies report potential Hippo/YAP and NOTCH pathway involvement. However, detailed knowledge about the timing and mechanisms underlying PR loss in human CRB1-associated retinal disease (CD) is limited. As such, we hypothesize that CD leads to a prolonged proliferative state and increased cell death, lowering the photoreceptor population.

**Methods:** Human retinal organoids (ROs) were generated from induced pluripotent stem cell (iPSC) lines derived from a patient with homozygous CRB1 mutation (p.Q120X; p.Q120X) and a healthy donor. Every four weeks between weeks 8-12, immunofluorescent staining for proliferation, cell type-specific markers (progenitors: PAX6; photoreceptors: recoverin, CRX, OTX2; cones: ARR3; rods: NRL, rhodopsin; ganglion cells: BRN3a; Muller glia: SOX-9) and CRB1-related proteins (CRB1, ZO-1) was performed. RNA from bulk ROs were extracted and used in qRT-PCR to measure the expression of the NOTCH (NOTCH1, NOTCH2, Hes1, Hey1, Hey2) and Hippo/Yap (STK3, STK4, YAP1) pathways.

**Results:** Both healthy and diseased donor-derived ROs displayed sequential differentiation consistent with fetal development in vivo with positive staining for early retinal cell markers (ganglion cells: BRN3a, progenitor cells: PAX6, CHX10; photoreceptor/ bipolar cell progenitors: OTX2, CRX) at week 8, and positive staining for later markers (cones: ARR3, rods: NRL) at week 13. Compared to week 8, expression of CRB1, YAP1, NOTCH1, NOTCH2, and Hes1 significantly increased in healthy ROs at week 12. Initial observations of mature CRB1-mutant ROs showed less rhodopsin staining and shorter brush border compared to healthy ROs at week 34, which may suggest alterations to development of mature photoreceptors. Moreover, CRB1-mutated ROs showed more disruptions in outer neuroblastic layer compared to healthy ROs at week 8, which suggests structural disorganization at an early timepoint. Further analysis of CRB1-mutated ROs is ongoing.

**Conclusions:** Disease-specific retinal organoids derived from a CD patient showed differences in photoreceptor development compared to healthy ROs. Further study of protein and gene expression in an organoid model will clarify the effects of NOTCH1 and Hippo/Yap signaling in CD to facilitate the discovery of novel therapies.

## Realistic Generated Images using Latent Diffusion Models to Improve Retinal Disease Classification using Deep Convolutional Neural Networks

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**Introduction:** Generative AI for image creation, such as latent diffusion models (e.g. OpenAI DALL-E), is an emerging technology with potential applications in medical imaging and data augmentation. This study aimed to leverage latent diffusion probabilistic models (DDPMs) to generate highly realistic retinal images. The primary objective was to evaluate the quality of generated images using human experts and subsequently investigate the impact of incorporating generated images in the training of a previously published deep convolutional neural network ensemble (CNNs) for retinal disease classification.

**Methods:** A latent diffusion model, based on the Medfusion architecture, was trained to generate retinal fundus images across four disease categories: diabetic retinopathy (DR), glaucoma, age-related macular degeneration (AMD), and healthy eyes, using 144,513 real images from 13 public datasets. Eight human experts evaluated the realism of 48 generated images (12 per class) and classified them based on disease labels. Subsequently, varying numbers and combinations of generated and real retinal images were employed to augment training of deep convolutional ensembles (DCEs) for classifying retinal disease. Performance metrics, including accuracy, F-score, and area under the receiver operating characteristic (AUROC) curve, were measured on a test set of 100 real images.

**Results:** Eight board-certified ophthalmologists exhibited an average accuracy of 61.1% (range: 51.0 - 68.8%) in distinguishing between real and generated fundus images, with varied performance across disease categories. Augmenting the training set with generated images, especially in the smallest class (AMD), statistically significantly improved the DCE's classification performance: including an additional 238 generated fundus images of AMD improved the F-score and accuracy by 5.3% and 5.8% respectively compared to a previously published baseline model (Pandey et al., 2023) trained only with real images.

**Conclusion:** This study establishes the efficacy of latent diffusion models in generating high-fidelity realistic retinal fundus images, as graded by board-certified ophthalmologists. Furthermore, the integration of generated images into the training of deep convolutional neural networks resulted in statistically significant improvements in the multi-class classification of retinal diseases. These findings underscore the potential of generative models in augmenting data and improving algorithm classification performance without the need for additional real data.

**Association Between Sociodemographic, Clinical Access, and Regional Factors with Diabetic Retinopathy in the National Health Interview Survey: A Cross-sectional, Population-Based Analysis**

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**Introduction:** Diabetic retinopathy (DR) is the most common microvascular complication of diabetes and the leading cause of blindness in working class adults in the United States. The impact of diverse social determinants of health (SDH) on the prevalence of DR is poorly understood. This study aimed to investigate the relationship between sociodemographic and healthcare access factors with DR prevalence in a large, nationally representative sample of the United States population.

**Methods:** This cross-sectional analysis included respondents to the 2017 National Health Interview Survey (NHIS) who answered the question, "Have you ever been told by a doctor or other health professional that you had diabetic retinopathy?" Univariable and multivariable logistic regression was used to examine the association between DR prevalence and sociodemographic factors. The primary outcome was DR and the exposures included the following SDH: 1) healthcare access and quality, 2) economic stability, 3) education access, 4) neighborhood and built environment, and 5) social and community context.

**Results:** Of 26,966 eligible NHIS respondents (81.4%), 26,699 participants were eligible for participation, of whom 266 (1.0%) self-reported a DR diagnosis. Most participants were white (80.46%) and aged 50-64 (26.11%). Multivariable analysis found a significant association between DR prevalence and the following social determinants of health: poorer health status (OR=6.10; 95%CI=3.75-9.92;  $p < 0.001$ ), disability (OR 2.07; 95%CI 1.33 - 3.21;  $p = 0.001$ ), no employment (OR=1.77; 95%CI= 1.12 - 2.81;  $p = 0.015$ ), and living in Southern America (OR= 1.85; 95%CI= 1.072- 3.20;  $p = 0.028$ ). Having a usual place for healthcare (OR 0.28; 95% CI 0.12 - 0.69;  $p = 0.005$ ) and female sex (OR= 0.58; 95%CI= 0.42 - 0.82;  $p = 0.002$ ) was negatively associated with DR prevalence.

**Conclusions:** Multiple sociodemographic factors are associated with DR prevalence. Health care providers and policymakers should tailor future interventions to address the social determinants of health in a holistic model of DR screening and care.



## Postoperative Aniseikonia in Patients with Unilateral Rhegmatogenous Retinal Detachment: A Systematic Review

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**Introduction:** Rhegmatogenous retinal detachments (RRD) can be repaired using scleral buckle (SB), pars plana vitrectomy (PPV), or pneumatic retinopexy (PnR). Although retinal reattachment rates are generally high, poor functional outcomes are still a reality. One of the most prevalent post-operative symptoms is aniseikonia, which is a binocular difference in the size or shape of the perceived image. This systematic review aimed to investigate the incidence and characteristics of aniseikonia in patients after RRD repair.

**Methods:** A systematic review of literature in concordance with the PRISMA guidelines was completed. Ovid MEDLINE, EMBASE, and Cochrane CENTRAL were searched for peer-reviewed publications between January 1st, 2000 and October 22nd, 2022. Our primary outcome was the presence and/or severity of aniseikonia following SB, PnR, or PPV to treat unilateral RRD. Our data were reported through descriptive statistics.

**Results:** Our search captured 383 relevant articles and ultimately 14 studies were included. From 14 included studies, data from 1463 patients were analyzed. Most patients were male and the mean age was  $58.3 \pm 4.33$  years old. All studies showed an improvement in best-corrected visual acuity post-surgery. However, there was a great variability in visual function. The incidence and severity of aniseikonia varied between studies and procedures. The incidence of aniseikonia ranged from 5% to 60%, with micropsia being the most common. More than half of the included studies had patient populations with greater than 50% having aniseikonia post-surgery. Aniseikonia was measured qualitatively in 2 included studies, while the remainder utilized quantitative methods.

**Conclusions:** Aniseikonia is commonly found in patients post-RRD repair. Further research with a more robust methodology should be undertaken to understand the relationship between surgical techniques and perioperative factors with aniseikonia.

## Evolution of Asymptomatic Pentosan Polysulfate Maculopathy Following Medication Discontinuation: A Case Report

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**Introduction:** Pentosan Polysulfate Sodium maculopathy (PPSM), first reported in 2018, is a newly characterized retinal disease associated with long-term use of PSS, a semisynthetic sulfated polysaccharide, which is the only Food and Drug Administration approved oral entity for interstitial cystitis. Most patients with experience progressive nyctalopia, central scotoma, and potentially severe vision loss. Asymptomatic cases have been seldom reported in the literature. Herein, we describe the clinical course of a patient receiving pentosan polysulfate (PPS) for interstitial cystitis, who developed asymptomatic PPS maculopathy (PPSM) that nonetheless persisted and evolved for four years after medication discontinuation.

**Methods:** Case report of one patient at a tertiary retina clinic. The charts of the given patient were reviewed for their clinic visits between 2016 and 2023.

**Results:** A 48-year-old female with a history of interstitial cystitis was referred to our retina clinic for query findings of age-related macular degeneration, despite endorsing no vision complaints. She had no relevant past ocular history. She had been taking PPS for 10 years for interstitial cystitis, first consuming 600mg/day for eight years, followed by 200mg/day for two years. At first presentation in 2016, examination revealed macular pigmentary clumping in both eyes. In subsequent years, pigmentary changes were confirmed by optical coherence tomography (OCT) which showed progressive macular thinning in both eyes. In 2019, the patient discontinued PPS; however, she continued to exhibit PPSM progression for years thereafter. At four-year follow-up after discontinuation of PPS, the patient returned with stable vision, but showed changes in macular lipofuscin deposits with outer retinal and retinal pigment epithelial alterations. Across the entire span of follow-up, she did not report a consistent constellation of visual symptoms, nor did she endorse the typical progressive symptoms of PPSM.

**Conclusions:** This case demonstrates sustained and evolving PPSM even after drug discontinuation, suggesting that active PPS may have a prolonged half-life in the retina and retinal pigment epithelium. Further, we report a rarer case of asymptomatic PPSM, despite clinically progressive findings.

## Differential Characteristics in Enrollment in Age-Related Macular Degeneration Clinical Trials: A Cross-Sectional Study

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**Introduction:** Evidence indicates inequitable enrollment of some demographics into trials for certain ophthalmic diseases. Representative trial enrollment is necessary to accurately extend conclusions on safety and efficacy to real-world populations. This study investigates demographic characteristics in age-related macular degeneration (AMD) trial enrollment.

**Methods:** Cross-sectional study. We included AMD patients enrolled in US-registered, high-quality, randomized controlled trials (RCTs). Clinicaltrials.gov was searched with “age-related macular degeneration” to identify RCTs with double, triple, or quadruple masking. Trial (e.g., study location, phase, masking, trial initiation year, and sponsor origin) and demographic data were collected. Sex-based AMD disease burdens were retrieved from the Global Burden of Disease database to calculate pooled female population-to-prevalence ratios (PPRs). Equitable trial enrollment was defined as PPR between 0.8-1.2. Demographic proportions were evaluated across trial characteristics using the Kruskal-Wallis test ( $\alpha=0.05$ ) followed by post-hoc comparisons. Pooled PPR for female enrollment. Secondary outcomes of interest included the association of trial characteristics with sex, race, and ethnicity.

**Results:** From 1999 records, we included 106 eligible trials spanning between 1990-2020. All trials (N=77,939) reported sex demographics with a pooled female PPR of 0.88 (95% confidence interval [CI]: 0.82, 0.94). Female enrollment was 36,109 (46.3%) out of 77,939 participants. Of the 74 (69.8%) trials that adequately detailed race, White participants comprised the largest group (N=57,917; 82% of total participants). Thirty-seven (34.9%) trials adequately detailed ethnicity.

**Conclusions:** This study primarily sought to determine whether AMD trials adequately enrolled female participants. Our results indicate representative female enrollment compared to their disease burden, thereby furthering confidence in their generalizability to this population. Female enrollment held consistent across strata of all trial characteristics (study phase, region, sponsor, initiation year, and intervention type). However, race and ethnicity were often under-reported and minority groups composed a minority of participants, which generally held across trial characteristics. Future studies should prioritize representative racial and ethnic enrollment to optimize trial result generalizability.

## Comparison of Intravitreal Corticosteroids for Management of Diabetic Macular Edema: A Scoping Review of Long-Term Randomized Trials

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**Introduction:** A significant proportion of patients with diabetic macular edema (DME) require second-line corticosteroid therapy after insufficient response to anti-vascular endothelial growth factor (anti-VEGF) treatment. Currently, dexamethasone implant, fluocinolone acetonide inserts, and intravitreal triamcinolone acetonide are approved for second-line intravitreal corticosteroid therapy. However, there are scarce evidence-based guidelines advising the delivery of these corticosteroids for DME. Current guidelines recommend subjective clinical judgement to guide management. It also remains unclear whether there is sufficient evidence in the literature to support the creation of such guidelines. This study aimed to summarize the published repertoire of long-term randomized controlled trials (RCTs) that evaluate current corticosteroid treatments for DME patients.

**Methods:** Scoping review of RCTs following PRISMA guidelines. Using a validated search strategy, MEDLINE, EMBASE, and Cochrane CENTRAL were searched to April 2022 for RCTs evaluating monotherapy or combination steroid (with laser or anti-VEGF) treatments against control (placebo, sham, or observation), laser (grid or panretinal photocoagulation), or anti-VEGF agents (bevacizumab, ranibizumab, or aflibercept). Exclusion criteria included studies with patients undergoing concomitant ocular surgery at baseline (as a co-intervention), prophylaxis studies, follow-up fewer than 6 months, and duplicate publications. Paired independent reviewers conducted title and abstract screening, full-text selection, and data extraction. Information related to patient enrollment, study interventions, and study durations were abstracted for each trial included in the final summary.

**Results:** From 2906 records, we identified 55 RCTs across 7014 patients (7294 eyes) comparing corticosteroid treatments against other treatment modalities (median follow up: 6 months). Of most concern, there were zero published trials directly comparing corticosteroid monotherapies (dexamethasone implant, fluocinolone acetonide insert, or intravitreal triamcinolone acetonide) against one another. As well, we identified zero studies directly comparing different corticosteroids through combination regimens. This result precluded summary of the comparative efficacy between corticosteroids. However, between studies, RCTs overwhelmingly compared all corticosteroid agents against common comparator mono-interventions (control: n=9 studies; anti-VEGF agents: n=27 studies; laser therapy: n=18 studies).

**Conclusions:** RCTs predominantly compare corticosteroid treatments against other treatment modalities. However, to-date, there is insufficient evidence directly comparing available corticosteroids to identify an agent that optimizes patient outcomes and safety. Corticosteroid therapy remains a viable option for patients who cannot adhere to monthly anti-VEGF treatment. Our results indicate need for head-to-head corticosteroid trials to further substantiate evidence-based DME treatment guidelines. Although such trials require prolonged longitudinal follow-up, we report sufficient evidence for network meta-analyses to derive preliminary evidence comparing corticosteroid monotherapy and combination regimens.

## Intracameral Moxifloxacin Prophylaxis for Postoperative Endophthalmitis: Dose Optimization for Posterior Capsular Rupture and Secondary IOL Cases

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**Introduction:** Previously, we developed a mathematical model for optimizing drug delivery of prophylactic intracameral moxifloxacin (ICM) after routine cataract surgery with in-the-bag IOL implantation. This model ultimately recommended injecting 0.55 mL (150 ug/0.1 mL) of ICM to reliably achieve a retained mass of 500 ug ICM in the anterior chamber at the conclusion of surgery, which according to literature, should eliminate known pathogens to cause postoperative endophthalmitis with negligible risk of toxicity. However, even with adoption of ICM prophylaxis at the end of surgery, evidence suggests statistically higher rates of postoperative endophthalmitis after complex cases involving intraoperative posterior capsular rupture (PCR) and secondary intraocular lens (IOL) implantation. The purpose of this work was to adapt the model to these more complicated cases to optimize the prophylactic ICM dose and administration method at the end of surgery.

**Methods:** We employ mathematical modelling, specifically first order mixing methods accounting for simultaneous fluid injection and leak from the anterior chamber, to predict achieved drug delivery. We have extended our previous mathematical model to these two previously unconsidered scenarios (which have different volume and compartment properties than simple pseudophakic eyes after routine cataract surgery) based on the surgeon's ability or inability to reinstate a "posterior capsular barrier". For both groups of scenarios, we then propose an enhanced dose and method to deliver ICM which may reduce their reported increased infection rates.

**Results:** We identified two groups (Group 1, in which the capsular barrier is reinstated, and Group 2, in which the barrier cannot be reinstated). Unlike the 0.5 mL volume of a newly pseudophakic eye after cataract surgery, the working volumes were determined to be separated 0.5mL and 1.0mL compartments in Group 1, and a single 1.0 mL compartment for Group 2. For Group 1, our suggested approach is to inject 0.55 mL (150 µg/0.1mL) ICM just prior to IOL implantation, directed towards the vitreous, and another 0.55 mL moxifloxacin through the side port at the end of the case after the main incision has been sealed. For Group 2, we recommend injecting a total injection of 1.1 mL (150 µg/0.1mL) ICM, which can be achieved using the same technique as for Group 1.

**Conclusions:** We suggest an enhanced ICM protocol for PCR and secondary IOL implantation cases to more accurately achieve the desired POE prophylactic dose of 500 µg per 0.5 mL volume in the at-risk increased anterior chamber and anterior vitreous volumes.

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

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**Introduction:** There is an absence of validated patient-reported outcome measures (PROMs) that evaluate treatment outcomes of 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 well-validated PROM that evaluates appearance-based outcomes of craniofacial patients. This prospective observational and qualitative study evaluated FACE-Q's content validity for use in CA, RB, and SB patients.

**Methods:** Cognitive debriefing interviews were conducted with CA, RB and SB patients  $\geq 8$  years old, and parents of patients  $< 8$  years old, hard of hearing or developmentally delayed. The interviews were part of a two-round process, using "think aloud" and verbal probing to obtain feedback on seven FACE-Q scales measuring eye-related (3/7), appearance-based (2/7) and psychosocial outcomes (3/7), as well as the need for any additional scales. Modifications were made to the FACE-Q based on feedback obtained from round 1 and additional input from a panel of scientific and clinical stakeholders and patient advocates. The modified FACE-Q was evaluated for its acceptability and relevance in round 2.

**Results:** Most FACE-Q content was comprehensible and relevant to CA, RB, and SB patients. After interviewing participants (n=36) in round 1, modifications, including expanding recall periods, removing concepts irrelevant to patients' lived experiences or conditions, subdividing scales to better reflect the diversity of patients' experiences, rewording instructions and existing items or adding examples to enhance comprehensibility, and adding missing condition-specific concepts were made. In round 2, participants (n=36) indicated that these modifications were relevant and acceptable, making the modified FACE-Q more relevant, comprehensible, and comprehensive compared to the original version. To further enhance the comprehensiveness of the modified FACE-Q for RB patients, a novel scale was developed with input from 6 RB patients, 4 eye trauma patients, and a prosthetic-specific panel, for reporting of appearance-based outcomes specific to the prosthetic eye.

**Conclusions:** The study suggests that FACE-Q may be a suitable PROM to adapt to measure appearance-based outcomes in CA, RB, and SB patients. With lived expertise, clinical, and scientific input, FACE-Q was modified to enhance its relevance, comprehensibility, and comprehensiveness for ophthalmic patients. The addition of the prosthetic scale broadened the applicability of the modified FACE-Q for patients with prosthetic eyes as well. Next steps include validation and psychometric evaluation of the modified FACE-Q.

**Effects of relative anterior chamber depth and relative anterior microphthalmos on intraocular lens power calculation accuracy.**

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**Introduction:** To determine the accuracy of various intraocular lens (IOL) power formulas in eyes with high anterior chamber depth (ACD) to axial length (AL) ratio (ACD:AL), eyes with low ACD:AL, and eyes with relative anterior microphthalmos (RAM).

**Methods:** All patients who received IOLMaster700 biometry from Feb 2019 to Jan 2021 were included in a retrospective consecutive case series. Patients were sorted by ACD:AL and patients in the top 5% of ACD:AL, patients in the bottom 5% of ACD:AL, and patients with RAM (defined as  $AL \geq 20$  mm, white-to-white  $\leq 11$  mm, and  $ACD \leq 2.2$  mm) were included in our analysis. % Patients within  $\pm 0.50D$  error was determined for Barrett Universal II, Cooke K6, EVO, Hill-RBF v3, Hoffer QST, Kane, Pearl DGS, Haigis, SRK/T, Hoffer Q, Holladay 2, Holladay 1; and compared to determine which formula(s) performed best for the three scenarios.

**Results:** For eyes with high ACD:AL ( $n=14$ ), there were no differences ( $p>0.05$ ) between formulas in %eyes within  $\pm 0.25$ ,  $0.50$  and  $0.75D$  error. Barrett Universal II, EVO, and Hoffer QST had the highest at 61% eyes within  $0.50D$  error, and Holladay 1 had the lowest at 53. For eyes with low ACD:AL ( $n=32$ ), there were no differences ( $p>0.05$ ) between the formulas in %eyes within  $\pm 0.25$ ,  $0.50$  and  $0.75D$  error. Haigis, EVO, Hill-RBF, and Hoffer QST achieved  $>70\%$  within  $\pm 0.50D$ , and Hoffer Q had the lowest at 53%. For RAM eyes ( $N=6$ ), there were no differences ( $p>0.05$ ) between the formulas in %eyes within  $\pm 0.25$ ,  $0.50$  and  $0.75D$  error. Formulas ranged from 20-50% within  $\pm 0.50D$  error. There were also no differences in MAE for any formula in any of the groups.

**Conclusion:** All formulas performed poorly (53-61% within  $0.50D$  error) in eyes with high ACD:AL ratio. Some formulas could achieve  $>70\%$  within  $0.50D$  error in eyes with low ACD:AL ratio. All formulas performed poorly (20-50% within  $0.50D$  error) in RAM eyes.

### **Preoperative Fasting for Ambulatory Cataract Surgery: A Time-Interrupted Prospective Randomized Study (The PRACTICE Study)**

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**Introduction:** Traditional fasting guidelines recommend nil per os (NPO) from midnight the night before elective surgery. Evolving recommendations from the American Society of Anesthesiologists and other jurisdictions suggest more flexible fasting durations for elective surgery, acknowledging minimal risks and potential benefits of reduced patient discomfort and increased scheduling flexibility without increased risk. We evaluated patient reported experience and distress of traditional versus modified fasting guidelines on patients undergoing routine cataract surgery.

**Methods:** In this prospective, time-interrupted, randomized study, adult patients undergoing routine cataract surgery at Kensington Eye Institute were included. Experimental group patients consumed up to 400mL of specified liquids up to three hours before their scheduled surgery time and were compared to patients who followed traditional fasting guidelines. Participants completed a validated questionnaire for fasting burden related to hunger, thirst, voice hoarseness, weakness, anxiety, and nausea both before and after surgery. Primary outcome was total fasting burden scores and secondary endpoints included individual questionnaire items, surgery cancellations, and aspiration incidence. Continuous data was reported as means with standard deviations, and categorical data as proportions with 95% confidence intervals. Data was analyzed with univariable and multivariable regression models. A p-value of less than 0.05 deemed statistically significant.

**Results:** 451 participants were recruited (241 controls). Average fasting durations were 14.26±6.80 for both solids and liquids and 3.80±1.15 hours for liquids for the control and experimental groups, respectively. Survey responses showed no statistically significant difference between the groups in total fasting-related burden, both pre- and post-operatively. Univariable model showed statistically significant decrease in anxiety level in the experimental group both pre-operative (0.243) and post-operative (0.171). Multivariable linear regression analysis revealed significant associations between the demographic patterns of: age and pre-operative hunger (0.022), post-operative weakness (0.014); time of surgery and pre-operative hunger (0.423), pre-operative thirst (0.298), pre-operative voice hoarseness (-0.306); gender and pre-operative thirst (0.451), post-operative thirst (0.439), post-operative weakness (0.409); amount of liquid consumed and pre-operative hunger (-1.965, -1.972, -2.987, respectively); amount of liquid consumed and pre-operative nausea (-1.195) and pre-operative voice hoarseness (1.291).

**Conclusions:** Statistically significant difference between the control and experimental group was not found yet, our intervention did show a statistically significant decrease in level of anxiety in the univariable model. However, this decrease was not seen in our multivariable model controlling for confounding factors. Other variables found to influence patient fasting-related burden were age, gender, time of surgery, and total amount of liquids consumed.



## Macular Retinal Ganglion Cell Thickness After Ischaemic Stroke, With and Without Visual Pathway Involvement

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**Introduction:** There is limited evidence on the impact of social determinants of health (SDH) on rare pediatric eye cancer (R-PEC) outcomes in Canada. We examined the association of R-PEC patient SDH with (a) medical visit attendance, (b) age and stage at diagnosis, (c) clinical outcomes, and (d) emergency visits.

**Methods:** This retrospective cohort study between 1-June-2018 and 6-October-2023 included R-PEC patients managed at The Hospital for Sick Children and resided in Ontario. Data collected included: sociodemographic variables, diagnosis details, medical visit attendance and clinical outcomes. Postal code was used to deduce neighborhood income quintile, Ontario marginalization index (OMI), geographic location, distance from hospital, and urbanicity. Pearson Chi-squared analysis and multivariable regression with adjusted odds ratios (aOR) and 95% confidence intervals (CI) were performed (significance was set at  $p < 0.05$ ).

**Results:** There were 324 study subjects with R-PECs affecting the retina (64.2%), optic nerve (28.7%), orbit (5.2%), eyelid (0.9%), and other structures of the eye (0.6%). Rescheduled or no-show medical visits were associated with: highest quintile (most marginalized) of the OMI dimensions material resources ( $p=0.049$ , aOR=1.576, 95% CI=1.003-2.477) and household dwellings ( $p=0.015$ , aOR=1.112, 95% CI=1.021-1.211); living >75 km from the hospital ( $p=0.028$ , aOR=1.109, 95% CI=1.011-1.216); and non-white race ( $p < 0.001$ , aOR=1.758, 95% CI=1.051-2.942). Higher stage at diagnosis was associated with: the highest quintile of the OMI dimensions material resources ( $p=0.046$ ), household dwellings ( $p=0.015$ ), age labor force ( $p=0.004$ ), and racialized and newcomer populations ( $p < 0.001$ ); low neighborhood income quintile ( $p=0.038$ ); and non-white race ( $p < 0.001$ ). Older diagnosis age was associated with: highest quintile of the OMI dimensions material resources ( $p < 0.001$ ), household dwellings ( $p < 0.001$ ), age labor force ( $p=0.013$ ), and racialized and newcomer populations ( $p=0.002$ ); living >75 km from the hospital ( $p < 0.001$ ); low neighborhood income quintile ( $p=0.017$ ); rural residence ( $p < 0.001$ ), and non-white race ( $p < 0.001$ ). Greater visual impairment was associated with the highest quintile of the OMI dimensions material resources ( $p=0.003$ ), household dwellings ( $p=0.013$ ), and racialized and newcomer populations ( $p=0.042$ ); low neighborhood income quintile ( $p < 0.001$ ); rural residence ( $p < 0.001$ ); and non-white race ( $p < 0.001$ ). Having >1 emergency room visit was associated with: low neighborhood income quintile ( $p=0.022$ ); highest quintile of the OMI dimension racialized and newcomer populations ( $p=0.002$ ), and non-white race ( $p=0.041$ ).

**Conclusions:** Addressing unfavorable SDH could serve to improve clinic attendance, age and stage at diagnosis, final visual outcome and reduce emergency room visits among patients with R-PECs.

## Modelling the Impact of the Autism Gene SCN2A on Retinal Development Using Human Stem Cell-Derived Organoid Models

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**Introduction:** De novo protein-truncating or missense variants in the central nervous system-specific neuronal voltage-gated sodium channel, SCN2A (Nav1.2), is responsible for a range of neurological disorders that includes autism spectrum disorder/intellectual disability (ASD/ID) and visual impairment. While the source of vision disorders in SCN2A patients is thought to be cortical, SCN2A is expressed in many cell types in the eye (eg. retinal ganglion cells and bipolar cells) and in retinal organoids (ROs), suggesting impaired SCN2A function in the retina may contribute to vision disorders. Given that loss-of-function mutations in SCN2A, generally associated with ASD, impair excitatory synaptic transmission in cortical neurons, SCN2A may play a role in synaptic transmission in the retina. Therefore, we hypothesize that ASD-mutations in SCN2A cause vision disorders by impairing the development and function of retinal synapses.

**Methods:** I have generated two isogenic human embryonic stem cell lines – one heterozygous for a novel ASD-specific G1744\* mutation and one homozygous knock-out (KO), to reveal how complete or partial loss of SCN2A function impacts human retinal development and synaptic function. ROs and cerebral organoids (COs) are an emerging 3D stem cell-derived model that recapitulates most aspects of retinal development and gene expression patterns compared to the human retina and brain in vivo. We first examined the impact SCN2A would have in cortical development using COs given its primary expression in the brain. COs were generated using STEMdiff™ Cerebral Organoid Kit by STEMCELL Technologies and assayed at Day 90, a time of high neuron diversity of maturation, for cytoarchitecture and single-cell RNAseq.

**Results:** Using single-cell RNAseq, we found cell type-specific changes in developmental trajectories in mutant organoids. Specifically, SCN2A mutant organoids showed reduced proportion of deep- and upper-layer neurons. Conversely, we observe precocious production of DLX+ inhibitory neurons resembling those derived from the caudal ganglionic eminence.

**Conclusions:** Our results suggest that the loss of SCN2A leads to impaired neuron development and disrupts normal excitatory-inhibitory balance. Given these findings in a cortical forebrain model, it is possible SCN2A may regulate similar aspects in the retina and contribute to the pathophysiology of vision disorders observed in some SCN2A patients.

**Navigating the Medico-Legal Challenges of Ophthalmology: Insights, Impacts, and Recommendations**Loukman Ghouti<sup>1</sup> (BSc.), Bonnie He<sup>2</sup>, (MD), Armaan Jaffer<sup>3</sup><sup>1</sup>Faculty of Medicine, Dalhousie University<sup>2</sup>Department of Ophthalmology, Dalhousie University<sup>3</sup>Faculty of Science, Queen's University

**Introduction:** Ophthalmology faces a rise in medical malpractice claims due to the intricate nature of procedures, the surge in elective oculoplastic and cosmetic treatments, and heightened patient expectations. This study explores these challenges, providing insights and recommendations.

**Methods:** Study design: A literature review. A systematic search using keywords and phrases related to ophthalmology litigation, malpractice, and subspecialties was conducted. Medical Subject Headings and Boolean operators were used. A total of 68 papers were reviewed.

**Results:** Ophthalmologists face malpractice claims once every 15 years, with cataract surgeries and refractive procedures being more susceptible to claims. A growing trend in claims, often exceeding \$1 million in compensation in the U.S., is evident. In Canada, about half of malpractice cases favor ophthalmologists; cases primarily involve surgical procedures (46.2%), misdiagnoses (32.7%), and non-surgical procedures (21.2%), with a median award of CDN \$308,202. Cases involving refractive treatments mainly comprise LASIK (74.2% over 50 years), while PRK represents only 5.5% of claims. Cataract surgeries lead in claims due to issues during pre-operative, intra-operative, and post-operative phases. In oculoplastics, procedures like blepharoplasty (63.8%) and brow lifts (11.6%) are commonly involved in claims, with common allegations including excessive scarring, lagophthalmos, and visual defects. Mean payment is US \$455,703. Oncology malpractice is rare (1.5% of cases), often involving uveal melanoma (31.3%), retinoblastoma (12.5%), and sebaceous cell carcinoma (12.5%), with a mean payment of US \$511,244.88. Pediatric cases often include traumatic ocular injuries (22.1%), retinopathy of prematurity (17.6%), and endophthalmitis (8.8%); they often favor plaintiffs and have larger financial awards (mean US \$4,815,693). Glaucoma claims account for 10% of cases in the U.S. from 1985-2005, often due to medication errors, diagnostic errors, and failure to monitor patients, with a mean award of US \$179,000. In neuro-ophthalmology, a high misdiagnosis rate (60-70%) leads to claims. Most claims resulted from failures in diagnosing conditions like stroke (30.2%); overdiagnosis was also a concern, especially in IHH. Effective communication, particularly during the informed consent process, is paramount in mitigating the risk of litigation.

**Conclusions:** Medical malpractice is common in ophthalmology, particularly in cataract surgeries and refractive procedures. Oculoplastics and ocular oncology are also implicated but to a lesser extent. These issues largely stem from perioperative negligence and inadequate informed consent. Residents' involvement in litigation highlights the need for improved training focusing on patient-physician relationships. Effective communication, particularly during informed consent, is vital in reducing litigation risks.

## Advanced Open-Source Machine Learning Tool for Hyperspectral Fluorescence Imaging in Ophthalmology

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**Introduction:** The eye, a complex optical system, consists of multiple layers, each with unique optical properties, including the cornea, sclera, uvea, and retina. These layers exhibit autofluorescence, observable through fluorescence microscopy, which is often considered as background noise when detecting signals from exogenous fluorescent probes targeting specific molecules. By integrating fluorescence microscopy with hyperspectral imaging technology, we have been able to acquire datasets with enhanced spectral and spatial resolutions. Recent advancements have demonstrated that the distinct autofluorescence spectral signatures of eye layers can be utilized for segmentation purposes. Nevertheless, the visualization and analysis of Hyperspectral Fluorescence Microscopy Imaging (HFMI) data present significant challenges. Our objective is to develop an open-source desktop application designed for the preprocessing, visualization, semantic segmentation, and boundary detection of hyperspectral images of eye tissue sections

**Methods:** This platform was developed utilizing hyperspectral datacubes (210 X 210 X 54), derived from frozen sections of pigmented and albino mouse eyes, captured using a snapshot Image Mapping Spectrometer imager (54 wavelengths from 528 to 836 nm) mounted on a fluorescence microscope. The aim is to devise segmentation and boundary detection algorithms for examining the distribution of biomolecules exhibiting endogenous fluorescence within specific layers of eye tissue. The algorithms, including Spectral Information Divergence Spectral Angle Mapper (SIDSAM) with an optional unmixing feature, and Spatial Fuzzy C-means (FCM) clustering integrated with a Sobel edge detector, have been incorporated into the application. This app provides a comprehensive suite of functionalities for data preprocessing—such as normalization, denoising, and superpixel generation—alongside visualization tools. These tools enable 2D and 3D spectral-based interactive exploration, selection of regions of interest (ROI), calculation and display of average spectral curves, and the preliminary identification of eye layer signatures through segmentation tools.

**Results:** The segmentation algorithms and additional tools integrated into the application offer an effective approach for analyzing Hyperspectral Fluorescence Microscopy Imaging (HFMI) across different environments. This integration facilitates the unsupervised, label-free segmentation of eye layers, including the retina, choroid, and sclera, significantly diminishing the time required for experts to label these layers for subsequent quantitative analysis.

**Conclusions:** The described desktop application, featuring label-free segmentation algorithms, enables users to derive insights from and add significance to complex biomedical hyperspectral data. Intended for release as an open-source tool, it is adaptable for use with various tissues beyond its initial scope. Ultimately, this application is poised to expedite research efforts aimed at validating clinical imaging techniques through hyperspectral imaging.

## Comparison of ChatGPT and Gemini in Surgical Planning for Orbitotomy

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**Introduction:** There has been an increasing use of artificial intelligence to aid radiologic imaging interpretation and to complement clinical decision making. However, their role in ophthalmologic surgical decision making has not been assessed. This study aims to assess the ability of ChatGPT and Gemini to interpret diagnostic imaging reports and to recommend appropriate surgical approaches for patients undergoing orbitotomy.

**Methods:** We conducted a consecutive, retrospective case series of all adult orbitotomy cases from July 2021 to September 2023 of three oculoplastic surgeons at University of Toronto, Ontario, Canada. Thirty-four patients underwent an orbitotomy. For each patient, the computed tomography (CT) or magnetic resonance imaging (MRI) report was input into ChatGPT 3.5 and Gemini 1.0. A standardized script was used to ask four questions: 1) Top 3 differential diagnosis; 2) Single most likely diagnosis; 3) Most appropriate biopsy type (incisional vs. excisional); and 4) Recommended surgical approach to access the lesion. Our outcomes included the proportion of cases where the differential diagnosis included the final pathology diagnosis and where the recommended biopsy type and surgical approach matched the surgeon's operative choice.

**Results:** The analysis included 30 patients. Gemini only answered the script questions for a subset of 17 patients, and declined to give medical advice for the remainder. For this subset, ChatGPT and Gemini performed very similarly. The top 3 differential diagnoses based on CT or MRI report findings included the final pathology diagnosis in 71% of cases for both. The proposed most likely diagnosis matched the pathology diagnosis in 53% vs. 47% of cases ( $p=1.0$ ), respectively. The suggested biopsy type (incisional vs. excisional) matched the surgeon's choice in 67% vs. 47% ( $p=0.25$ ). When asked regarding the most appropriate surgical approach to access the lesion, their recommendation matched the surgeon's choice in 45% vs. 36% ( $p=1.0$ ). Looking at only ChatGPT data for all 30 patients, its performance was: 1) 50%; 2) 38%; 3) 72%; and 4) 39%. For 5 patients, ChatGPT indicated neither type of biopsy as appropriate as the suspected diagnosis was inflammatory in nature. In two patients, it indicated neither biopsy was appropriate and suggested different biopsy techniques such as stereotactic biopsy or fine-needle aspiration biopsy.

**Conclusions:** ChatGPT and Gemini demonstrate potential in diagnostic imaging interpretation and in aiding preoperative surgical planning. However there remains limitations in their ability to accurately interpret radiologic imaging findings without clinical context and to select an appropriate surgical approach, illustrating the complexity and nuance of this decision.

### Geographic and Sociodemographic Perspectives on Ophthalmic Plastic and Reconstructive Surgery Providers in the United States

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**Introduction:** Ophthalmic plastic and reconstructive surgeons are trained to address complex ocular and facial disorders, considering functional and esthetic dimensions. These ophthalmologists are experts in the management of eyelid, orbit, and tear duct pathologies. Ensuring equitable access to their services is essential for comprehensive healthcare and optimal quality of life. To date, no study has evaluated the demographic and geographic disparities in access to oculoplastic care. This study characterizes oculoplastic surgeons in the United States (U.S.) and maps their service coverage areas (SCAs).

**Methods:** Using the 2024 American Society of Ophthalmic Plastic and Reconstructive Surgery (ASOPRS) directory, we identified all U.S.-based practicing ASOPRS-trained providers (referred to as OPRS) and confirmed their primary practice location. We further recorded their ASOPRS teaching site (when applicable), gender and degrees. Their primary practice addresses were converted into latitude and longitude coordinates using LocationIQ (Unwired Labs). These geographic coordinates were inputted in ArcGIS Pro (Esri) to perform geospatial coverage analyses. We delineated SCAs by generating regions within a 90-minute drive time from each provider address. The most recent American Community Survey data (ACS) from the U.S. Census Bureau were then layered onto the provider distribution map to characterize the population within and outside the SCAs. Social determinants of health of the population within and outside the SCAs were compared using chi-square tests.

**Results:** Of the 741 practicing OPRS, 186 (25.1%) worked at an ASOPRS teaching site, 527 (71.1%) were men, and 55 (7.4%) had a Masters/Doctorate degree. States with the most OPRS were California (n=117 OPRS, 15.9%), Texas (n=54, 7.3%) and Florida (n=53, 7.2%), while no OPRS practiced in Montana, North Dakota, South Dakota, and Wyoming. Of the 336,586,609 Americans nationwide, 294,070,172 (87.4%) lived within a 90-minute driving time from an OPRS office. The population living outside a 90-minute drive from OPRS was significantly more likely to be White, Non-Hispanic, without university education, receiving social security income, residing in a household below the federal poverty level, and lacking health insurance, compared to the population living inside 90-minute SCAs (each  $P < 0.001$ ).

**Conclusions:** Inequitable geographic distribution in OPRS across the U.S leads to service deserts, disproportionately affecting patients in rural areas and those with lower socio-economic status. Similar patterns have been observed in studies across various ophthalmic subspecialties, including pediatric uveitis, glaucoma, and neuro-ophthalmology. Recognizing these geographical and social obstacles to oculoplastic care access can inform future policies aimed at reducing these barriers.

**Comparative Analysis of Bacterial vs Culture-Negative Endophthalmitis**

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**Introduction:** Endophthalmitis can be caused by numerous infectious etiologies, but differences in visual acuity outcomes between etiological agents have not been extensively compared. This retrospective study aimed to assess visual acuity outcomes in patients with endophthalmitis based on microbiology results.

**Methods:** The data were collected from the electronic medical records of a vitreoretinal surgeon in Toronto from March 2011 to March 2023. After excluding patients with no follow up, the data from adult individuals with infectious endophthalmitis were extracted. Patients were categorized based on their microbiology report as having either bacterial or culture-negative microbiology. Univariable and multivariable linear and logistic regression were conducted to assess the differences in visual acuity outcomes after treatment for endophthalmitis based on microbiology, adjusting for age and sex. Statistical analyses were carried out in Microsoft Excel.

**Results:** Overall, 47 patients with infectious endophthalmitis were included. There was a more negative coefficient in the linear association between mean visual acuity and bacterial cultures (R-squared = 0.606,  $p = 0.008$ ) compared to the association between mean visual acuity and culture-negative samples (R-squared = 0.645,  $p = 0.003$ ). This suggests that mean VA improved more quickly in the bacterial group than the culture-negative group. However, on multivariable logistic regression, there was no significant difference in visual improvement between samples with bacterial culture or culture-negative from baseline to 1 month post-treatment ( $p = 0.11$ ) and baseline to 12 months post-treatment ( $p = 0.57$ ).

**Conclusions:** This linear and multivariable analysis found no significant difference in VA recovery between endophthalmitis patients with bacterial or culture-negative infections. Further large clinical trials would be helpful in further exploring the association between culture results with different microorganisms and their functional outcomes.

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**Sex Disparities in Operating Room Utilization among Cataract Surgeons: A 10-Year Retrospective Population-Based Analysis**

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**Introduction:** Sex-based differences in operating room (OR) distribution have not been extensively studied in ophthalmology. This is the first study to use objective, population-level data to assess sex differences in the number of OR days amongst cataract surgeon in Ontario.

**Methods:** In this retrospective population-based analysis, physician billing data between 2010 and 2019 were analyzed to identify all cataract surgeries in this timeframe. The number of cataract surgeries per day and number of OR days per year were extracted. Data were stratified by surgeon sex and career stage (defined as early: <45, middle: 45-55; and late: >55 years of age).

**Results:** Between 2010 and 2019, 1.05 million cataract surgeries were performed in Ontario. There was an average of  $195 \pm 3$  comprehensive cataract surgeons per year, of which  $39 \pm 5$  were female. The proportion of females increased from 16.8% of all surgeons in 2010 to 24.4% in 2019. The greatest proportion of male surgeons were in the late phase of their career, whereas the greatest proportion of female surgeons were in the early stage of their career. On average, males had  $44.9 + 1.90$  OR days per year and females had  $32.5 + 1.90$  OR days per year, resulting in females averaging  $12.45 + 1.90$  fewer OR days every year. The OR utilization remained consistent across career stages. The greatest number of OR days per year for both sexes occurred during mid-career. Case volumes per OR day were similar across sexes, but males performed on average  $172.7 \pm 30.6$  more surgeries per year.

**Conclusions:** Despite performing similar case volumes per OR day, female surgeons had less OR time compared to their male counterparts, and this remained consistent across career stages and over the 10-year period. Metrics used to determine OR allocation should be well-defined and transparent to achieve sex parity.



**Glaucoma Medication Persistence Rates in Ontario – A Retrospective Population-Based Study**

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**Purpose:**

Despite the success of intraocular pressure lowering therapy, glaucoma medication persistence - defined as the act of continuing the treatment for the prescribed duration - remain suboptimal. To date, there has been no comprehensive population-based studies examining glaucoma medication persistence rates. We conducted a retrospective population-based study utilizing data from a universal publicly funded system. This is the first study that employs a big-data approach to elucidate treatment persistence patterns for glaucoma eye drops.

**Methods:**

All individuals diagnosed with glaucoma who initiated ocular hypotensive medication between January 1, 2011, and December 31, 2016, were included in the study. Glaucoma was defined as patients using one or more glaucoma medications, accompanied by at least one visual field test within four months before or up to two years after medication initiation. Medication persistence was defined as maintaining a continuous supply of medications for up to two years. Partial persistence was for patients who intermittently maintained medications within the 2-year period; and transient users had less than 3 refills. We further analyzed potential factors, such as age, sex and socioeconomic status (SES), that influenced medication persistence.

**Results:**

From the ICES database, we identified 75,055 glaucoma patients. Among them, 13,150 were transient medication users (Group 1). In contrast, 61,905 patients belonged to the consecutive group. Of these, 17,462 (28.2%) achieved full persistence (Group 2); 31,125 (50.3%) patients (Group 3) experienced >90 days of medication interruption but later resumed their medications. The non-persistent group (Group 4, 21.5%) typically discontinued medications after 3 consecutive refills. The average age, average number of comorbidities, SES and sex distribution in each group are outlined in Figure 1. There were significant associations between the persistence group and SES ( $p < 0.01$ ), and with gender ( $p < 0.001$ ). Specifically, the non-persistence group have higher proportion of patients with low SES than the full-persistence group.

**Conclusions:**

Our study underscores the prevalence of low persistence (28.2%) for glaucoma medications over a 2-year period. This knowledge will facilitate the refinement of both medical practice and social policies, with the aim of providing enhanced support to individuals who are grappling with these challenges.

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