Department of Ophthalmology and Vision Sciences
University of Toronto

Sixty-Fifth Annual Research Day
and
Forty-Second Clement McCulloch Lecture
and
Dr. Martin J. Steinbach Lecture

Friday, May 26th, 2023
7:30 AM – 5:00 PM

SickKids
Peter Gilgan Centre for Research and Learning
686 Bay St
Toronto, Ontario
M5G 0A4

Meeting Chairperson

Matthew Schlenker, MD, MSc (Clin Epi), FRCSC
Director of Resident Research

Glaucoma, Cataract, & Anterior Segment Surgeon
Assistant Professor
Department of Ophthalmology and Vision Sciences
University of Toronto

UHN-Toronto Western Hospital
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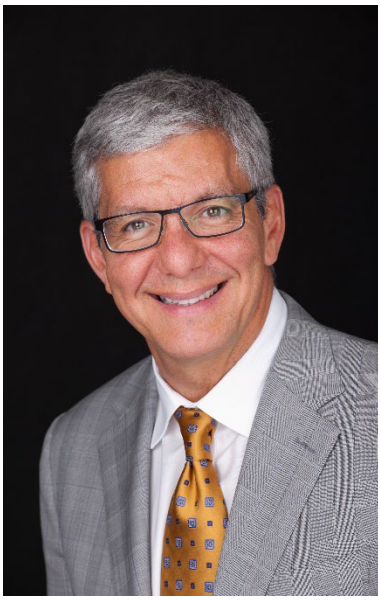
Chair's Message

Department of Ophthalmology and Vision Sciences 65th Annual Research Day



It is a pleasure for me to welcome you to the University of Toronto Department of Ophthalmology and Vision Sciences 65th Annual Research Day. Vision science is a vital part of our mandate in the department and plays an essential role in defining who we are. We have established ourselves as leaders in providing the most advanced vision care and continue to break new ground. Our research-intensive department is measured by the excellent faculty and by the innovative nature of our research program. Our commitment to scientific discovery enables close interactions between clinicians and scientists which ultimately transfers into tangible 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 and challenging accepted dogma to continually refine our understanding and management of ophthalmic conditions. A large part of our mission at the Department of Ophthalmology and Vision Sciences at the University of Toronto is to train ophthalmologists in research and critical thinking regardless of whether they become university or community-based; comprehensive or subspecialist. We hope this research training will lead to lifelong critical thinking and ongoing inquiry, a deeper understanding of vision science, and a relentless quest for better treatments of eye disease. The Department's primary goal 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 translational endeavours.

This year, with the leadership of Dr. Matt Schlenker, the research day program will return to an in-person meeting. The program will begin at 7:30 AM and there will be 3 sessions during the day with 3 breakout room sessions during the second session. During each session, we will feature the trainee presentations that scored highest by the abstract reviewers along with expert presentations. There will also be fewer oral presentations, though each will be longer to allow the speakers to fully explain their research. In addition, all other submitted abstracts will be provided with 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.Susan E. Quaggin, MD, FRCP(C), FASN. Dr.Quaggin is a graduate of the University of Toronto where she completed her residency and served as chief medical resident for the University's St.Michael's Hospital. She completed her nephrology fellowship at the University of Toronto and Yale University, where she also completed research and post-doctoral training. Dr. Quaggin's research focuses on fundamental processes needed to establish and maintain the integrity of the specialized vascular beds in the kidney and eye. Translation of her group's findings regarding the vasculature reveals pathogenic mechanisms and new therapeutic targets for several diseases, including diabetic kidney and eye disease, nephrotic syndrome, and glaucoma. Currently, she is the Charles Horace Mayo professor of medicine at Northwestern University where she serves as the Chief of the Division of Nephrology and Hypertension and Director of the Feinberg Cardiovascular and Renal Research Institute. Dr. Quaggin was elected to the American Society for Clinicl Investigation in 2006, the Association of American Physicians in 2013, the National Academy of Meidicne in 2019, the National Academy of Investors in 2021 and the American Academy of Arts and Sciences in 2023 and is past President of the American Society of Nephrology and councilor of the Association of American Physicians.

In addtion to our guest speaker, Dr. Ashwin Millipatna and Dr. Peter Kertes will be presenting their academic work on their respective research endeavours.

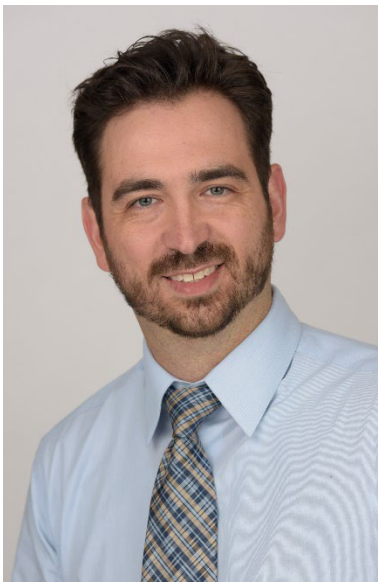
Dr. Matthew Schlenker, our Director of Resident Research, has been instrumental in planning this important event and we are grateful to him for his hard work contributing to the success of this day. I also would like to express my gratitude to all the supporting staff for the assistance they provided Dr. Schlenker in the preparation of the program and manual. A special thanks to Mano Chandrakumar for all his efforts.

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

As we continue our journey through this challenging but exciting time of new research discovery and achievements, I hope that you will enjoy our sessions, I know that you will leave with new, relevant, and interesting knowledge in our exciting field.

Sherif El-Defrawy MD, PhD, FRCSC
Nanji Family Chair in Ophthalmology and Vision Sciences
Professor and Chair
Department of Ophthalmology and Vision Sciences,
University of Toronto

Research Day Chairperson's Remarks



The Department of Ophthalmology and Vision Sciences at the University of Toronto has a long track record for research excellence. Many of our pre-clinical, clinic, and research trainees start their journey into the research realm at this very Research Day, including myself. 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 65th Ophthalmology Departmental Research Day and the 42nd Clement McCulloch Lecture. We would like to welcome Dr.Susan E. Quaggin, MD, FRCP(C), FASN, a renowned clinician-scientist who will share her unique research endeavours. The title of her talk is ***Under Pressure: High 'TEK' Solutions for Glaucoma***.

This scientific gathering would not be possible without the generous support from our sponsors. I would like to thank the members of the different committees, moderators, and ancillary staff who are responsible for the success of Research Day. Specifically, I would like to thank Mano Chandrakumar who spent countless hours assisting with the organization of this year's Research Day. I would also like to thank our Faculty members who judged the abstracts and then assessed the presentations. And a special thanks to all of the supervisors of our trainees. Finally, thank you all for your participation in this year's Research Day, which has returned to the traditional in person format.

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
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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

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Assistant Professor
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Research Day 2023 Committees

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Jeremy Sivak, PhD
Brian Ballios, MD, PhD, FRCSC
Matthew Schlenker, MD, MSc., FRCSC
Kamiar Mireskandari, MBChB, FRCSEd, FRCOphth, PhD

A look at the past …
University of Toronto
Department of Ophthalmology and Vision Sciences
Annual Research Meetings

1st Annual Research Day	February 27, 1959
2nd Annual Research Day	1960
Guest of Honour:	V.E. Kinsey, Detroit, U.S.A.
3rd Annual Research Day	March 18, 1961
Guest of Honour:	H.M. Burian, University of Iowa, Iowa, U.S.A.
4th Annual Research Day	1962
Guest of Honour:	Endre A. Balazs, MD, Boston, Massachusetts, U.S.A.
5th Annual Research Day	March 22, 1963
Guest of Honour:	L. Simovitch, Toronto, Canada
6th Annual Research Day	March 20, 1964
Guest of Honour:	P.A. Cibis, St. Louis, Missouri, U.S.A.
7th Annual Research Day	May 1, 1965
Guest of Honour:	G. Wald, Professor of Biology, Harvard University, Cambridge, Massachusetts, U.S.A.
8th Annual Research Day	April 30, 1966
Guest of Honour:	Maurice E. Langham, PhD, Baltimore, Maryland, U.S.A.
9th Annual Research Day	April 29, 1967
Guest of Honour:	J.E. Harris, Minneapolis, Minnesota, U.S.A.
10th Annual Research Day	April 26, 1968
Guest of Honour:	Herbert E. Kaufman, MD, Professor, Department of Ophthalmology, University of Florida, Gainesville, Florida, U.S.A.
11th Annual Research Day	May 9, 1969
Guest of Honour:	T. Leeson, Professor, Department of Anatomy, University of Alberta, Edmonton, Alberta, Canada
12th Annual Research Day	May 6, 1970
Guest of Honour:	Jin H. Kinoshita, PhD, Associate Professor of Biomechanical Ophthalmology, Harvard University Medical School, Boston, Massachusetts, U.S.A.

13th Annual Research Day	May 13, 1971
Guest of Honour:	M. Alpern, Professor of Physiological Optics, Department of Ophthalmology and Physiology, University of Michigan, Ann Arbor, Michigan, U.S.A.
14th Annual Research Day	May 11, 1972
Guest of Honour:	Ben S. Fine, MD, Ophthalmic Pathology, Armed Forces Institute of Pathology, Washington, DC, U.S.A.
Guest of Honour:	M. Mathieu, Director, Department of Ophthalmology, Hospital Maionneuve, Montreal, Quebec, Canada
15th Annual Research Day	June 7, 1973
Guest of Honour:	Jose A. Zadunaisky, MD, PhD, Department of Ophthalmology, Yale University, School of Medicine, New Haven, Connecticut, U.S.A.
16th Annual Research Day	June 13, 1974
Guest of Honour:	P.E. Hallet, Associate Professor, Department of Physiology, University of Toronto, Toronto, Canada
Guest of Honour:	C. Dyson, Department of Ophthalmology, University of Western Ontario, London, Ontario, Canada
17th Annual Research Day	June 12, 1975
Guest of Honour:	David H. Hubel, MD, Professor of Neurobiology, Harvard Medical School, Boston, Massachusetts, U.S.A.
18th Annual Research Day	May 27, 1976
Guest of Honour:	G.R. O'Connor, Director, Francis I. Proctor Foundation for Research in Ophthalmology, University of California, California, U.S.A.
19th Annual Research Day	May 18, 1977
20th Annual Research Day	June 9, 1978
21st Annual Research Day	May 18, 1979
Guest of Honour:	Ramesh Tripathi, MD, PhD, Professor of Ophthalmology, University of Chicago, Illinois, U.S.A.
22nd Annual Research Day	June 6, 1980
Guest of Honour:	John R. Trevithick, PhD, Department of Biochemistry, University of Western Ontario, London, Ontario, Canada

23rd Annual Research Day	June 5, 1981
Guest of Honour:	B. Jackson, Boston Biomedical Research Institute, Boston, Massachusetts, U.S.A.
1st Clement McCulloch Lecturer	Arnall Patz, MD, The Wilmer Institute, The John Hopkins University School of Medicine, Baltimore, Maryland, U.S.A. *Lecture: Clinical Application of New Studies on Retinal Neovascularization*
24th Annual Research Day	May 31, 1982
2nd Clement McCulloch Lecturer	Arthur Neufeld**,** PhD, Eye Research Institute of Retina Foundation, Harvard Medical School, Boston, Massachusetts, U.S.A *Lecture: Adrenergic Mechanisms Regulating lntraocular Pressure*
25th Annual Research Day	May 27, 1983
3rd Clement McCulloch Lecturer	Mathea Allansmith**,** Eye Research Institute of Retina Foundation, Harvard Medical School, Boston, Massachusetts, U.S.A. *Lecture: Giant Papillary Conjunctivitis*
26th Annual Research Day	May 10, 1984
4th Clement McCulloch Lecturer	Ronald F. Fisher**,** Institute of Ophthalmology, University of London, England *Lecture: The Mechanics of Accommodation in the Human Eye - Theories New and Old*
27th Annual Research Day	May 24, 1985
5th Clement McCulloch Lecturer	Richard F. Brubaker, MD, Mayo Clinic, Rochester, Minnesota, U.S.A. *Lecture: The Use of Fluorophotometry for measuring aqueous production*
28th Annual Research Day	April 4, 1986
6th Clement McCulloch Lecturer	Max Cynader, PhD, Dalhousie University, Halifax, Nova Scotia, Canada *Lecture: Neuronal Mechanisms in Experimental Amblyopia*
29th Annual Research Day	April 3, 1987
7th Clement McCulloch Lecturer	Dean Bok, PhD, Jules Stein Eye Institute, University of California, Los Angeles, California, U.S.A. *Lecture: Recent Advances in our knowledge of the visual cycle*
30th Annual Research Day	April 8, 1988
8th Clement McCulloch Lecturer	David A. Robinson, PhD, The Wilmer Institute, The John Hopkins University School of Medicine, Baltimore, Maryland, U.S.A. *Lecture: Signal Processing in the Oculomotor System*

31st Annual Research Day	April 7, 1989
9th Clement McCulloch Lecturer	Keith Green, PhD, DSc, School of Medicine, Medical College of Georgia, Augusta, Georgia, U.S.A. L*ecture: Free Radical Induced Ocular Disease*
32nd Annual Research Day	April 6, 1990
10th Clement McCulloch Lecturer	Prasanta K. Basu, MD**,** Department of Ophthalmology, University of Toronto, Toronto, Ontario, Canada *Lecture: My Research Experience at the University of Toronto Since 1955*
33rd Annual Research Day	April 5, 1991
11th Clement McCulloch Lecturer	Henk Spekreijse, PhD, Dutch Interuniversity Eye Institute, Amsterdam, Netherlands *Lecture: Ophthalmology, and the Validity of the Monkey Model of the Human Visual System*
34th Annual Research Day	April 30, 1992
12th Clement McCulloch Lecturer	Pat Stewart, Department of Anatomy, University of Toronto, Toronto, Ontario, Canada *Lecture: Blood Brain Barrier as it Relates to the Eye*
35th Annual Research Day	April 2, 1993
13th Clement McCulloch Lecturer	Helene Boisjoly, MD, MPH, Department of Ophthalmology, University of Laval, Quebec, Canada *Lecture: Corneal Transplantation - Current Research Overview*
36th Annual Research Day	June l7, 1994
14th Clement McCulloch Lecturer	Jack Rootman, MD, FRCSC, Department of Ophthalmology, University of British Columbia, British Columbia, Canada *Lecture: Is Clinical Research Relevant*
37th Annual Research Day	May 26, 1995
15th Clement McCulloch Lecturer	Clement McCulloch, MD, Department of Ophthalmology, University of Toronto, Professor and Chair, 1961-1982, Toronto, Ontario, Canada *Lecture: 50 Years*
38th Annual Research Day	June 14, 1996
16th Clement McCulloch Lecturer	David McLeod, MD, FRCS, Department of Ophthalmology, University of Manchester, Manchester, England *Lecture: Surgical Pathology of Advanced Diabetic Eye Disease*
39th Annual Research Day	May 30, 1997
17th Clement McCulloch Lecturer	Edwin M. Stone, MD, PhD, Department of Ophthalmology, The University of Iowa, Iowa, U.S.A. *Lecture: Molecular Genetics for the Ophthalmologist*

40th Annual Research Day **18th Clement McCulloch Lecturer**	May 8, 1998 Alan Bird, MD, Professor of Clinical Ophthalmology, Institute of Ophthalmology, Moorfields Eye Hospital, London, England *Lecture: ARMD; where do we go from here?*
41st Annual Research Day **19th Clement McCulloch Lecturer**	April 30, 1999 Sylvain Chemtob, MD, PhD, Department of Pediatrics & Pharmacology, Hospital Ste. Justine, Montreal, Quebec, Canada *Lecture: Retinopathy of prematurity: Mechanisms and potential therapies*
42nd Annual Research Day **20th Clement McCulloch Lecturer**	May 12, 2000 Desmond Archer, OBE FmedSci, FRCS, FROOphth, Professor of Ophthalmology, The Queen's University of Belfast, Belfast, Ireland *Lecture: Retinal New Vessels – A Brief Odyssey*
43rd Annual Research Day **21st Clement McCulloch Lecturer**	May 11, 2001 John Flannery, PhD, Department of Vision Science and Helen Wills Neuroscience Institute, University of California, Berkeley, California, U.S.A. *Lecture: Gene Therapy for Inherited Retinal Degeneration*
44th Annual Research Day **22nd Clement McCulloch Lecturer**	May 17, 2002 Mansoor Sarfarazi, PhD, Professor of Human Genetics and Scientific Director, Surgical Research Center, Molecular Ophthalmic Genetics Laboratory, University of Connecticut Health Center, Farmington, Connecticut, U.S.A. *Lecture: Impact of Molecular Genetics on Management and Diagnosis of glaucoma*
45th Annual Research Day	May 23, 2003 (Visiting Professor cancelled due to SARS)
46th Annual Research Day **23rd Clement McCulloch Lecturer**	June 4, 2004 Lawrence Tychsen, MD, Professor, Department of Ophthalmology & Visual Sciences, Washington University in St. Louis *Lecture: Causing and Curing Infantile Strabismus in Macaque Monkeys*
47th Annual Research Day **24th Clement McCulloch Lecturer**	June 2, 2005 Mark Tso, MD, Professor of Ophthalmology & Pathology, Johns Hopkins University, Baltimore, Maryland, U.S.A. *Lecture: Retinal Microglia: Novel Inflammation In Macular And Retinal Degenerations And A New Therapeutic Approach*

48th Annual Research Day **25th Clement McCulloch Lecturer**	June 9, 2006 David C Beebe, Janet & Bernard Becker Professor of Ophthalmology & Visual Sciences, Professor of Cell Biology & Physiology, Washington University School of Medicine, St Louis, Missouri, U.S.A. *Lecture: The Cause & Prevention of Nuclear Cataracts; Oxygen & The Vitreous Body*
49th Annual Research Day **26th Clement McCulloch Lecturer**	June 15, 2007 Paul Kaufman, Peter A Duehr Professor & Chair, Department of Ophthalmology & Visual Sciences, University of Wisconsin School of Medicine & Public Health, Madison, WI, U.S.A. *Lecture: Medical Therapy for Glaucoma – The next 20 Years*
50th Annual Research Day **27th Clement McCulloch Lecturer**	May 8 & 9, 2008 Alfredo A Sadun, The Flora Thornton Chair of Vision Research, Professor of Ophthalmology & Neurological Surgery, Doheny Eye Institute, USC-Keck School of Medicine, Los Angeles, CA U.S.A. *Lecture: Leber's Hereditary Optic Neuropathy & the Intracellular Time Bomb*
51st Annual Research Day **28th Clement McCulloch Lecturer**	June 11 & 12, 2009 Randy H Kardon, Professor & Director of Neuro-ophthalmology, Pomerantz Family Chair of Ophthalmology, Dept of Ophthalmology & Visual Sciences, University of Iowa & Veterans Administration Hospitals, Iowa City, Iowa, U.S.A. *Lecutre: Clinical Application of the Physiology of the Melanopsin Retinal Gnaglion Cell & Pupil Light Reflex for Diagnosing Photoreceptor Disease*
52nd Annual Research Day **29th Clement McCulloch Lecturer**	May 28, 2010 Elizabeth Engle, Professor of Neurology and Ophthalmology, Harvard Medical School, Neurology, Ophthalmology, & Medicine, Children's Hospital Boston Investigator, HHMI, Boston, U.S.A. *Lecture: Complex Strabismus and Disordered Axon Guidance*
53rd Annual Research Day **30th Clement McCulloch Lecturer**	May 27, 2011 Martin Friedlander, Professor, Dept of Cell Biology, The Scripps Research Institute, Director, Retina Services, Division of Ophthalmology, Scripps Clinic, La Jolla, CA, U.S.A. *Lecture: Progenitor Cell Based Therapies for Retinal Vascular and Degenerative Diseases*

54th Annual Research Day **31st Clement McCulloch Lecturer**	May 25, 2012 Terri L. Lewis, Professor, Department of Psychology, Neuroscience & Behaviour, McMaster University, Adjunct Professor, Department of Ophthalmology and Vision Sciences University of Toronto, Adjunct Scientist, The Hospital for Sick Children Research Institute *Lecture: Visual Development and Critical Periods Revisited*
55th Annual Research Day **32nd Clement McCulloch Lecturer**	May 31, 2013 Thomas C. Lee, Director, The Vision Center, Children's Hospital Los Angeles, Associate Professor of Ophthalmology, Keck School of Medicine, University of Southern California *Lecture: A Robert Frost Approach to Academic Ophthalmology*
56th Annual Research Day **33rd Clement McCulloch Lecturer**	May 9, 2014 Emily Chew**,** Deputy Director of the Division of Epidemiology and Clinical Applications (DECA), National Eye Institute National Institutes of Health in Bethesda, Maryland *Lecture: The Age-Related Eye Disease Study 2 (AREDS2): The Power of Randomized Controlled Clinical Trials*
57th Annual Research Day **34th Clement McCulloch Lecturer**	May 29, 2015 Dr. Sanjay Sharma, BSc, MD, MSc (Epid), MBA Professor of Ophthalmology & Epidemiology, Queen's University Editor-in-Chief, medskl.com *Lecture: The Equation: How to Innovate, Deliver Quality Care and Stay Sane in these Turbulent Times of Ophthalmic Practice*
58th Annual Research Day **35th Clement McCulloch Lecturer**	May 27, 2016 Dr. Napoleone Ferrara, MD Distinguished Adjunct Professor of Ophthalmology Senior Deputy Director for Basic Science Moores Cancer Center University of California, San Diego *Lecture: New insight into the regulation of ocular angiogenesis*
59th Annual Research Day **36th Clement McCulloch Lecturer**	May 19, 2017 Friedrich E. Kruse, MD Professor and Chairman Department of Ophthalmology Erlangen University Medical School, Erlangen Germany *Lecture: New insight in the concept of limbal stem cells for ocular surface reconstruction*
60th Annual Research Day **37th Clement McCulloch Lecturer**	May 18, 2018 Paul P. Lee, MD, JD F. Bruce Fralick Professor and Chair Department of Ophthalmology University of Michigan Medical School *Lecture: Balanced Scorecards in Eye Care*

61st Annual Research Day	May 24, 2019
38th Clement McCulloch Lecturer	Dr. Balwantray Chauhan, BSc, Ph.D., PDF Mathers Professor and Research Director Department of Ophthalmology & Visual Sciences, Department of Physiology and Biophysics, Glaucoma Research Group, Department of Medical Neuroscience Dalhousie University *Lecture: Imaging in Glaucoma: Current Possibilities and Future Expectations*
62nd Annual Research Day	May 7,14,21, & 28 2020
39th Clement McCulloch Lecturer	Peter Kertes, MD, FRCSC Professor & Ophthalmologist-in-Chief Department of Ophthalmology & Vision Sciences Sunnybrook Hospital & University of Toronto *Lecture: The CanTreat Compendium: The Many Lessons Learned from a Large Multicentre Canadian Randomized Clinical Trial*
63rd Annual Research Day	April 27th, May 4th, & 11th 2021
40th Clement McCulloch Lecturer	Jonathan Crowston, MD MSCI Clinician-Scientist and Professor of Ophthalmology, Duke-NUS Medical School, Singapore. *Lecture: Neurorecovery in retinal ganglion cells*
64th Annual Research Day	April 26th, May 3rd, & 10th 2022
41st Clement McCulloch Lecturer	Dr. Ian MacDonald MSc, MD CM Served 4 terms as Department Chair of Ophthalmology and Visual Sciences at the University of Alberta and is currently Acting-Chair and Acting Edmonton Zone Chief of Ophthalmology for Alberta Health Services *Lecture: What should I know about Ocular Gene Therapy?*

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.

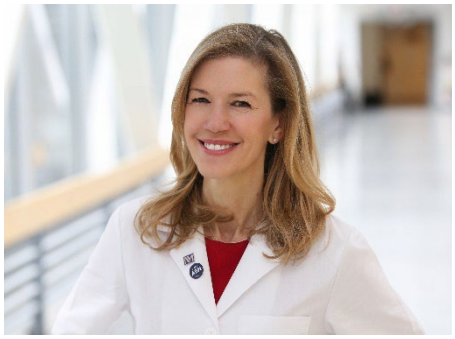
Dr. McCulloch passed away in early 2007. With this lectureship, Dr. McCulloch’s legacy will continue to live on.

42nd Clement McCulloch Lecture

(Speaker of the Royal College of Physicians and Surgeons of Canada, Region #3 Advisory Committee)

Susan Quaggin, MD, FRCP(C), FASN

Charles Horace Mayo professor of medicine at Northwestern University
Chief of the Division of Nephrology & Hypertension and Director of the Feinberg Cardiovascular and Renal Research Institute



Susan Quaggin, MD, FRCP(C), FASN, is a graduate of the University of Toronto where she completed her residency and served as chief medical resident for the University's St. Michael's Hospital. She completed her nephrology fellowship at the University of Toronto and Yale University, where she also completed research and post-doctoral training. Dr. Quaggin's research focuses on fundamental processes needed to establish and maintain the integrity of the specialized vascular beds in the kidney and eye. Translation of her group's findings regarding the vasculature reveals pathogenic mechanisms and new therapeutic targets for several diseases, including diabetic kidney and eye disease, nephrotic syndrome, and glaucoma.

Currently she is the Charles Horace Mayo professor of medicine at Northwestern University where she serves as the Chief of the Division of Nephrology & Hypertension and Director of the Feinberg Cardiovascular and Renal Research Institute. Dr. Quaggin was elected to the American Society for Clinical Investigation in 2006, the Association of American Physicians in 2013, the National Academy of Medicine in 2019, the National Academy of Inventors in 2021 and the American Academy of Arts and Sciences in 2023 and is past President of the American Society of Nephrology and councilor of the Association of American Physicians.

Her presentation will focus on **" Under Pressure: High 'TEK' Solutions for Glaucoma"**

Glaucoma is a leading cause of blindness worldwide. Primary congenital glaucoma is a severe form of the disease in children, characterized by maldevelopment of Schlemm's canal (SC). The SC develops from veins in the iridocorneal angle just after birth in mice and in late gestation in humans. Absent or hypo-morphic SC reduces outflow of aqueous humor from the anterior chamber leading to elevated intraocular pressure (IOP) and progressive loss of retinal ganglion cells (RGCs). Our group identified a key role for the Angiopoietin-Tie/TEK vascular tyrosine kinase signaling pathway in development of the SC. Loss of signaling in mice results in maldevelopment of the SC, resembling human PGC. We further showed that loss of function mutations in the genes encoding Angiopoietin 1 (*ANGPT1*) or the Angiopoietin receptor (*TEK*) cause PGC in children. Inhibition of Angiopoietin-Tie2/TEK signaling in adult non-human primates results in rapid onset of high-pressure glaucoma, suggesting this pathway is also important in maintenance of AH outflow from the eye. Using single cell analysis, we have identified additional modulators of Angiopoietin-Tie signaling that represent new candidate genes for glaucoma. Finally, activation of the Tie2/TEK receptor with an Angiopoietin-mimetic rescues the glaucoma phenotype in mice and lowers IOP in adult mice when injected intravitreally. Taken altogether, Angiopoietin-Tie/TEK signaling is able to improve SC development and outflow facility and represents an exciting candidate target to treat high pressure glaucoma.

University of Toronto
Department of Ophthalmology and Vision Sciences
Annual Research Day Winners

John Gaby Prize
(Best 1st Year Research Day Paper)

1962 George Cobb
1963 Jerome Kazdan
1964 Ian Drysdale
1965 James Miller
1966 Warren Allin
1967 David Chubb
1968 Michael Easterbrook
1969 David Anderson
1970 H. Tauzer
1971 R.F. Stevenson
1972 P. Teal
1973 Gordon T. Hand
1974 H.S. Wang
1975 Trevor Chin Fook
1976 Judy Verbeeten
1976 Aaron Goldberg
1977 Steve Arshinoff
1977 Murray Christianson
1978 Michael Motolko
1979 Jonathan Rodgers
1980 Stephen Kraft
1981 Dennis Galbraith
1981 Robert Baker
1982 Pamela Velos

John Gaby Prize
(Best Fellow Research Day Paper)

1983 T. Moore
1984 Christine Corriveau
1984 Patricia Hinton
1985 M. Tyfla
1985 Raul Garcia-Salinas
1987 Hugh McGowan
1988 Margaret Irons
1988 Heather Sheardown
1992 Elise Héon
1993 Andrew Apel
1994 Andrew Apel
1995 David Yan
1996 Alan Burnstein
1997 Craig Donaldson
1998 Hungh Ming Lee
1999 Boon Long Quah
2000 Agnes Wong
2001 Alison Duckett
2002 Jeffrey Lim
2003 Colin Willoughby
2004 Sohel Somani
2005 Juan P. Lopez
2006 David M Assaad
2007 Igor Kaiserman
2008 Paul Tesha
2009 Fiolmento Cortese
Delan Jinapriya
2010 Darana Yuen
2011 Sana Muhsen
2012 Alejandro Lichtinger
2013 Roxane Hillier
2014 Johanna Gonzalez-Rodriguez
2015 Talal Alabduljalil
2016 Yael Chavez
2017 Alaa Al Ali
2018 Avner Belkin
2019 Sameh Soliman
2020 Riddhi Dharia
2021 Wei Wei Lei
2022 Bryon R. McKay

Alumni Award
(Best Resident Annual Research Day Paper)

1974 Brenda Gallie
1975 Wing Chan
1976 Gerald Goldlist
1977 Heinz Smirmaul
1978 Gerald Walman
1979 Steve Arshinoff
1980 Michael Motolko
1981 Emily Chew
1982 Patricia Harvey
1983 Dennis Galbraith
1984 Mary Lou Jackson
1985 Patricia Hinton
1986 Raul Garcia-Salinas
1987 Robert Devenyi
1988 Blair Fearon
1989 Jeff Machat
1990 Tom Klein
1992 Edsel Ing
1993 Jill Hopkins
1994 Jonathan Heston
1995 David Yan
1996 David Yan
1997 Agnes Wong
1998 David Lane
1999 David Weinstock
2000 Iqbhal Ahmed
2001 Eric Tam
2002 Arthur Sit
2003 Kylen McReelis
2004 Marisa Sit
2005 Rajeev Muni
2006 Feisal A Adatia
2007 Efrem Mandelcorn
2008 Jason Noble
2009 Matthew C Bujak
2010 Stephen J Dorrepaal
2011 Carla Lutchman
2012 Talal Alabduljalil
2013 Matthew B. Schlenker
2014 Hannah Chiu
2015 Panos Christakis
2016 Victoria Leung
2017 Stephanie Low
2018 Brian Ballios
2019 Brian Ballios
2020 Marko Popovic
2021 Austin Pereira
2022 Marko Popovic

Best 2nd Year Resident Award

1993-94 Stephen De Souza
1994-95 Sanpatna Rutnin

Best Student Annual Research Day Paper

1995 Tara Young
1996 John Janevski
1997 David DiCiommo
1998 Rachel Panton
1999 Kim Dorval
2000 Irina Burcescu
2001 Chloe Gottieb
2002 David Taylor
2003 Tim Corson
2004 Jacky Yeung
2005 Maryam Fesharaki
2006 Michael Richards
2007 Michael Richards
2008 Matthew Schlenker
2009 Kim Le
2010 Kay Lam
2011 Alex Tam
Ewa Niechwiej-Szwedo
2012 Natalie Pankova
2013 Krista R. Kelly
2014 Yelin Yang
2015 Michael Mak
2016 Alex Lai Chi Tam
2017 Shicheng Tony Jin
2018 Tina Felfeli
2019 Saba Samet
2020 John Liu
2021 Prem Nichani
2022 Michael Balas

Best VSRP Annual Research Day Paper

2001 Kim Dorval
2002 Tara Young
2003 Ted Erclik
2004 Nima Noordeh
2005 Slobodan Beronja
2006 Slobodan Beronja
2007 Marek Pacal
2008 Marek Pacal
2009 Ekta Lakhani
2010 Loksum Wong
2011 Calvin Mok
2012 Rana Arham Raashid
2013 Emily Mathieu
2014 Emily Mathieu
2015 Emily Mathieu
2016 Michael Richards
2017 Shireen Khattak

Best Annual Research Day Poster

2003 Adrian Fawcett
2004 Ishtiaq Ahmed
2005 Pieter Gouws
2006 Raquel Heskin
2007 Giuseppe Mirabella
2008 Michael Smith
2009 Loksum Wong
2010 Rachel Leeder
2011 Daniel Rootman
2012 Rachel Leeder
2013 Ken Olsen
2014 Lee-Anne Khuu
2015 Nevena Vicic
2016 Jonathan A. Micieli
2017 Yael Chavez
2018 Austin Pereira
2019 Matthew-Mina Reyad
2020 NA
2021 Jovi Wong
2022 Tina Felfeli

Dr. Martin J. Steinbach Research Award

2018 Runjie Bill Shi
2019 Nicole Yan
2020 Ajay David
2021 James Dunbar
2022 Runjie Bill Shi

65th Annual Research Day

and

42nd Clement McCulloch Lecture

and

Dr. Martin J. Steinbach Lecture

Program

65th Annual Ophthalmology Research Day
and
42nd Clement McCulloch Lecture
and
Dr. Martin J. Steinbach Lecture
Department of Ophthalmology and Vision Sciences
SickKids Peter Gilgan Centre for Research and Learning

Friday, May 26th, 2023 (7:30 am – 4:00 pm)

PROGRAM

7:30-8:00 **Continental Breakfast**

8:00-8:05 **Department Chair's Welcome**
Dr. Sherif El-Defrawy

8:05-8:10 **Annual Ophthalmology Research Day Chair Welcome**
Dr. Matthew Schlenker

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

8:10 -9:29 AM **Session moderator: Dr. David Wong**
Format: **8 - 10 min. Presentation + 2-4 min. Discussion**

8:10-8:24	Red Reflex Screening Reimagined: Empowering Early Retinoblastoma Detection.	Ashwin Mallipatna (Faculty)
8:25-8:39	A comparison between notched Iodine-125 plaque brachytherapy and external beam radiotherapy in the management of juxtapapillary choroidal melanoma *Supervisor: Hatem Krema*	Adwaita Nag (F)
8:40-8:50	Mapping Choroidal and Retinal Thickness in a Mouse Model of Spaceflight-Associated Neuro-ocular Syndrome *Supervisor: Yeni Yücel*	Arya Zarrinbakhsh (VS)
8:50-9:00	A Population-Based Analysis of Long-Term Costs, Re-attachment Rate and Adverse Events Following Pneumatic Retinopexy and Pars Plana Vitrectomy *Supervisor: Donald A. Redelmeier & Rajeev Muni*	Marko Popovic (R)
9:00-914	Investigating Adeno-Associated Virus (AAV) Transduction Efficiency in Human Corneal Endothelial Cells as a Treatment for Fuchs Endothelial Corneal Dystrophy *Supervisor: Stephan Ong Tone*	Ness Little (U)
9:15-9:29	Early Pressure-Induced Response in ex-vivo Organotypic Human Eyes *Supervisor: Jeremy M Sivak*	Jenny Zhang (VS)

9:30 - 10:30 AM

COFFEE BREAK
+
POSTER SESSION

Even numbered posters are judged

10:30-12:00 PM **BREAK ROOM SESSIONS**
Format: **12 - 15 min. Presentation + 2-6 min. Discussion**

BASIC SCIENCE - **Moderator: Dr. Jeremy Sivak**

10:30-10:51	Rescuing Cone Photoreceptor Death With the Sustained Release of RdCVF from a Biocompatible Hydrogel *Supervisor: Molly Shoichet*	Lia Huo (VS)
10:53-11:14	A human chimeric retinal organoid model for studying donor-host cell interactions in cell therapies of inherited retinal disease. *Supervisor: Brian Ballios*	Cassandra D'Amata (U)
11:16-11:37	Functional analysis of axon guidance programs in developmental and therapeutic photoreceptor connectivity *Supervisor: Valerie A. Wallace*	Victor Q.B. Pham Truong (VS)
11:39-12:00	Retinal cell differentiation and maturation is controlled by glycolytic flux *Supervisor: Carol Schuurmans*	Joseph Hanna (VS)

RETINA - **Session moderator:** Brian Ballios

10:30-10:51	The Association of Outer Retinal Morphologic Stage and Postoperative Visual Acuity in Fovea-Involving Rhegmatogenous Retinal Detachment *Supervisor: Rajeev H. Muni*	Isabela Martins Melo (RF)
10:53-11:14	Posterior Hyaloid Discontinuity on Optical Coherence Tomography in Patients with Vitreomacular Traction and Posterior Vitreous Detachment: A Retrospective Cross-Sectional Study *Supervisor: David T. Wong*	Grace Yin (M)
11:16-11:37	Reattachment Rate with Pneumatic Retinopexy for Rhegmatogenous Retinal Detachment with a Single Break in Detached Retina *Supervisor: Rajeev H. Muni*	Aurora Pecaku (RF)
11:39-12:00	Association between Magnitude of Retinal Displacement and Functional Outcomes Following rhegmatogenous Retinal Detachment Repair *Supervisor: Rajeev H. Muni*	Reut Shor (RF)

EPIDEMIOLOGY - **Session moderator: Dr. Matthew Schlenker**

10:30-10:51	Conversational AI Models for Ophthalmic Diagnosis: Comparison of ChatGPT and the Isabel Pro Differential Diagnosis Generator *Supervisor: Edsel B. Ing*	Michael Balas (M)
10:53-11:14	Presenting Characteristics and Healthcare Utilization of Patients Diagnosed with Functional Vision Loss *Supervisor: Edward Margolin*	Irina Sverdlichenko (M)
11:16-11:37	The Association Between Sociodemographic, Clinical Access, and Regional Factors with Vision Difficulty *Supervisor: Radha P. Kohly*	Lana Moayad (M)
11:39-12:00	Delisted routine eye exams and the increased use of family physicians and ophthalmologists for glaucoma diagnosis *Supervisor: Ya-Ping Jin*	Wongel Bogale (VS)

12:00 - 1:00 PM

LUNCH
+
POSTER SESSION

Odd numbered posters are judged

1:00-1:10 **Introduction to Dr. Susan E. Quaggin**
The 42nd Clement McCulloch Lecturer: Dr. Matthew Schlenker

1:10-2:10 **The 42nd Clement McCulloch Lecture:**
Under Pressure: High 'TEK' Solutions for Glaucoma

2:10 - 3:00 PM

COFFEE BREAK
+
POSTER SESSION

All remaining posters are judged

3:00-4:00 PM	**Session moderator: Dr. Kamiar Mireskandari**
Format:	**8 - 10 min. Presentation + 2-4 min. Discussion**

3:00-3:14	The TALON study: Balancing durability with risk	Peter Kertes (Faculty)
3:15-3:25	Quantitative Mapping of Uveoscleral and Lymphatic Drainage Pathways From the Suprachoroidal Space *Supervisor: Yeni H Yucel*	Babishaa Sauntharrajan (U)
3:26-3:36	Choroidal hypoperfusion and reduced retinal function in retinopathy of prematurity – a collaborative tale of two cities. *Supervisor: Kamiar Mireskandari*	Tianwei Ellen Zhou (R)
3:37-3:47	Primary Iris Claw Intraocular Lens Implantation in Children *Supervisor: Asim Ali*	Caludia Castro (CF)
3:48-3:58	Novel Ultrafast Visual Field Testing with The Toronto Portable Perimeter (TPP) *Supervisor: Willy Wong*	Runjie (Bill) Shi (VS)

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

4:00 – 5:00

POSTER SESSION

5:00	**Meeting Adjourned**

* 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. *

POSTERS (Total of 63)

1. **Amina Adama (VS)**
   Identification of an LXB4 Transcriptional Response in Neuroprotective Signalling

2. **Louis Abraham Batalla Zavala (F)**
   Brillouin Spectroscopy for Corneal Biomechanics on Glaucoma patients

3. **Panagiota Antonopoulou (F)**
   Gonioscopy-Assisted Transluminal Trabeculotomy in the Management of Paediatric Glaucoma

4. **Kristen Ashworth (VS)**
   Establishing a model of USH2A-associated retinitis pigmentosa using 3D human retinal organoids

5. **Yewande Babalola (F)**
   Clinical profile and outcomes of endophthalmitis in children and adolescents

6. **Abed Baiad (M)**
   A meta-analysis of neurodevelopmental outcomes following intravitreal bevacizumab for the treatment of retinopathy of prematurity

7. **Michael Balas (M)**
   Adaptive Optics Imaging in Diabetic Retinopathy: A Prospective Cohort Study

8. **Michael Balas (M)**
   Oculoplastic Procedures: Use of Text-To-Image AI Models for Pre-Operative Counseling

9. **Mostafa Bondok (M)**
   Accessibility of Canadian ophthalmology department webpages for the visually impaired

10. **Hillary Chan (M)**
    Optic disc appearance in arteritic compared to non-arteritic anterior ischemic optic neuropathy

11. **Hillary Chan (M)**
    Bilateral sequential vision loss from giant cell arteritis with persistently low inflammatory markers

12. **Kelvin Chau**
    Development of 3D Printed Eye Models with Normal and Abnormal Red Reflexes

POSTERS (Continued)

13. Lina Chen (RF)
Decreased cone density in circular retinal regions at the outer edge of full thickness macular hole edema in adaptive optics imaging

14. Milena Cioana (M)
Postoperative dry eye symptoms and secondary healthcare utilization in patients prior to, during, and after the COVID-19 pandemic

15. Milena Cioana (M)
Post-procedural endophthalmitis visual outcomes by microorganism: A systematic review and meta-analysis

16. Aditya Damani
Computerized Simulation of Retinoblastoma Treatment Using Focused Ultrasound

17. Fowad Daud
Combined versus Sequential Pars Plana Vitrectomy and Phacoemulsification for Macular Hole and Epiretinal Membrane - A Systematic Review and Meta-Analysis

18. Narisa Dhupar (G)
Validation of Preloaded DMEK Donor Tissues: A Laboratory Based Study on Endothelial Cell Viability

19. Tina Felfeli (R)
Anatomical and Functional Outcomes of Short-Term DensironXTRA Heavy Silicone Oil for Rhegmatogenous Retinal Detachments: A Comparative Case Series

20. Victoria Romero Fresno (F)
GCC changes in wet AMD patients treated with intravitreal injection according to treat and extend protocol in comparison to non-treated dry AMD.

21. Justin Grad (M)
Surgical drainage methods during pars plana vitrectomy for rhegmatogenous retinal detachment: a meta-analysis

22. Alicia Harracksingh (VS)
Functional characterization of optic phototaxis behaviours in lymnaea stagnalis- A new in vivo model for visual phototransduction

23. Amin Hatamnejad (U)
Combined anti-vascular endothelial growth factor and steroid treatment compared with standalone anti-vascular endothelial growth factor treatment for macular edema secondary to retinal vein occlusion: a meta-analysis

POSTERS (Continued)

24. Amin Hatamnejad (U)
Efficacy and safety of anti-vascular endothelial growth agents for the treatment of polypoidal choroidal vasculopathy: a systematic review and meta-analysis

25. Maggie Mengjia Huang (VS)
SNAP-25 but not SNAP-23 is essential for photoreceptor function and survival in mice

26. Omer Jamal (VS)
Quantifying the Availability of Social Determinants of Health Data in the Electronic Health Record of Pediatric Ophthalmology Patients

27. Stephanie Jarvi (M)
Human Placental Tissue and Cell derived HLA-G+ Extracellular Vesicles for the Treatment of Corneal Injury and Corneal Transplant Rejection

28. Aaditeya Jhaveri (M)
Outer Retinal Hyperreflective Dots, A Potential Biomarker In Rhegmatogenous Retinal Detachment

29. Aaditeya Jhaveri (M)
Systemic Arterial and Venous Occlusions Associated with Anti-VEGF Injections: A Meta-Analysis

30. Aaditeya Jhaveri (M)
Optical coherence tomography biomarkers as potential predictors for visual function and response to intravitreal therapy in diabetic macular edema: a review

31. Jeeventh Kaur (M)
The impact of eyewear insurance coverage on utilization of eye care providers in a publicly funded healthcare system

32. Farheen Khan (VS)
Evaluation and Adaptation of the FACE-Q Patient-Reported Outcome Measure for Ophthalmology Patients

33. Farbod Khorrami (G)
Amyotrophic Lateral Sclerosis Mice Eyes Reveal Retinal Nerve Fiber Layer Changes Over Time: An *In Vivo* Imaging Study

34. Yaroslav Kravchenko
Analysis of the Electroretinogram with Machine Learning to Identify Patients with Retinal Disease

POSTERS (Continued)

35. Rebecca Lena (M)
Evaluation of Pars Plana Vitrectomy with and without Supplemental Scleral Buckle for the Repair of hegmatogenous Detachment due to Inferior Retinal Breaks: A Systematic Review

36. Yan Li (VS)
A data-driven model for simulating longitudinal visual field tests in glaucoma

37. Hedy Liu (G)
Combinatorial expression of the proneural genes Ascl1 and Neurogenin2 restricts retinal progenitor cells to an amacrine cell fate

38. Andrew Mihalache
Pars plana vitrectomy with or without internal limiting membrane peel for macular hole and epiretinal membrane: a systematic review and meta-analysis

39. Andrew Mihalache
Performance of an Artificial Intelligence Chatbot for Ophthalmic Knowledge Assessment: a Cross-Sectional Study

40. Sumana Naidu (M)
Disparities in Cataract Surgical Training at Kensington Eye Institute Based on Sex and Medical Graduate Type

41. Sumana C. Naidu (M)
Gender-Based Disparities in OR Resources, Cataract and Teaching Volumes at the University of Toronto's Eye Institute

42. Georges Nassrallah (F)
An Orbital Differential Diagnosis Spreadsheet

43. Jia Ng (U)
Grading System for Choroidal Effusion Following Glaucoma Surgery Using Fundus Photographs

44. Alexandra Nitoiu (VS)
Biallelic Variants in IFT57 May Cause BBS-like Ciliopathy with Retinal Dystrophy

45. Samantha Orr (RF)
Utilization of Enface OCT and Deep Learning-Based Automated Segmentation to Quantify Area of GA: ECLIPSE study

POSTERS (Continued)

46. Samantha Orr (RF)
Novel Features of Degenerative Retinoschisis Identified Using Ultra-Widefield Multicolor Channels: A Review of 139 Eyes

47. Rahma Osman (U)
Optical Properties, Dimensions, and Pigment Concentrations in the Pediatric Eye: A Scoping Review

48. Alissa Pak (U)
Deciphering the role of Pten in maintaining Müller glia in quiescence in the mouse retina

49. Bhadra Pandya (M)
The Causes of Optic Disc Edema in Patients Presenting with Significantly Compromised Vision: A Retrospective Study

50. Bhadra Pandya (M)
The Use of Preoperative Visual Acuity Thresholds in Pars Plana Vitrectomy for Epiretinal Membrane: A Systematic Review

51. Paula Pietraszkiewicz (VS)
Tracing connections of the inner retina to identify circuits resilient to photoreceptor degeneration

52. Kavin Selvan (VS)
Validation of patient-reported outcome measures in adolescent patients with Inherited Retinal Diseases

53. Irina Sverdlichenko (M)
Anemia and Idiopathic Intracranial Hypertension: a Prospective Study

54. Irina Sverdlichenko (M)
Antivirals versus antivirals and steroids for treatment of Herpes-Zoster related ophthalmoplegia: A case series and systematic review

55. Irina Sverdlichenko (M)
Yield of Investigations in Young Patients Presenting with Transient Monocular Vision Loss

56. Michal Syonov (VS)
A dual role for the RGMc protein in retinal angiogenesis

POSTERS (Continued)

57. Carter Teal (VS)
Directed Evolution Enables Simultaneous Controlled Release of Multiple Therapeutic Proteins from Biopolymer-Based Hydrogels

58. Priscilla Valentino (VS)
Characterization of Spalt, the Drosophila homolog of the vertebrate SALL genes, in the developing fly visual system

59. Charbel Wahab (F)
Applications of Artificial Intelligence for Diabetic Retinopathy Screening: An analysis of the Toronto Tele-Retinal Screening Program.

60. Charbel Wahab (F)
Acquired focal choroidal excavation secondary to pachychoroid choroidal neovascular membrane following central serous chorioretinopathy.

61. Judy Yan (RF)
Investigating the role of epithelial to mesenchymal transition (EMT) regulators TCF4 and TGF-β in Fuchs endothelial corneal dystrophy

62. Grace Yin (M)
A Systematic Review of Toxicities of Densiron-68 in the Surgical Management of Retinal Detachment

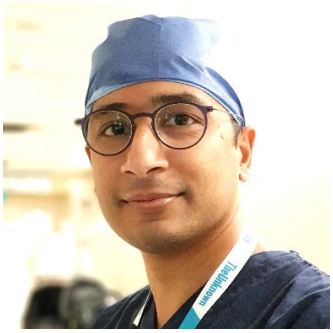
63. Chris Zajner (M)
Relationship between Disease and Treatment Factors in Diabetes Mellitus with Vision Difficulty in the National Health Interview Survey: A Cross-sectional, Population-Based Analysis

ABSTRACTS FOR ORAL PRESENTATIONS

Ashwin Mallipatna | Faculty Speaker | Time: 8:10 - 8:24

Red Reflex Screening Reimagined: Empowering Early Retinoblastoma Detection

Abstract:
The early detection of retinoblastoma and childhood blindness poses significant challenges. While red-reflex screening is the conventional method for early detection, this presentation starts by addressing its limitations in low-resource contexts. We examine the use of compact digital cameras for red-reflex screening, including their ability to detect abnormalities in children and the implementation of a training program for community health workers in Rural South India.
We start being comparing the results of red-reflex screening using a direct ophthalmoscope (DO) and a compact digital camera in a study conducted in Bangalore, India, to demonstrate that cameras have a high sensitivity for detecting “severe” abnormalities relative to DO (87.5%). However, sensitivity was reduced (36.6%) for less apparent abnormalities. In healthy eyes, we also encountered instances of pseudo-leukocoria and pseudo-loss of red reflex, highlighting the need for cautious interpretation.
Based on these findings, we devised and pilot-tested a training program for community health workers in rural and urban India to use compact digital cameras for red-reflex screening of preschool children. In addition, we compared standard red-reflex testing to instrument-based infrared photo screeners for detecting amblyogenic refractive errors and vision-threatening ocular abnormalities in preschool children.
This presentation concludes by discussing the challenge of detecting retinoblastoma through red-reflex screening alone, highlighting the significance of carer awareness regarding leukocoria or strabismus. In addition, we investigate the rationale for and initial efforts toward reforming the pedagogy of red reflexes in medical school curricula. This research can potentially improve the early detection and treatment of childhood blindness and retinoblastoma, particularly in settings with limited resources.



Short Bio:
Dr. Mallipatna is a pediatric ophthalmologist specializing in retinoblastoma. He completed his fellowship at the Hospital for Sick Children in Toronto, Canada in 2009 and was honored as the Student Humanitarian of the Year during his training. Motivated by a desire to improve care for underserved populations, he established a retinoblastoma service in India, gaining recognition as an international expert in the field.
Dr. Mallipatna's research on the use of periocular Topotecan received recognition from F1000Prime for its potential in advancing retinoblastoma management. Collaborating with researchers from various institutions, including Université de Montréal, the University of Toronto, and the University of Adelaide, he contributed to the early detection of retinoblastoma using camera flash red-reflex, earning prestigious accolades such as the Massachusetts Institute of Technology's Young Innovators Award in India.
To address the needs of patients in resource-limited settings, Dr. Mallipatna co-founded Iksha Foundation, an NGO dedicated to supporting retinoblastoma care across multiple cities in India. His involvement with the American Joint Committee on Cancer (AJCC) in developing retinoblastoma staging has significantly influenced international treatment protocols, leading to more evidence-based approaches. The AJCC recognized his substantial and lasting contributions to the 8th Edition of the AJCC Cancer Staging Manual.
In 2020, Dr. Mallipatna returned to Toronto as an Assistant Professor at the University of Toronto, where he is now the Head of the Retinoblastoma Program at the Hospital for Sick Children, continuing the teams commitment to providing the best possible care for children with retinoblastoma.

A comparison between notched Iodine-125 plaque brachytherapy and external beam radiotherapy in the management of juxtapapillary choroidal melanoma

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   University of Toronto, Toronto, Ontario, Canada
2. Filiberto Altomare MD, FRCS(C)
   Ocular Oncology Service, Department of Ophthalmology and Visual Sciences
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3. Beiki-Ardakani Akbar Ph.D
   Department of Radiation Medicine
   University of Toronto, Toronto, Ontario, Canada
4. Normand Laperriere MD, FRCPC
   Department of Radiation Oncology
   University of Toronto, Toronto, Ontario, Canada
5. Hatem Krema MD, FRCS(C)
   Ocular Oncology Service, Department of Ophthalmology and Visual Sciences
   University of Toronto, Toronto, Ontario, Canada

Type of research/ Category: Clinical research/ Ocular Oncology
Financial interests: NIL
Conflicts of interest: NIL

Introduction: Conventionally, juxtapapillary choroidal melanomas (JPCM) were treated with External Beam Radiotherapy (EBRT). Brachytherapy using standard round episcleral plaques does not provide adequate radiation coverage of juxtapapillary tumors since the orbital part of the optic nerve poses a physical hindrance for correct plaque placement. The advent of notched plaques enabled the treatment of JPCM. Herein, we compare the treatment efficacy and radiation complications between notched Iodine-125 plaque brachytherapy and Photon EBRT in the management of JPCM.

Methods: We retrospectively reviewed consecutive patients with JPCM who were treated with radiotherapy from January 2016 to December 2020. Eyes in which the posterior edge of the choroidal melanoma was touching, encircling, overhanging, or within 2mm of the optic disc were included. Patients were divided into two cohorts: brachytherapy (A) and Photon EBRT (B). Group A was treated with Iodine-125 plaque delivering 8500 centigray (cGy) to the tumor apex at a mean dose rate of 50 cGy/h. Group B was treated with 5000 cGy to the tumor apex in 5 fractions. Outcome measures were local tumor control, radiation complications, globe salvage, metastasis-free survival, and final visual acuity.

Results: 84 eyes were included in group A and 37 eyes were included in group B. On comparing the pre-treatment clinical data and tumor characteristics, there were no statistically significant differences between groups A and B. The median follow-up periods were 38.7 months and 38.17 months in groups A and B respectively. The actuarial rates of local tumor control, globe salvage, and metastasis-free survival in the two groups at 1 year, 3 years, and 5 years are depicted in table 1. Radiation complications in groups A and B included cataracts in 17.3% and 57.7%, radiation retinopathy in 42% and 63.3%, radiation papillopathy in 7.4% and 46.7%, vitreous hemorrhage in 6.2% and 20%, and neovascular glaucoma in 6.2% and 53.3% respectively. Final visual acuity equal to or less than 20/200 (including enucleated eyes) was noted in 48.1% of eyes in group A and 93.3% of eyes in group B.

Conclusion: Both iodine-125 plaque brachytherapy and Photon EBRT have similar efficacy in local control of JPCM. However, brachytherapy has significantly lower rates of secondary enucleation, lesser radiation complications, and better final visual acuity as compared to stereotactic radiotherapy, leading to increased patient comfort and acceptance. Despite being surgically challenging, notched plaque brachytherapy provides a significantly better outcome in the treatment of JPCM.

Mapping Choroidal and Retinal Thickness in a Mouse Model of Spaceflight-Associated Neuro-ocular Syndrome

Arya Zarrinbakhsh[1,2], Haaris M. Khan[1,7,8], Shuo Chen[9], Xun Zhou[1,3], You Liang[10], Mirza F. Beg[9], Eduardo V. Navajas[8], Neeru Gupta[1-3,6,8], Yeni Yücel[1-5]

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[7] School of Population and Public Health, Faculty of Medicine, University of British Columbia
[8] Department of Ophthalmology and Visual Sciences, Faculty of Medicine, University of British Columbia
[9] School of Engineering Science, Faculty of Applied Sciences, Simon Fraser University
[10] Department of Mathematics, Faculty of Science, Toronto Metropolitan University

Type of research: Basic research
Category: Retina

Introduction: Spaceflight is increasingly being democratized, making astronaut health concerns and space medicine a public affair. Spaceflight-Associated Neuro-ocular Syndrome (SANS) is a major risk of long-duration spaceflight affecting almost half of astronauts within a month. Increased choroidal and retinal thicknesses (CT and RT) are hallmark findings of SANS, yet the etiology remains unknown. Our lab previously described that CSF flows into the optic nerve in a glial-cell-dependent manner. We hypothesized that microgravity-induced fluid shifts involving this pathway and others may increase CT and RT. With no established animal model of SANS, we performed a longitudinal experimental study to test the ocular effects of hindlimb unloading (HU), a mouse microgravity analog. We also developed a novel machine-learning-based CT and RT measurement pipeline.

Methods: An HU protocol was developed in which mice were suspended from the tail at approximately 30º for 21 days. Ten 8-month-old male B6(Cg)-Tyrc-2J/J albino mice were randomly categorized into control ($n = 4$) and HU ($n = 6$) groups. Serial *in vivo* enhanced depth imaging optical coherence tomography (EDI-OCT; Spectralis, Heidelberg Engineering) of the eyes was performed before suspension (day 0), and during suspension (days 8, 14 and 21) to evaluate CT and RT. Body weight measurements were performed concurrently. Control mice were not suspended and underwent the same data acquisition protocol. Retinal and choroidal boundaries were manually marked on EDI-OCT B-scans to train a deep neural network for automatic segmentation. Segmented EDI-OCT B-scans were then further corrected by masked trained experts. CT and RT were calculated using a *k*-nearest neighbours algorithm and interpolated between B-scans for the left eyes. Linear mixed models were used to longitudinally analyze sectoral and total thickness changes in control and HU groups.

Results: Mixed model regression revealed choroidal thickening in the inner nasal ($p < 0.0001$), inner temporal ($p < 0.0001$), inner inferior ($p = 0.025$), outer temporal ($p = 0.025$) and outer inferior ($p = 0.035$) sectors, driving total choroidal thickening ($p = 0.0003$) during suspension. No significant choroidal thickness changes were observed in the remaining eye sectors during suspension. No significant retinal thickness changes were observed in any sector during suspension ($p > 0.05$).

Conclusion: In a mouse model mimicking microgravity conditions, automatic choroidal and retinal segmentation showed choroidal but not retinal thickening. These findings may be relevant to understanding the mechanisms underlying visual distrubances due to SANS seen in astronauts.

Acknowledgement: We acknowledge the support of the Canadian Space Agency [19HLSRM02] (YHY, NG), the Henry Farrugia Research Fund (YY), the Canadian Foundation for Innovation Leaders Opportunity Fund [31326] (YY), the Dorothy Pitts Chair of Ophthalmology and Vision Sciences (NG), the Natural Science and Engineering Research Council of Canada – Canada Graduate Scholarships (AZ), and the Vision Science Research Program Award (AZ).

Marko Popovic | Resident | Time: 8:50 - 9:00

A Population-Based Analysis of Long-Term Costs, Re-attachment Rate and Adverse Events Following Pneumatic Retinopexy and Pars Plana Vitrectomy

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Conflicts of Interest: MMP: Financial support (to institution) – PSI Foundation, Fighting Blindness Canada. PJK: Advisory board – Novartis, Alcon, Bayer, Roche, Novelty Nobility; Financial support (to institution) – Bayer, RegenXBio, Roche, Novartis; Financial support – Novartis, Bayer; Equity owner – ArcticDx. RHM: Advisory board- Alcon, Bausch + Lomb, Bayer, Novartis, Allergan, Roche; Financial Support (to institution)- Bayer, Novartis, Roche. RPK: Financial Support (to institution) – Bayer, Novartis.

Introduction: Rhegmatogenous retinal detachment is an ocular emergency that can be treated with pneumatic retinopexy (PnR) or pars plana vitrectomy (PPV). The objective of this study was to examine the cost effectiveness, re-attachment rate, and complications of PnR compared to PPV using a comprehensive analysis within a universal healthcare system.

Research Type/ Category: Cohort Study/ Retina

Methods: In this retrospective, population-based, multi-center, consecutive, longitudinal cohort study, we identified consecutive adults aged 50 and older requiring surgery for primary rhegmatogenous retinal detachment over a 20-year interval between April 1, 2002 and March 31, 2022. The date of initial surgery was considered the index date for analyses. The primary analysis investigated the mean annualized healthcare costs comparing PnR to PPV patients over the two years following initial surgery. Secondary analyses examined the primary reattachment rate and other possible complications comparing PnR to PPV using logistic regression.

Results: In total, 28,162 eligible patients were identified, with 8,794 undergoing PnR and 16,871 undergoing PPV. The mean patient age was 65 years and 39% were women. The mean annualized costs after PnR was $8,924 CAD and $11,937 CAD after PPV (mean difference: $3,013, 95% confidence interval [CI]: $2,533 to $3,493, $p<0.001$). The primary reattachment rate at 90 days for PnR was 83% and for PPV was 93% (62% relative reduction in odds, 95% confidence interval [CI]: 59% to 65%, $p<0.001$). There was a lower risk of subsequent cataract and glaucoma surgery following PnR, and a higher risk of subsequent ophthalmology clinic visits, intravitreal injections and diagnoses of anxiety. Total hospitalizations and long-term disability were less frequent after PnR surgery.

Conclusions: In this cohort study, PnR compared to PPV surgery was associated with lower long-term healthcare costs. These findings can be considered for treatment decision-making in patients with retinal detachment.

Investigating Adeno-Associated Virus (AAV) Transduction Efficiency in Human Corneal Endothelial Cells as a Treatment for Fuchs Endothelial Corneal Dystrophy

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Genome editing in the eye provides therapeutic advantages including accessibility and immunoprivilege. AAVs offer advantages to other viral vectors as they induce a mild immune response, remain primarily episomal after transduction, avoiding random integration into the host genome, and are already in human clinical trials for the treatment of ocular diseases. However, limited studies have explored AAV as a delivery tool to the human corneal endothelium (CE). Gene transfer to the CE has many potential applications, including the treatment of Fuchs endothelial corneal dystrophy (FECD). The most common genetic mutation in FECD is a trinucleotide CTG repeat expansion in the third intron of the transcription factor 4 (TCF4) gene, making it a compelling candidate for gene therapy.

Purpose: This study aims to screen and optimize AAV transduction efficiency with different serotypes in human corneal endothelial cells (CECs) derived from normal donor and FECD specimens.

Study Design: Laboratory-based investigation.

Methods: Seventeen different AAV serotypes (AAV2/-1, -2, -4, -5, -6, -7, -8, -9, -Rh10, -DJ, -DJ8, -Retro, -phpB, -phpeB, -phpS, -phpN, -phpV1) with different multiplicity of infection (MOI) and incubation times were tested to maximize transduction and minimizing vector toxicity in normal CECs. AAV serotypes expressing GFP under the CAG promoter were screened using an MOI of 100 000 and 200 000 for each serotype. Cells were monitored for GFP expression using the IncuCyte S3 Live-Cell Analysis System. Images were acquired at a 20x magnification every 6 hours. Cells were fixed on day 4 with paraformaldehyde and counterstained with propidium iodide. GFP positive cells and total nuclei were quantified from 2 to 4 representative images. The top 4 AAV serotypes were selected to undergo further validation in 2 FECD cell lines and ex-vivo specimens.

Results: We observed the highest transduction efficiency with AAV2/-2,-5,-6,-DJ in normal CECs. We validated that AAV transduction efficiency with AAV2/-2,-5,-6,-DJ was still high in 2 FECD cell lines, FECD 54F and 61M. The highest transduction efficiency was observed with AAV2/-2 in FECD CECs, with an average transduction efficiency of 40.00%$\pm$24.88 in the 54F cell line (n=4) and 55.94%$\pm$9.70 in the 61M cell line (n=4). Similarly, AAV2/-2 showed the highest transduction efficiency, 41.47%$\pm$12.10, in normal ex-vivo corneas (n=2).

Conclusions: AAVs can transduce both normal and FECD CECs, where highest efficiency is observed with AAV2-/2. AAV could be further engineered to maximize transduction efficiency with the eventual goal of delivering genetic material to CECs as gene therapy.

Early Pressure-Induced Response in ex-vivo Organotypic Human Eyes

JW Zhang[1,3], D Chan[1,2], K Wigg[1], S Lively[1], P Portla[4], J Sivak[1,2,3].

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Financial or conflict of interest: non for all authors
Research Type: Glaucoma, basic research

Introduction: Glaucoma is a neurodegenerative disease characterized by progressive loss of retinal ganglion cells (RGCs) and axons of the optic nerve, prominently associated with increased intraocular pressure (IOP). The optic nerve head (ONH) is a glia-rich region that is considered the initial site of injury from elevated IOP. Early changes in the human eye following elevated IOP remain elusive due to the unique biomechanical properties of human eye. We generated a new model of acute IOP elevation based on a recently characterized organotypic human eye perfusion approach. This system enables us to study the initial response of the human eye *ex vivo* to pathologically relevant pressure insult. We hypothesize that elevated IOP will induce changes relevant to human glaucoma pathogenesis in our model.

Methods: Freshly donated human eyes were immersed in an optimized culture medium to preserve ocular tissue health. Fluid dynamic was restored in the eyes by infusion of synthetic aqueous humor into the anterior chamber over 6 hours. For each pair of eyes, one maintained a physiological IOP, and the contralateral eye maintained an elevated IOP. RGC survival, glial activation, and actin orientation were assessed in five pairs of perfused eyes using TUNEL assay, immunofluorescent staining, and phalloidin staining. Paired student's t-tests were used for statistical analysis. To examine the initial molecular changes in the ONH following IOP elevation, dissected ONH from four pairs of perfused eyes underwent mRNA sequencing on the Illumina platform, and results were analyzed bioinformatically.

Results: Whole-globe human eyes maintained a sustained physiological or elevated IOP for 6 hours. The retina and ONH cytoarchitecture were well preserved in all samples. There was minimal change in RGC number or RGC apoptosis after IOP elevation. Increased IOP led to significant change in retinal microglia distribution, increased intensity of astrocyte reactivity marker GFAP, and reorientation of actin filaments in the ONH. Paired bioinformatics analysis of RNA sequencing results revealed 25 differentially expressed genes in the ONH following elevated IOP. Functional enrichment analysis identified alteration of pathways related to neuroinflammation (particularly microglia activation) and cell-matrix interaction.

Conclusion: Our model produces sustained, elevated IOP in *ex-vivo* human eyes. The IOP insult induces rapid glial-mediated inflammation and ONH cytoskeletal remodeling that precedes visible neuronal injury, observed at morphological and molecular levels. These changes replicate findings in other early-stage glaucoma models, and provide insight into cellular events relevant to human glaucoma pathogenesis.

9:30 – 10:30 AM

COFFEE BREAK
+
POSTER SESSION

Even numbered posters are judged

ABSTRACTS FOR BREAK ROOM SESSIONS
(Basic Science)

Friday, May 26th, 2023

Lia Huo | VSRP Student | Time: 10:30 - 10:51

Rescuing Cone Photoreceptor Death With the Sustained Release of RdCVF from a Biocompatible Hydrogel

L. Huo[1], C. Teal[2], D. Isaacs[3], M. Ho[2], T. Léveillard[4], S. Albeck[5], T. Unger[5], R. Fluhr[6], M. Shoichet[1,2,3]

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***All stated authors have NO financial or other conflicts of interests to disclose.**

Introduction: Retinitis Pigmentosa (RP) is an incurable disease that can lead to blindness. Though rod-derived cone viability factor (RdCVF) is a promising therapeutic that improves cone survival in rodent models of RP, it cannot be translated to patient care because of its rapid clearance and limited bioavailability. To overcome these challenges, we designed a slow-release formulation of RdCVF, delivered by a biocompatible, bioresorbable, and injectable hydrogel with properties similar to the native vitreous. Here, we investigated the release profile of RdCVF and its bioactivity *in vitro*.

Methods: We expressed RdCVF with a Src homology 3 (Sh3) domain and modified an oxime-crosslinked hyaluronan (HA-oxime) hydrogel with Sh3 binding peptides to slow protein release through Sh3 and Sh3-binding peptide interactions (Figure 1). To investigate tunability of release, the hydrogel was made with increasing molar excesses (0, 10, and 50) of Sh3-binding peptide to Sh3-RdCVF, and released protein was quantified using an ELISA at different time points for 14 days (two-way ANOVA with Tukey's post-hoc test). To assess if the protein would retain its function after release, a transwell containing our HA-oxime gel loaded with Sh3-RdCVF was placed above chick retinal dissociates. After 6 days in culture, cone survival was quantified with immunofluorescence against cone-specific marker visinin and compared to treatment with Sh3-RdCVF alone, hydrogel vehicle alone, or mutant Sh3-RdCVF that does not bind to the RdCVF receptor basigin1 (one-way ANOVA with Tukey's post-hoc test).

Results: As the molar excess of Sh3 binding peptide increases with respect to the Sh3-RdCVF protein, the slower the protein release. Protein release from the gel with 0 molar excess plateaus at 2 days, which is extended to 14 days in the HA-oxime gel with 10- and 50-times molar excess of peptide. In addition, linear diffusion was extended, and relative diffusivity was decreased with increasing amounts of binding peptide, indicating that the release can be controlled with the addition of Sh3-binding peptide. Furthermore, the released protein was bioactive as shown by an increase in cone viability in chick retinal dissociates as compared to the hydrogel alone ($p=0.0018$) or Sh3-RdCVF mutant ($p=0.0162$). Therefore, the released RdCVF remains functional and is able to activate basigin1 to mediate cone survival.

Conclusion: The sustained release of RdCVF is not only controllable with our drug delivery system, but also bioactive, thereby laying the foundation for *in vivo* studies in disease models of RP.

Cassandra D'Amata | Undergraduate Student | Time: 10:53 - 11:14

A human chimeric retinal organoid model for studying donor-host cell interactions in cell therapies of inherited retinal disease

PURPOSE: There are currently no human models of retinal cell engraftment that enable the study of allogeneic donor-host cell interactions in a degenerating retina. Our lab has generated chimeric retinal organoids ("chimeroids") from a mixture of healthy human embryonic stem cell (hESC) and patient-derived, diseased induced pluripotent stem cell (iPSC) lineages. We hypothesize that **our chimeroids will represent a novel *in vitro* human model of retinal cell engraftment** in inherited retinal disease (IRD).

METHODS: Our pilot chimeroid experiments were performed using an iPSC line derived from a male patient with *USH2A*-associated retinitis pigmentosa (RP), and a healthy female H9 reporter hESC line expressing red-fluorescent protein (H9-RFP). The most common molecular cause of autosomal recessive RP are those pathogenic variants associated with *USH2A*. We combined H9-RFP and *USH2A* stem cells in a 1:1 ratio and co-cultured in 2D until 95% confluence, alongside age-matched single lineage controls. We then induced differentiation toward 3D retinal organoids following established protocols. We confirmed chimeroids in cryosection by non-overlap of H9-RFP+ nuclei and *USH2A* Y-chromosome-FITC+ nuclei.

RESULTS: We evaluated chimeroids and control organoids across development for retinal tissue structure and markers of retinal cell specification. *USH2A* control organoids showed disorganized lamination and a thin, sparsely-labelled presumptive outer nuclear layer, examined by expression of photoreceptor progenitor and mature cell markers (Otx2 and Recoverin, respectively) at Week 8 of differentiation. By comparison, chimeroids showed established retinal lamination and expression patterns similar to healthy controls. Quantitative RT-PCR analysis further confirmed expression of photoreceptor cell markers in Week 12 chimeroids, whereas *USH2A* controls did not express these markers. To improve our ability to analyze cell-cell interactions and chimeroid formation between different lineages, we engineered an *USH2A* reporter line using CRISPR/Cas9, where H2B promoter-driven GFP results in indelibly-tagged diseased cell nuclei in ongoing chimeroid lineage analysis and cell sorting experiments.

CONCLUSIONS: Our lab is able to successfully generate retinal chimeroids using a patient-derived diseased iPSC line. Our preliminary results suggest that the presence of healthy cells in a diseased host retina during development permits the specification and survival of photoreceptor cells. Further investigation will focus on determining a minimum required number of healthy cells to rescue a diseased organoid phenotype, by adjusting ratios in our co-cultures. A chimeroid platform could facilitate high-throughput analysis of donor-host cell interactions, and neuroprotective molecule screening, in potentially any IRD background for which human iPSC lines and an organoid phenotype exist.

Functional analysis of axon guidance programs in developmental and therapeutic photoreceptor connectivity

Victor Q.B. Pham Truong[1], Akshay Gurdita[1], Arturo Ortín-Martínez[2], James Dunbar[1], Mostafa Ibrahimi[1], Zhongda C. Liu[2], Matey Juric[2], Valerie A. Wallace[1,2,3]

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Background: Photoreceptor (PR) transplantation is an approach to treat PR degeneration diseases like macular degeneration and genetic retinopathies that result in permanent and untreatable visual deficits. However, many groups have observed that most donor PRs fail to connect with their correct synaptic partners. Despite the molecular composition of PR synapses being well characterized, there is also limited understanding regarding how PR axon outgrowth and target recognition are coordinated. Therefore, minimal donor cell connectivity remains a key challenge for therapeutic applications of PR replacement. The aim of this study is to investigate candidate genes that may play a role in proper PR axon and synapse development in the retina to improve donor-host connectivity.

Methods: Using data from bulk and single-cell PR RNA sequencing databases, candidate genes were selected based on cell surface expression, known roles in axon outgrowth, guidance, and synaptogenesis in other neuronal contexts, and expression during the peak period of PR synaptogenesis between post-natal days 0 to 6 (P0-6). RNAscope was used to probe for candidates in murine retina cryosections at P0, P7, and P14 to verify expression in PRs at key developmental timepoints. To investigate each gene's function, overexpression (OE) and knockdown (KD) experiments were conducted by sub-retinal injection and electroporation of either overexpression or short hairpin RNA plasmid vectors at P0. Retinas were collected 21 days post-injection and analyzed by immunohistochemistry for synaptic and morphological defects.

Results: EphA8 and Ncam1 are two candidates we have investigated so far. EphA8 expression was largely in the basal inner nuclear layer (INL) at P7 and P14, and EphA8 OE significantly reduced the dendritic field area of amacrine cells ($p < 0.05$). Ncam1 transcript variants 1, 3, and 4 (v1, v3, v4) were expressed throughout the neuroblastic layer at P0, localizing primarily to the INL at P7 and P14, while v2 expression increased in the outer nuclear layer at P7 and P14. Ncam1 v2 OE also caused synaptic defects including ectopic horizontal cell processes.

Discussion: We propose that Ncam1 may play a more essential role in rod PR development. Variant expression undergoes a temporal shift around a key developmental period of peak PR synaptogenesis and appears to impact proper synapse development suggesting it may be an imperative guidance or synaptogenic factor. Further insight into how PR axons develop and synapse, may reveal mechanisms that could be exploited for therapeutic treatment of vision loss.

Retinal cell differentiation and maturation is controlled by glycolytic flux

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6.

Commercial Relationships (All authors): None

Introduction: Sight begins when photosensitive retinal neurons, rod and cone photoreceptors, detect and convert light to electrical signals for visual function. During development, rods and cones are derived from multipotent retinal progenitor cells (RPCs) that give rise to all retinal cells in a defined temporal sequence. Here we investigated the role of PTEN, a lipid and protein phosphatase, and glycolysis in biasing RPC fate selection.

Methods: We knocked out Pten conditionally in retinal progenitor cells (RPC) by crossing Pax6::Cre mice with Ptenfl mice generating Pax6::Cre-Ptenfl/fl (Pten RPC-cKO) and Pax6::CrePtenfl/+ (controls). We then performed RNA sequencing at postnatal day (P) 0, at the peak of rod genesis. To assess glycolytic function, we performed a Seahorse assay on RPCs from Pten RPCcKO and controls. To assess the effect of glycolysis on photoreceptor differentiation and development, we grew wildtype CD1 mice P0 retinal explants with the glycolytic inhibitor 2- deoxy-d-glucose (2DG). We also injected 2DG daily intraperitoneal from P0-P7 in Pten RPC-cKO and controls to assess the effect of inhibited glycolysis on photoreceptor maturation. To dissect the mechanism, we investigated lactate production, which is a glycolytic byproduct that is shuttled out of the cell in high glycolysis, effectively increasing intracellular pH (pHi). To mimic these changes, we cultured retinal explants in acidic, basic, and neutral pH media. Results: We found accelerated timing of rod differentiation and outer segment maturation in Pten RPC-cKO. Pten RPC-cKO RNAseq, identified differentially expressed genes (DEG) in three gene ontology (GO) categories: (1) synapse/dendrite/axon formation and function, (2) metabolic processes, and (3) neural development/differentiation. Further data mining revealed upregulation of glycolytic genes in Pten RPC cKO cells, a metabolic pathway that we confirmed was upregulated using a Seahorse assay to quantify extracellular acidification rates(ECAR). Strikingly, artificially elevating RPC glycolysis using a cytoPfkfb3 conditional gain-of-function mouse model accelerated photoreceptor differentiation and outer segment maturation, phenocopying Pten RPCcKOs. Conversely, inhibiting glycolysis with 2-deoxy-d-glucose (2DG) inhibited RPC proliferation and delayed rod and cone marker expression in vitro, and blocked the precocious maturation of rod outer segments observed in Pten RPC-cKOs in vivo. In high pH 8.0 media, RPC proliferation was elevated and more Crx+ photoreceptor precursor cells were produced, whereas in low pH 6.5 media, RPC proliferation declined.

Conclusions: Glycolysis is thus a critical driver of RPC differentiation and maturation and acts in part by modulating pHi. These findings may help in designing novel regenerative therapies to restore vision and prevent blindness.

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ABSTRACTS FOR BREAK ROOM SESSIONS
(Retina)

Friday, May 26th, 2023

The Association of Outer Retinal Morphologic Stage and Postoperative Visual Acuity in Fovea-Involving Rhegmatogenous Retinal Detachment

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Type of Research: Clinical research

Category: Retina

Conflict of Interest: No conflicting relationship exists for any author.

Objective: To evaluate the association of baseline outer retinal morphologic stage of rhegmatogenous retinal detachment (RRD) and postoperative visual acuity (VA) in fovea-involving RRDs, using optical coherence tomography (OCT).

Methods: Single-centered retrospective study assessing 1,768 consecutive charts of fovea-off RRDs referred to St. Michael's Hospital, between January 2012-September 2022. Only patients with gradable baseline OCTs were included. VA was obtained at presentation, 3, 6 and 12 months postoperatively. OCTs were graded for the morphologic stage of RRD in the parafovea (as per *Melo et al.* 2022 – Fig.1) and photoreceptor integrity in the fovea. Visually significant cataracts were excluded from VA analysis.

Results: 351 patients were included, of which 68%(238/351) were male, with mean age of 61.2(±12.8) years, and 59%(206/351) were phakic. 13%(47/351) of patients presented in Stages 1 and 2; 15%(54/351) in Stage 3a, 36%(126/351) in Stage 3b, 24%(83/351) in Stage 4, and 12%(41/351) in Stage 5. Increasing presenting stage was significantly associated with worse foveal photoreceptor integrity, reduced mean baseline VA and longer duration of central vision loss ($p<0.001$). Mean 12-month logMAR VA by stage was 0.77(±0.64) for Stages 1 and 2, 1.00(±0.53) for Stage 3a, 1.36(±0.55) for Stage 3b, 1.33(±0.66) for Stage 4 and 1.55(±0.47) for Stage 5. Increasing stage of RRD on presentation was associated with reduced postoperative VA ($p<0.001$) at all time points. A subset analysis of acute detachments with photoreceptor-RPE-dysregulation (as per *Muni et al.* 2022) showed no difference in postoperative VA between RRDs presenting in Stages 1, 2 and 3a. However, 12-month VA was significantly better in patients presenting with Stages 1, 2 and 3a vs Stage 3b ($p=0.002$) and when comparing 3a vs 3b ($p=0.008$).

Conclusion: This study validates the clinical relevance of the staging system proposed by *Melo et al.* in 2022. Presenting stage was associated with worse baseline VA and longer duration of vision loss. Postoperative VA was significantly reduced in patients with worse presenting stage at all time points. In patients with RPE-photoreceptor-dysregulation, 12-month VA was significantly better in Stages 1, 2 and 3a vs Stage 3b. This suggests that Stages 1, 2, or 3a may have better retinal structure and function when compared with Stage 3b or worse. Stage 3b may represent a critical point where significant structural changes occur, leading to worse postoperative functional outcomes in acute RRDs. There may be a particular benefit of urgent intervention in patients presenting with RRDs in Stages 1, 2 or 3a.

Posterior Hyaloid Discontinuity on Optical Coherence Tomography in Patients with Vitreomacular Traction and Posterior Vitreous Detachment: A Retrospective Cross-Sectional Study

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Keywords: Posterior vitreous detachment, vitreomacular traction, macular hole, optical coherence tomography, posterior hyaloid discontinuity

Conflicts of Interest: GSY: Financial support – The Cambridge Trust Cambridge University. MMP: Financial support (to institution) – PSI Foundation, Fighting Blindness Canada. RHM: Advisory board- Bayer, Novartis, Allergan, Roche; Financial Support (to institution)- Bayer, Novartis. DTW: Consultant –AbbVie, Alcon, Apellis, Bayer, Bausch Health, Biogen, Boehringer Ingelheim, Novartis, Ripple Therapeutics, Roche,. Financial Support (to institution)- Bayer, Novartis, Roche. Research grants -Novartis, Roche

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Background : Posterior hyaloid discontinuity is a novel swept-source optical coherence tomography (SS-OCT) finding defined as an apparent break in the posterior hyaloid, with the potential for liquified vitreous to prolapse through this discontinuity. In this retrospective case series, we investigated patients with first presentation posterior vitreous detachment (PVD) or vitreomacular traction (VMT) to characterize features of posterior hyaloid discontinuity.

Methods : In this retrospective cross-sectional study, we analyzed all patients with available SS-OCT images between February 26, 2019 to September 30, 2022 who were diagnosed with PVD or VMT. Eyes with retinal detachment, proliferative diabetic retinopathy, neovascular age-related macular degeneration, or other visually significant ocular conditions were excluded. The posterior vitreous was assessed for signs of separation of the posterior hyaloid from the macula, peripapillary area, and other regions characterizing a partial PVD, or any tractional abnormalities such as VMT or macular hole (MH). Brightness and contrast were individually adjusted during vitreous imaging to enhance visualization. If present, the size and location of the posterior hyaloid discontinuity was recorded.

Results : 128 eyes from 99 patients were included. The median age was 63-years old (IQR 56-68). The mean best corrected visual acuity (BCVA) on the date of SS-OCT imaging was 0.24 (SD 0.31) logMAR (20/35 Snellen). The incidence of VMT, partial-thickness MH (PTMH), and full-thickness MH (FTMH) was 12.5% (n=16), 2.3% (n=3), and 9.4% (n=12), respectively. A total of 34.4% had a posterior hyaloid discontinuity on SS-OCT (n=43). Of these, the average linear diameter of discontinuity was 1302 μm (SD 1458 μm). The most common location of the discontinuity was peripheral (32%, n=15), followed by perifoveal or parafoveal (27%, n=13), foveal (23%, n=11), and peripapillary (16%, n=8). 8 eyes demonstrated formed vitreous prolapse through these discontinuities.

Conclusions : We describe and characterize a novel finding of a break through the posterior hyaloid via non-invasive imaging of the retina. Further studies should examine whether there is any predictive value for progression of PVD or VMT, which may be helpful for clinical decision-making.

Aurora Pecaku Research Fellow Time: 11:16 - 11:37

Reattachment Rate with Pneumatic Retinopexy for Rhegmatogenous Retinal Detachment with a Single Break in Detached Retina

Purpose: To assess reattachment rate with pneumatic retinopexy (PnR) for primary rhegmatogenous retinal detachment (RRD) in patients meeting PIVOT criteria with a single break in detached retina.

Methods: A post- hoc analysis of two prospective clinical trials that included primary RRDs referred to St. Michael's Hospital, Toronto, Canada between August 2012-April 2021. To be included in this study, patients had to meet PIVOT trial criteria (Hillier et al. 2018) but could have only one break in the detached retina, with any number of breaks or lattice degeneration in the attached retina.

Results:108 patients were included. All patients had a minimum of 3 months of follow-up and 99% (107/108) had a one-year follow-up. 32. 4% (35/108) of patients were female with a mean age of 62(±10.0) years and 52% (56/108) were phakic. 75.9% (82/108) were fovea-off at the time of presentation.

Primary anatomic reattachment rates at postoperative months 3 and 12 were 86.1% (93/108) and 85%(91/107) respectively. Mean logMar BCVA was 0.34(±0.4) at 3 and 0.2 (±0.3) at the 12-month post-operative evaluation.
The mean extent of RRD was 2.3±1 and 2±1 quadrants in patients who had primary reattachment with PnR versus those who required a subsequent operating room procedure.
40% (6/15) of patients who failed PnR were found to have additional breaks that were visualized at the time of pars plana vitrectomy (PPV).
Patients who failed PnR had a mean of 0.6 (SD±1) breaks in the attached retina vs 0.2 breaks (SD ±0.6) in patients who achieved reattachment with PnR.
The primary reattachment rate was 89.5% (77/86) in patients with no retinal breaks or suspicious pathology in the attached retina.

Conclusions: The primary reattachment rate in patients meeting PIVOT criteria was 80.8% in the trial. In this prospective cohort study, the primary reattachment rate increased to 86.1% at 3 months and 85 % at one year when only patients with a single break in the detached retina and any number of breaks or lattice degeneration in the attached retina were included. The primary reattachment rate increased to 89.5% in patients with no retinal breaks or suspicious pathology in the attached retina.
Pneumatic retinopexy provides long-term reattachment in a large proportion of patients with a single break in the detached retina that meets PIVOT trial criteria.

Association between Magnitude of Retinal Displacement and Functional Outcomes Following rhegmatogenous Retinal Detachment Repair

Reut Shor, MD[1,2], Sumana C. Naidu[3], Carolina L M Francisconi, MD[2], Samara B Marafon, MD[1,2], Varun Chaudhary, MD[5], Roxane J Hillier, MD[6], Nishaant Bhambra[1,2], Rajeev H. Muni MD[1-4]

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Research Type /Category: Clinical study/Retina
Funding/Financial Support: None
Financial Disclosures: No financial disclosures for all authors.

Introduction: Although a high proportion of patients achieve anatomic reattachment after rhegmatogenous retinal detachment (RRD) repair, many of them experience suboptimal post-operative functional outcomes. Retinal displacement is a common phenomenon seen on fundus autofluorescence imaging following RRD repair. We aim to evaluate the association between the magnitude of retinal displacement, calculated using a novel three- dimensional (3D) approach, and post- operative functional outcomes in patients treated with pars plana vitrectomy or pneumatic retinopexy for primary RRD.

Methods: This was a post- hoc analysis of the prospective, multicenter, non-randomized trial, "ALIGN". All patients with post-operative ultra-widefield fundus autofluorescence (UWF-FAF) images at 3- months and clinical follow-up, including visual acuity (VA), vertical and horizonal metamorphopsia (MV, MH) and aniseikonia (ASK) scores at 3- and 12- months post-operatively were included. 2D UWF-FAF images were projected to 3D using Optos software and retinal displacement vectors were calculated using the geodesic vertical, horizontal and total distances between points on retinal vessels and their corresponding retinal vessel printings (RVP).

Results: A total of 48 patients with a mean age of 63.3 years (SD=8.56) were included. There were significant correlations between VA at 3- months and total retinal displacement ($p<0.001$), VA at 12-months and horizontal retinal displacement ($p<0.001$), and between MV at 12-months and vertical retinal displacement ($p<0.001$). Multivariable regression models demonstrated effect sizes of 2.65 (mm/LogMar) ($p<0.001$), 3.26 (mm/LogMar) ($p=0.005$), and 2.16 (mm/M-chart score) ($p<0.001$), respectively for each correlation after adjusting for age, gender, and intervention group.

Conclusion: Post operative functional outcomes, including visual acuity and metamorphopsia were significantly correlated with magnitude of retinal displacement in patients following RRD repair.

ABSTRACTS FOR BREAK ROOM SESSIONS
(Epidemiology)

Friday, May 26th, 2023

Conversational AI Models for Ophthalmic Diagnosis: Comparison of ChatGPT and the Isabel Pro Differential Diagnosis Generator

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Declarations Of Interest: All stated authors have NO financial or other conflicts of interests to disclose.

Type of Research: Clinical Research

Category: Epidemiology / Public Health

ABSTRACT

Background: With the rapidly growing field of conversational artificial intelligence (AI), it is increasingly likely that this technology will revolutionize the way physicians diagnose and treat patients. The purpose of this study is to evaluate the use of conversational AI language models, specifically ChatGPT, for the diagnosis of ophthalmic disease, and to compare it to existing tools, namely the Isabel Pro Differential Diagnosis Generator.

Methods: Prospective, comparative evaluation of ChatGPT and Isabel in formulating provisional and differential diagnoses from a set of rich text case report descriptions. Ten ophthalmology patient cases were selected at random from a publicly available online database of ophthalmic case reports. The text details of each case were input into ChatGPT and Isabel. Their ability to identify the actual diagnosis and provide relevant differential diagnoses was compared.

Results: ChatGPT identified the correct diagnosis in 9/10 cases while having the correct diagnosis listed in all 10/10 of its lists of differentials. Isabel only identified 1/10 provisional diagnoses correctly, however it had the correct diagnosis in 7/10 of its differential diagnosis lists. The median position of the correct diagnosis in the ranked differential lists was 1.0 (IQR 1.0 to 2.8) for ChatGPT versus 5.5 (IQR 3.3 to 10.0) for Isabel.

Conclusions: Conversational AI models like ChatGPT have potential value in the diagnosis of ophthalmic conditions, particularly for primary care providers. As further iterations of models are deployed, additional studies investigating their capabilities are needed to determine the best ways to integrate them into practice.

Presenting Characteristics and Healthcare Utilization of Patients Diagnosed with Functional Vision Loss

Irina Sverdlichenko BHSc[1], Natalie Brossard MD[2], Jonathan Micieli, MD[2,3], Edward Margolin MD[2,4]

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Conflicts of Interest Disclosures: None

Financial Support: None

Introduction: Functional vision loss (FVL) is characterized by complaints of visual impairment without an organic cause. To avoid missing an organic cause, patients are often referred for unnecessary and costly medical testing. The purpose of this review is to characterize the presentation and healthcare utilization of patients with FVL.

Methods: 110 patients that were seen at two university-affiliated neuro-ophthalmology practices who were diagnosed with FVL were included. Medical records were evaluated, and data were collected on demographics, clinical presentation, ophthalmologic examination, neuroimaging, ancillary tests, and other healthcare provider visits and treatments.

Results: Over 70% (81/110) of participants were female with a mean age of 37 ± 15 years. The first point of contact with the healthcare system for thirty percent of individuals was an ophthalmologist or optometrist, with a presenting complaint of decreased vision in 71.8% (79/110) of participants. On ophthalmologic examination, visual acuity was normal or mildly reduced in 57.1% (97/170) of affected eyes, with generalized depression being the most common finding on visual field testing (42.5%, 68/160). Nearly half of participants (53/110) also endorsed at least one comorbid psychiatric condition. With respect to healthcare usage, each patient saw an average of 3.7 ± 2.6 different medical specialists (excluding neuro-ophthalmologists) for their visual complaint, and the average number of healthcare visits for this was 4.6 ± 4.4. As part of their work-up, patients underwent a mean of 2.2 ± 1.8 neuroimaging studies, and up to 10% had other ancillary tests done. Fifteen percent of patients also underwent unnecessary treatments, including steroids, visual therapy, and prisms.

Conclusion: FVL patients often present to three different healthcare specialists and attend four different visits for their visual complaints. Additionally, they undergo unnecessary testing and treatments; all this leads to significant healthcare utilization. To avoid needless workup and treatment, clinicians should refer suspect FVL patients directly to neuro-ophthalmologists, who can confirm the diagnosis and initiate appropriate management.

The Association Between Sociodemographic, Clinical Access, and Regional Factors with Vision Difficulty

Lana Moayad MD(C)[1,a] Chris Zajner MD(C) MA[2,a], Marko M. Popovic MD MPH[3], Gareth Mercer MD PhD[3], Peter J. Kertes MD CM FRCSC[3,4], Rajeev H. Muni MD MSc[3,5], Elizabeth Hall PharmD BCPS[6], Neha Goel MD[7], Mariam Rana MBBS FRCSC[8], Radha P. Kohly MD PhD FRCSC[3,4*]

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Conflicts of Interest: Lana Moayad: None. Chris Zajner: None. Marko M. Popovic: Financial support (to institution) – PSI Foundation, Fighting Blindness Canada. Peter J. Kertes: Advisory board – Novartis, Alcon, Bayer, Roche, Novelty Nobility; Financial support (to institution) – Bayer, RegenXBio, Roche, Novartis; Financial support – Novartis, Bayer; Equity owner – ArcticDx. Rajeev H. Muni: Advisory board- Alcon, Bausch + Lomb, Bayer, Novartis, Allergan, Roche; Financial Support (to institution)- Bayer, Novartis, Roche. Elizabeth Hall: None. Neha Goel: None. Mariam Rana: None. Radha P. Kohly: Financial Support (to institution) – Bayer, Novartis.

Introduction: Social determinants of health (SDH) are substantial factors that affect health outcomes and have been shown to determine 80-90% of a population's overall health. The effects of sociodemographic factors on vision health have not been extensively investigated, and studies to date remain limited in their scope. In this cross-sectional, population-based analysis, we investigate the relationship between domains of SDH with participant self-reported vision difficulty.

Methods: The National Health Interview Survey (NHIS) is an annual population-based survey based on the U.S civilian population aged 18 years and older. It provides self-reported data on demographic characteristics, socioeconomic factors, health status, and health care access. The 2021 NHIS database used in this study was based on data collected from January to December 2021. Adult participants of the NHIS who responded to the question "Do you have difficulty seeing, even when wearing glasses or contact lenses?" were included in this analysis. The relationship between vision difficulty was analyzed in relation to a list of sociodemographic factors through univariable and multivariable logistic regression analyses. From our regression models, we reported odds ratios with 95% confidence intervals. Statistical significance was determined at $p < 0.05$.

Results: The 2021 NHIS included 29,482 participants, of which 29,464 were included in our study. Univariable logistic regression showed there was an increased odds of self-reported vision difficulty among female (OR 1.28; 95% CI, 1.20-1.38; p <0.001), and gay, lesbian, or bisexual participants (OR 1.24; 95% CI, 1.04-1.49; p = 0.02). Those who possessed public compared to private insurance had higher odds of vision difficulty (OR 1.83; 95% CI, 1.69-1.99; p = <0.001), as did participants with less than a high school education (OR 1.88; 95% CI, 1.67-2.13; p < 0.001), or who had an income below the poverty threshold (OR 2.22; 95% CI, 1.96-2.51-0.67; p < 0.001). Multivariable analysis revealed an increased risk of vision difficulty reported amongst non-Hispanic Black participants (OR 1.65; 95% CI, 1.21-2.25; p = 0.002).

Discussion/Conclusion: In our multivariable analysis, the following variables were predictors of self-reported vision difficulty: age, race, sex, sexual orientation, health status, disability, insurance coverage, region of residence, and cost-related medical delays**.** Factors from each domain of SDH, including economic stability, healthcare access, education access, environmental context, as well as social and community context, showed strong relationships with vision difficulty. Our findings emphasize the importance of addressing SDH factors in the context of vision difficulty when considering policy decisions and implementation.

Delisted routine eye exams and the increased use of family physicians and ophthalmologists for glaucoma diagnosis

Wongel Bogale, BSc,[1] Graham E Trope, MB BCh, PhD, FRCSC,[2,3] Noah M Ivers, MD, PhD, CCFP,[4,5] Yvonne M Buys, MD, FRCSC,[2,3] Ya-Ping Jin, MD, PhD[1,2]

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Introduction: Government-insured routine eye exams by optometrists and physicians for individuals aged 20-64 were delisted in 2004 in Ontario. Since then, individuals affected by the policy may visit family physicians (FPs) for eye-related concerns to avoid out-of-pocket payment. We investigated if delisting was associated with increased use of FPs and ophthalmologists for glaucoma diagnosis.

Methods: Using population-based health service data from the Ontario Health Insurance Plan (OHIP) from 1997-2019, we compared the yearly proportion of people with a new glaucoma diagnosis claimed by FPs or ophthalmologists among the total number of individuals with a new glaucoma diagnosis claimed by all OHIP physicians. We conducted an interrupted time series analysis to assess if changes in the utilization of FPs or ophthalmologists before and after delisting was the result of chance alone or policy change. Ontarians aged 20-64 were in the policy-affected group. Those aged 65+ were in the policy-unaffected group.

Results: In the policy-affected age groups, the utilization rate of FPs for glaucoma diagnosis significantly increased immediately following delisting: 14.6% (95% confidence interval [CI] 11.0%~18.3%) for the 20-39 age group and 9.9% (95% CI 8.2%~11.5%) for the 40-64 age group. The utilization of ophthalmologists for glaucoma diagnoses increased substantially post-delisting: 41.5% (95% CI 37.8%~45.3%) for the 20-39 age group and 40.3% (95% CI 35.7%~45.0%) for the 40-64 age group. There was a significant increase in the number of glaucoma referrals from FPs to optometrists immediately after delisting (569, 95% CI 445~694) and from FPs to ophthalmologists after 2006 (1471, 95% CI 769~2174).

In the policy-unaffected 65+ group, the utilization rate of FPs (1.9% (95% CI 0.6%~3.2%)) and ophthalmologists (4.4% (95% CI 0.4%~8.4%)) for glaucoma diagnoses increased minimally post-delisting. The number of glaucoma referrals did not significantly change post-delisting from FPs to ophthalmologists (-11, 95% CI -315~293) and increased marginally from FPs to optometrists after 2010 (38, 95% CI 3~73).

12:00 - 1:00 PM

LUNCH
+
POSTER SESSION

Odd numbered posters are judged

The 42nd Clement McCulloch Lecture:

Under Pressure: High 'TEK' Solutions for Glaucoma

Dr. Susan Quaggin, MD, FRCP(C), FASN

Charles Horace Mayo Professor of Medicine
Northwestern University
Chief of the Division of Nephrology & Hypertension
Director of the Feinberg Cardiovascular and
Renal Research Institute

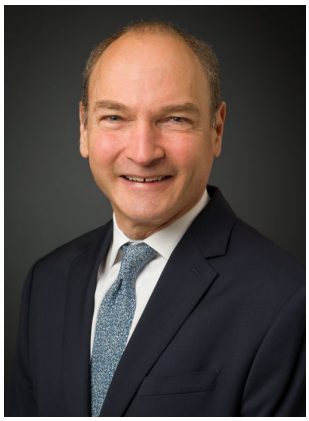
2:10 – 3:00 PM

COFFEE BREAK
+
POSTER SESSION

All remaining posters are judged

Red Reflex Screening Reimagined: Empowering Early Retinoblastoma Detection

Abstract:
TALON was a 64 week prospective Phase IIIb superiority study evaluating the efficacy and safety of brolucizumab 6 mg compared with aflibercept 2 mg using a matched (Treat-and-Extend) treatment regimen in patients with nAMD
Methods Seven hundred and thirty seven patients were randomized to receive Brolicizumab (BRO) 6mg or Aflibercept (AFL) 2mg at Weeks (W) 0, 4, 8, and 16, followed by 4W interval adjustments depending on disease activity (DA) up to q16w.
Results At W64, more BRO patients had a last treatment interval with no DA of q16w while more AFL patients had a q4w interval need. Mean BCVA gains were comparable to AFL and 24.3% (BRO) vs 24.7% (AFL) patients gained ≥15 letters from baseline. BRO achieved greater average reductions in Central Subfield Thickness (CSFT) on OCT at W60 and W64 and fewer BRO patients had intraretinal and/or subretinal fluid (26.6% vs 34.4%). Adverse events of special interest occurred in 22 (6.0%) BRO vs 6 (1.6%) AFL patients with 2 BRO patients losing ≥15 letters from baseline vs 0 in AFL arm.
Conclusions BRO achieved longer treatment intervals, greater reductions in anatomical outcomes and comparable visual gains to AFL.
Knowing that BRO is a more durable superior drying agent, with a small but significant risk of vision threatening intraocular inflammation (IOI), a decision analysis was then carried out to try to determine how much more durable does BRO have to be to justify the risk of IOI.



Short Bio:
Dr. Peter Kertes is the incoming chair and a Professor in the Department of Ophthalmology & Vision Sciences of the University of Toronto and an Associate member in the Institute of Medical Science at the Temerty Faculty of Medicine. He is an affiliate scientist at the Sunnybrook Research Institute and served as Ophthalmologist-in-Chief at the John and Liz Tory Eye Centre at Sunnybrook Health Sciences Centre from 2010 to 2021. He also holds appointments at The Hospital for Sick Children and Kensington Health. Dr. Kertes obtained his MD at McGill University before completing residency at the University of Ottawa and a 2-year vitreo-retinal surgical fellowship at Louisiana State University in New Orleans. He also holds an AB in molecular biology from Princeton University.

A vitreo-retinal surgeon, Dr. Kertes has a special interest in pediatric retinal diseases and in international ophthalmology and has participated in 28 development projects throughout the world. Dr. Kertes' has nearly 150 peer-reviewed publications and has been the principal, senior or co-author in nearly 300 peer-reviewed conference proceedings at major ophthalmology meetings at home and abroad. A recipient of several teaching awards, Dr. Kertes has supervised more than fifty adult and pediatric vitreo-retinal surgery fellows and participated in the education of more than one hundred ophthalmology residents.

Quantitative Mapping of Uveoscleral and Lymphatic Drainage Pathways From the Suprachoroidal Space

Sauntharrajan, Babishaa[5, 7]; Zhou, Xun[7]; Gumeler, Ekim[7,8]; Koletar, Margaret[4]; Lam, Wilfred W.[4]; Stanisz, Greg[4, 6]; Gupta, Neeru[1, 3]; Yucel, Yeni H.[2,7]

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Purpose: This study quantitatively evaluates the tracer distribution and drainage following suprachoroidal (SC) injection using a near-infrared (NIR) fluorescent tracer and Magnetic Resonance Imaging (MRI).

Methods: A NIR fluorescent tracer, CF770 conjugated with bovine serum albumin (MW:70kDa, 0.5µL) was injected into the SC space of the right eye of adult mice (C57BL/6; n=6). Non-injected left eyes (n=6) were used as controls. Mice were sacrificed 20 minutes post-injection. Infrared reflectance and fluorescence images of the neck lymph nodes were obtained using a scanning laser ophthalmoscope (Spectralis, Heidelberg Engineering, Germany). Orbit specimens were processed and serially sectioned with a cryostat. Frozen sections were imaged using NIR epifluorescence microscopy mounted with sCMOS camera. The mean pixel intensities (MPI) were measured in the sclera and orbital tissue using ImageJ (NIH, v1.53q). Wilcoxon and student's t-test were used for statistical analysis. A second set of adult mice (C57BL/6; n=2) received SC injection of galbumin (human serum albumin conjugated with gadolinium and rhodamine; MW:70kDa; 0.5µL, BioPAL, USA) into the right eye. In vivo MRI scans were collected for 50 minutes with a 7T pre-clinical scanner (BioSpec 70/30 USR, Bruker BioSpin) covering the orbits. A 3D fast low angle shot sequence was used, and images were reconstructed using the 3D Slicer software.

Results: 20 minutes after tracer injection into right eye, the MPI of the NIR fluorescent signal within the right sclera was greater compared to left sclera (3.592±4.230 vs. 0.031±0.002, right and left sclera respectively; p=0.0244). The tracer signal was also greater in the right orbit compared to left orbit (7.359±1.965 vs. 0.028±0.006, right and left orbit respectively; p=0.0025). In vivo MRI scans demonstrated that tracer drains through the medial pathway into the orbit. Ex vivo NIR fluorescent imaging showed that tracer drains into the right accessory submandibular lymph node.

Conclusion: This study provides the first quantitative evidence that SC tracer injection exits the eye through a medial route into the orbital tissue and drains into the neck lymph node. This new multimodal imaging approach may lead to in vivo quantitative assessment and screening of drugs targeting the uveoscleral/lymphatic drainage pathway for the treatment of glaucoma and other eye diseases.

Tianwei Ellen Zhou	Resident	Time: 3:23 - 3:33 PM

Choroidal hypoperfusion and reduced retinal function in retinopathy of prematurity – a collaborative tale of two cities.

Tianwei Ellen Zhou MDCM, PhD[1]; Allison Dorfman PhD*[2]; Anna Polosa PhD*[3]; Elizabeth Youn*[4]; Valentina Parra*[4]; Patrick Hamel MD*[2]; Thuy Mai Luu MD*[5]; Anik Cloutier PhD*[5]; Anne-Monique Nuyt MD*[6]; Sylvain Chemtob MD, PhD*[6]; Peter John Kertes MDCM[1,7]; Nasrin Najm-Tehrani MBBCh, MSc[1,8]; Cynthia, Qian MDCM*[2,3]; Kamiar Mireskandari, MBChB, PhD[1,8].

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No conflicts of interest.

* The University of Montreal group that performed the study on retinal function. Conception: Drs. Ellen Zhou, Cynthia Qian and Sylvain Chemtob. PI: Dr. Cynthia Qian.

Introduction: Retinopathy of prematurity (ROP) is the leading cause of childhood visual impairment worldwide. Many believe that ROP only affects the retinal vessels during its active phase. Emerging evidence has shown that choroidal insufficiency is a salient feature of ROP, and can carry long-term impacts on photoreceptors, which solely relies on the choroid as its blood supply. In this project, we provided structure-function analyses of photoreceptors and choroid in patients formerly affected by ROP.

Methods: At SickKids, ROP patients who received treatments from 2011–2020 were identified in the intravenous fluorescein angiography (IVFA) database. Three experts (PK, NT and KM) were asked to categorize each image based on: image quality, the presence or absence of choroidal hypoperfusion at the arteriovenous phase, and the location of choroidal hypoperfusion. Inter-rater agreement was assessed by Fleiss' κ.
At Saint-Justine Hospital, school-aged patients were recruited and divided into three groups: former premature babies diagnosed with ROP ("Ex-ROP"), former premature babies without ROP ("Preterm") and full-term age-matched controls ("Full term"). Participants underwent a complete ophthalmological examination including electroretinogram (ERG).

Results: 118 ROP patients from Sickkids were identified for review; among them, 74 had high-quality images that enabled further analyses. The average BW was 600.4 grams, and the average GA was 23.9 weeks. The majority (69.4%) had zone I, stage 3+ ROP. The average chronological age at receiving IVFA was 11.5 months. 68 eyes (91.9%) demonstrated choroidal hypoperfusion that overlapped the macula. In some patients, choroidal hypoperfusion persisted years after the initial phase of ROP had resolved. Fleiss' κ for interrater agreement was 0.85 (almost perfect). In our prospective school-aged cohorts from Ste-Justine (average age = 11.2 year-old), the Ex-ROP group had significantly higher refractive errors and intraocular pressure. More interestingly, significant differences were observed in some of the photopic and scotopic ERG parameters between the Ex-ROP group and controls.

Conclusions: Our collaborative study illustrated that the vast majority of patients with treatment-required ROP sustained choroidal hypoperfusion at the macula. This striking feature was observed after acute ROP had resolved, spanned a critical period of retinal maturation, and was persistent in certain cases. Meanwhile, a history of ROP is associated with diminished retinal function in a group of school-aged children. To our knowledge, this is the first study to provide a potential connection between choroidal hypoperfusion and photoreceptor deficit in ROP. Further investigation is needed to strengthen this link.

Claudia Castro	Clinical Fellow	Time: 3:34-3:44 PM

Primary Iris Claw Intraocular Lens Implantation in Children

Claudia Castro, MD; Larissa Gouvea, MD; Sara Williams, MSc; Asim Ali, MD, FRCSC

Introduction: Few long-term studies support the safety and efficacy of primary intraocular lens (IOL) implantation in the pediatric population in the absence of capsular support. This study aims to report outcomes and complications of primary iris claw IOL implantation in children with ectopia lentis.

Method: The medical records of children who underwent primary iris claw aphakia IOL implantation for ectopia lentis over a period of nine years were reviewed retrospectively. Best-corrected visual acuity (BCVA), intra- and postoperative complications, reoperations, and corneal endothelial cell loss (ECL) were evaluated.

Results: 31 eyes of 19 children were included. The mean age at surgery was 9 years (range 4-17). Mean follow-up after surgery was 5.3 years (range 0.6-9.7 years) with 43.8 % more than 5 years. Mean BCVA improved from 0.62 to 0.2 logMAR ($p<0.001$). No eyes had decreased BCVA at the end of follow-up. One (3.2%) intraoperative and 16 (51,6%) postoperative complications occurred. Eleven reoperations in 8 eyes were needed, 6 (54.5%) for IOL dislocation with the majority secondary to trauma. 68.8% of the complications arose after 18 months of surgery. The mean ECL was 9.7% one year after surgery. Four patients had ECL over 20%, 2 of which were associated with prior IOL dislocation. No patients needed IOL explantation.

Conclusion: Our study demonstrates that primary iris claw IOL implantation in children resulted in good visual outcomes. A considerable number of late complications occurred. ECL following surgery was similar to that reported in previous studies of secondary implantation.

Novel Ultrafast Visual Field Testing with The Toronto Portable Perimeter (TPP)

Runjie (Bill) Shi[1,2] (BASc), Moshe Eizenman[5] (PhD), Michael Balas[2] (BS), Gareth Leung[3] (BS), Yan Li[4] (MEng), Myrna Lichter[5] (MD, FRCSC), Steve Arshinoff[5] (MD, FRCSC), Willy Wong[1,4] (PhD)

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Financial Disclosures: Shi and Eizenman: Inventors of the Toronto Portable Perimeter.Arshinoff: Alcon Laboratories Inc.-C; Rayner-C; iMed Pharma-C; Arctic Dx-C; Zeiss-C. Other authors have no financial disclosures.

Introduction: Approximately half of all Canadian glaucoma patients already have moderate-to-severe visual field defects at initial diagnosis. A more accessible visual field test may be used to detect vision loss earlier in these patients. Current standard automated perimeters are difficult to use in community screening programs because they are non-portable, expensive, technical and tests are long. Here we evaluate a new TPP-Ultrafast test for the Toronto Portable Perimeter (TPP), a head-mounted virtual-reality perimeter.

Method: Algorithms based on the Sequentially Optimized Reconstruction Strategy (SORS) to estimate contrast sensitivity thresholds were trained to match the expected visual fields from a general population. SORS is a data-driven algorithm that continuously predicts visual field thresholds during the test to achieve significant speed-up over traditional approaches. Unlike other supra-threshold screening tests, the TPP-Ultrafast test estimates true thresholds in decibels and outputs standard field indices.

Glaucoma patients with stable visual fields were recruited from the York Finch Eye Institute in Toronto. Each patient performed an HFA SITA-Fast 24-2 test and a TPP-Ultrafast test. Visual fields with at least one cluster of three neighboring locations with pattern deviation $p<5\%$ were considered a "detection." Each eye's last two SITA-Fast tests were analyzed and compared against the TPP-Ultrafast results. The more reliable of the two SITA-Fast tests was used as "reference" to establish the status of the visual field, while the other SITA-Fast test was treated as "retest" to measure test-retest performance of the HFA.

Results: N=33 eyes from 18 patients (age: 72±8 years (mean±sd), Mean Deviation (MD): -4.4±6.9 dB) were tested. In 11 "no detection" eyes on the SITA-Fast reference field, the TPP-Ultrafast test achieved specificity of 91% (10/11) versus 64% (7/11) for the SITA-Fast retest. In eight eyes with moderate-to-severe field defect (MD worse than -6 dB), TPP-Ultrafast and SITA-Fast both achieved 100% sensitivity. In 14 eyes with mild field defect (MD better than -6 dB), TPP-Ultrafast achieved 50% (7/14) sensitivity versus 86% (12/14) on the HFA. TPP-Ultrafast tests were on average 55% shorter in moderate-to-severe fields (mean: 131 vs 292 seconds, Wilcoxon $p=0.008$) and 57% shorter in mild and healthy fields (mean: 95 vs 196 seconds, Wilcoxon $p<0.001$). Overall, TPP-Ultrafast always achieved better sensitivity when matched specificity ≥73%. (See figure)

Conclusion: The TPP-Ultrafast test has very good specificity and can reliably detect moderate-to-severe visual field loss in half the time of a SITA-Fast test, making it a promising tool for visual field testing in the community.

ABSTRACTS FOR POSTER PRESENTATIONS

Friday, May 26th, 2023

Identification of an LXB_4 Transcriptional Response in Neuroprotective Signalling

Aminat S Adama, Karen G Wigg, Alessandra Tuccitto, Jeremy M Sivak

Background: Despite clinical advances, Glaucoma remains the global leader of irreversible blindness. This incurable condition encompasses a group of optic neuropathies that present as a slow and progressive loss of peripheral vision. A primary characteristic is the degeneration of retinal ganglion cells (RGCs) and the optic nerve. We previously reported on the neuroprotective activity of the lipid mediators Lipoxin A_4 (LXA_4) and its isomer Lipoxin B_4 (LXB_4) in acute and chronic models of glaucomatous injury. LXB_4 was found to be substantially more potent, with its activity mediated through a separate mechanism than LXA_4. Unlike LXA_4, LXB_4 signalling and its associated targets have yet to be identified. LXB_4 is most potent as a pre-treatment 1 hour before injury, suggesting transcriptional changes contributing to these effects. We sought to capture these changes and to develop a preliminary molecular signature describing LXA_4 and LXB_4 transcriptional changes in neuronal cells.

Methodology: RNA Sequencing: HT22 neuronal cells were seeded at $1x10^6$ cells/well in DMEM media overnight. 4 groups; LXA_4, LXB_4,15-HETE (inactive LXB_4 precursor) and Vehicle were treated at 1μM 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. **Retinal Staining:** C57BL/6 mice were intravitreally injected with 10μM LXB_4 and Vehicle 1-hour before 10mM kainic acid (KA) insult. Retinas were dissected at 3 hours and 20 hours post-insult respectively and sectioned for immunofluorescence imaging. **qPCR:** HT22 cells were treated with 1μM LXB_4 for 1 hour and RNA was isolated and reverse transcribed into cDNA. cDNA was quantitatively analyzed using SyBR Green and gene expression calculated by the ΔΔCt method, with TBP as a reference gene.

Results: Compared to Vehicle, 242 LXB_4-specific genes, 539-LXA_4, and 440 15-HETE-specific genes were identified ($p<0.01$). Interestingly, only 23 genes were common between LXA_4 and LXB_4. 10 LXB_4-specific genes passed the statistical test of $p.adj<0.05$ and log_2FC -3</>3 to be used in subsequent analyses. *In-vivo* staining of mice retinas treated with KA and LXB_4 showed a significant decrease in SPT6 signal 3 hours following injury. Similarly, TERT staining suggested a signal increase specific to LXB_4 treatment that was confirmed in qPCR data.

Conclusion: A preliminary neuronal molecular signature for LXA_4 and LXB_4 signalling was identified, consisting of altered transcripts unique to each treatment. Next steps include validation of signature genes to determine their relation to LXB_4 neuroprotective activity.

Brillouin Spectroscopy for Corneal Biomechanics on Glaucoma patients

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Elevated intraocular pressure (IOP) is a major risk factor for glaucoma progression and interventions to reduce it have been proven to delay progression of the disease. Glaucomatous optic neuropathy seems to have continuous deterioration in up to 45% patients despite 5.1mmHg or 45% of IOP reduction with treatment. This fact has brought into attention other factors such as biomechanical properties of the eye.
Corneal biomechanics have been largely studied and it has been determined that corneal properties such as corneal hysteresis (CH) play a major role in the disease and these parameters are significantly reduced in glaucoma patients and appear to be a risk factor for glaucoma progression.
Brillouin spectroscopy measures the interaction of narrow-banded laser light and phonons in matter. Phonons are wavelets produced by molecular vibrations and occur universally in tissue at room temperature traveling inside matter with a velocity that is related to the elastic moduli, which is closely related to stiffness properties. Measuring the Brillouin frequency shift in a cornea gives a noninvasive access to the so called bulk elastic modulus M of the cornea. The Brillouin Optical Scanner System (BOSS) is a new technology with potential to add determinant information as to when and how aggressive an intervention has to be made.

Patients included in the first phase of the study are the ones with new diagnosis of early or advanced glaucoma and a control group. Exclusion criteria include connective tissue diseases, previous laser vision correction surgery, corneal dystrophies and corneal scarring.

For the second phase of the study, patients recruited on the first phase that started topical medical therapy with a Prostaglandin analogue will undergo a second BOSS measurement two months after starting treatment

Results: pending.

Panagiota Antonopoulou	Fellow	Poster #3

Gonioscopy-Assisted Transluminal Trabeculotomy in the Management of Paediatric Glaucoma

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Introduction: Gonioscopy Assisted Transluminal Trabeculotomy (GATT) is an increasingly popular procedure for the treatment of childhood glaucoma as it allows up to 360° cleavage of the trabecular meshwork at one operation. We present the results of GATT using an illuminated microcatheter device in our paediatric patients with glaucoma.

Methods: This is a retrospective single-center case series. Research ethics board approval was obtained. The electronic records of all paediatric patients (<18 years) who underwent GATT and had follow up of more than 3 months were reviewed. Failure of the procedure was determined based on the 2008 World Glaucoma Association consensus.

Results: We identified a total of 46 eyes (42 patients) to which GATT using an illuminated microcatheter device was attempted. Surgeries were performed by 3 experienced surgeons. In 30% of cases (14 eyes) the procedure was converted to standard goniotomy as the microcatheter persistently tracked into false passages out of Schlemm's canal and these cases were not included in this study. Three eyes were also excluded as they did not meet the follow up criterion. Therefore, 29 eyes (27 patients with mean age 8.9 years) were included in the analysis. In the majority of cases the diagnosis was glaucoma associated with an acquired ocular condition (n=13) while other diagnoses were PCG (n=4), glaucoma following cataract surgery (n=4), glaucoma associated with a non-acquired systemic disease (n=3), juvenile open angle glaucoma (n=3) and glaucoma associated with a non-acquired ocular anomaly (n=2). Preoperatively, the mean intraocular pressure (IOP) was 30.0±8.8 mmHg while postoperatively, the mean IOP was 16.0±6.0 mmHg at 3 months (n=25) and 14.0±3.9 mmHg at 12 months (n=17). The mean use of glaucoma drops was 3.3±1.1, 1.4±1.4 and 0.7±1.1 at preop, 3 months and 12 months respectively. Two eyes had an IOP spike associated with persisting hyphaema at one month follow up. Over a median follow up period of 25.9 months, 9 eyes (31%) failed, while absolute success was observed in 13 eyes (45%) and qualified success in 7 eyes (24%).

Discussion/ Conclusion: These early data suggest that GATT using an illuminated microcatheter is safe and effective in cases of childhood glaucoma. However, our study shows that in the paediatric population there is a large percentage of cases where the procedure is technically not possible and predictive factors for that risk need to be explored.

Establishing a model of *USH2A*-associated retinitis pigmentosa using 3D human retinal organoids

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Type of Research: Basic research / **Category**: Retina

Introduction: Pathogenic variants in over 300 genes have been discovered in association with monogenic inherited retinal diseases (IRDs), but mutations in the USH2A gene are the most common cause of autosomal recessive retinitis pigmentosa (RP). Animal models of USH2A-associated retinopathy are limited in the way they recapitulate human disease. We developed an USH2A retinal organoid model to characterize the human disease phenotype using patient-derived induced pluripotent stem cells (iPSCs). We are developing a humanized model of a common IRD to study the pre-clinical application of human cell therapies, including cell transplantation. We hypothesize that USH2A organoids will display abnormal molecular and morphological patterns of development at multiple stages of retinal maturation.

Methods: Retinal organoids were developed from healthy human H9 embryonic stem cells and iPSCs derived from a patient with USH2A-associated RP (hereafter USH2A cultures) to compare healthy and diseased phenotypes. Phase images of H9 and USH2A cultures were taken at Weeks 1 and 3 of 2D differentiation to assess morphological differences in organogenesis during neural induction. At Week 4 of 2D differentiation (optic vesicle formation and initiation of organoid structures), cultures were moved to 3D growth, considered Week 1 of organoid development. Week 1 healthy and diseased organoids were fixed, and immunofluorescence was performed (staining for the retinal progenitor marker Pax6) to assess differences in cellular organization and morphology in early stages of retinal development.

Results: Compared to healthy H9 controls, USH2A cultures displayed increased apoptosis during neural induction (Weeks 1 to 3 of 2D differentiation). At Week 1 of 3D growth, USH2A cultures had markedly lower yield of organoids and were smaller in size compared to controls. USH2A organoids displayed disorganized retinal lamination compared to controls at Weeks 1, 2 and 3 of 3D growth. Staining of Pax6 at Week 1 of 3D growth confirmed both control and diseased organoids continue retinogenesis following neural induction. Pax6 was properly localized to the outer lamina in both groups and no obvious differences in localization and fluorescent intensity between groups was observed.

Conclusions: During early neural retinal development, USH2A cultures 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.

Clinical profile and outcomes of endophthalmitis in children and adolescents

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Research type: Clinical
Category: Retina

Introduction

Endophthalmitis is rare and devastating condition that leads to severe vision loss in high percentages of cases. Unlike adults, children might not be able to recognise or explain their symptoms, making it more difficult to promptly diagnose and treat endophthalmitis in the paediatric population. There is a paucity of studies looking at endophthalmitis in the paediatric patients. The aim of this study is to get a better understanding of the aetiology, risk factors, culture results, management and visual and anatomical outcomes of patients with endophthalmitis presenting to a single centre over the last 20 years.

Methods

A retrospective review of medical records of patients under the age of 18 with a diagnosis of endogenous and exogenous endophthalmitis in Hospital for Sick Children from 2001 to 2021 was carried out. Clinical features, aetiology, causative organisms, management as well as visual and anatomical outcomes were analysed.

Results

17 eyes of 14 children were identified. Age ranged from 3weeks old to 16years old. Endogenous endophthalmitis (64.7%) and previous ocular surgery (29.4%) were the most common aetiologies. 8 (47%) eyes had final visual acuities of 20/50 or better, 1 (5.8%) eye 20/600, 4 (23.5%) eyes has no light perception and 2 (11.8%) eyes were enucleated. Visual acuity unavailable for 2 (11.8%) eyes as 1 patient with bilateral endogenous endophthalmitis died. 2 (11.8%) eyes developed phthisis bulbi, 3 (17.6%) eyes developed retinal detachments, 1 (5.9%) eye developed secondary cataract. 10 (71%) of patients had positive cultures. Gram positive organisms isolated in 6 patients, Gram negative in 3 patients and fungi in 1 patient.

Conclusion

Endogenous endophthalmitis was the most common cause of endophthalmitis in our cohort of patients. In this research the visual outcomes were variable. Patients with post operative endopthalmitis had worse visual outcomes than those with endogenous endophthalmitis. *Streptococcus pneumoniae* is the most commonly identified organism in exogenous endophthalmitis and *Candida species* in endogenous endophthalmitis.

A meta-analysis of neurodevelopmental outcomes following intravitreal bevacizumab for the treatment of retinopathy of prematurity

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Conflicts of interest: AAB: None IZK: None. MMP: Financial support (to institution) – PSI Foundation, Fighting Blindness Canada. GK: None. RHM: Advisory board- Bayer, Novartis, Allergan, Roche; Financial Support (to institution)- Bayer, Novartis. KM: Advisory board – Santen Inc, Bayer, Novartis; Financial Support (to institution) – Bayer. NNT: Financial Support (to institution) – Bayer. TEZ: None. PJK: Advisory board – Novartis, Alcon, Bayer, Novelty Nobility; Financial support (to institution) – Allergan, Bayer, Roche; Financial support – Novartis, Bayer; Equity owner – ArcticDx.

Purpose: To evaluate neurodevelopmental safety of intravitreal bevacizumab (IVB) monotherapy compared to laser photocoagulation (LPC) for retinopathy of prematurity (ROP).

Clinical relevance: ROP is the most common cause of preventable blindness in preterm infants. First-line treatments include LPC or IVB. Despite promising efficacy and increasing clinical use over the last decade, concerns for the safety of IVB have been raised.

Methods: MEDLINE, EMBASE and Cochrane databases were searched up to September 2022 to select studies comparing IVB alone to LPC in infants with type 1 ROP or to observation in infants with ROP not requiring treatment. Studies were included if they reported at least 12-month follow-up of primary outcomes such as severe neuro-developmental impairment (sNDI), cerebral palsy (CP), and hearing impairment (HI). Secondary outcomes were moderate-to-severe impairment (msNDI) and Bayley Scores of Infant Development 3rd Edition (BSID-III). A random effects meta-analysis was performed.

Results: Overall, 1998 articles were identified. 1231 patients from 11 comparative studies were included. Quality of evidence was rated low for all outcomes. IVB was associated with a higher risk for sNDI (risk ratio [RR]=1.25, 95% confidence interval [CI] 1.01, 1.53, *P*=0.04) and CP (RR=1.40, CI [1.08, 1.81], *P*=0.01) compared to LPC. However, an additional analysis comprising 4 articles comparing IVB for infants with type I ROP to infants with ROP not requiring treatment suggested no statistically significant differences in the risk of sNDI (RR=1.41, CI [0.93, 2.14], *P*=0.11). There was no significant difference between IVB and LPC for msNDI (RR=1.15, CI [0.98, 1.35], *P*=0.08) and HI (RR=1.43, CI [0.86, 2.39], *P*=0.17). BSID-III percentile scores were similar between IVB and LPC, with weighted mean differences of 1.51 [CI=-1.25, 4.27], 2.43 [CI=-1.36, 6.22] and 1.97 [CI=-1.06, 5.01] for cognitive, language, and motor domains, respectively (*P*>0.05).

Conclusion: To our knowledge, this is the largest meta-analysis on neurodevelopmental outcomes and the first to rigorously examine IVB monotherapy in ROP treatment. Compared to LPC, there was a marginally increased risk for sNDI and CP with IVB but little or no difference in the risk of msNDI and HI. Moreover, infants who received IVB performed similarly on Bayley-III scales as infants who received LPC or no treatment. Further randomized studies are needed to strengthen these findings.

Adaptive Optics Imaging in Diabetic Retinopathy: A Prospective Cohort Study

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Declarations Of Interest: All stated authors have NO financial or other conflicts of interest to disclose.

Type of Research/Category: Clinical Research/Retina

Background: Adaptive optics (AO) imaging is a non-invasive, ultrahigh-resolution technology that allows for direct visualization of the retina at a microscopic resolution. It enables quantitative evaluation of the retinal vasculature and can count individual photoreceptors. There is currently limited literature on the clinical utility of AO imaging in diabetic retinopathy (DR). The objective of this study was to quantitively evaluate the relationship between DR severity and microscopic retinal and vascular changes based on AO imaging.

Methods: This prospective cohort study recruited consecutive adult participants with healthy eyes or a diagnosis of DR presenting to the Kensington Eye Institute in 2021. DR stage was classified using the Early Treatment Diabetic Retinopathy Study (ETDRS) system and participants were grouped into the following categories: (1) control or mild non-proliferative DR (NPDR); (2) moderate or severe NPDR; (3) proliferative DR. Upon enrollment, subjects underwent AO imaging using the RTX1 retinal camera in addition to fundus colour photo acquisition and non-contact ocular biometry with the IOLMaster 700. AO parameters were measured at 2° and 4° degrees of eccentricity from the fovea in four quadrants (superior, inferior, nasal, and temporal) and in both eyes while correcting for axial-length and performing manual quality assurance. To account for the correlation between multiple retinal images and both eyes of the same participant, we performed a repeated measures analysis using non-parametric generalized estimating equations (GEE).

Results: AO imaging photoreceptor data was collected from 48/48 participants (724 scans, mean age: 61, 79% male), while vascular data was collected from 39/48 participants (325 scans, mean age: 59, 77% male). Within the first 2° of retinal eccentricity in the univariable analysis, there were significant differences ($p<0.05$) between DR groups for all photoreceptor parameters (i.e. regularity, dispersion, density, spacing) and the wall-to-lumen ratio. All other vascular parameters (i.e. total vessel diameter, wall thickness, lumen diameter, vascular wall cross-sectional area) were non-significantly different between DR severity groups. While accounting for eye laterality, age, sex, axial length, and imaging depth, multivariable GEE modelling demonstrated that the strongest predictors for disease severity were cone density ($p<0.001$) and dispersion ($p<0.001$).

Conclusion: To date, this is one of the largest studies evaluating the use of AO in DR, demonstrating its ability to differentiate between various levels of disease severity in DR. These results have implications for the potential use of AO in research and clinical practice for diagnostic and treatment response evaluation at the microstructural level.

Michael Balas | Medical Student | Poster #8

Oculoplastic Procedures: Use of Text-To-Image AI Models for Pre-Operative Counseling

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DECLARATIONS OF INTEREST: All stated authors have NO financial or other conflicts of interests to disclose.

Type of Research/ Category: Clinical Research/Oculoplastics

Background: Pre-operative education and counseling are essential components of patient care, particularly when there will be lasting cosmetic effects. Thus, it is important for patients to fully understand the potential risks and benefits of the procedure, as well as the expected outcomes. To aid this process, we piloted the use of "DALL·E 2", a state-of-the-art text-to-image AI model, for the purpose of creating images that predict the results of oculoplastic surgery.

Methods: Publicly available pre- and post-operative photos of two patients were uploaded to the DALL·E editor interface. One patient was a 54-year-old female with right-sided ptosis and the other was a 48-year-old female with thyroid-associated orbitopathy. We used the DALL·E editor to mask pathological regions in the patient images and provided textual descriptions for how the masked area should be replaced. DALL·E operates by passing user-specified text into Transformer Language Models, producing text embeddings which are then subsequently used to synthesize images with Diffusion Probabilistic Models.

Results: After examining several variations of predicted post-operative images generated by DALL·E, we selected the image that we believed was most accurate and likely to resemble the actual post-surgical appearance of the patient. This entire process, from capturing the photo to uploading and modifying it on the DALL·E editor and having the AI generate the image, was achieved in less than three minutes.

Conclusions: Image editing software for pre-operative counseling is not a new phenomenon, however most products available today are proprietary, expensive, and have a demanding learning curve. The use of text-to-image AI models for pre-operative counseling has the potential to significantly improve the experience for both patients and providers. In addition, the speed and ease of use of this technology allows users to tailor images to the specific needs and concerns of each individual patient. This can help manage expectations and reduce anxiety and uncertainty, leading to improved patient satisfaction. Although this technology is still in its infancy, our results already highlight the potential of these models as useful adjuncts in the preoperative discussion.

Accessibility of Canadian ophthalmology department webpages for the visually impaired

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Authorship Financial Disclosures: None.
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Key Words: Visual Impairment, Ophthalmology, Accessibility technology, Medical Education
Study Design: Cross-sectional study of CUODW.

Purpose: We reviewed Canadian university ophthalmology department webpages (CUODW) to determine their web content accessibility for users with visual impairment or colour vision deficiency.

Methods: The compatibility of fifteen CUODW with the Web Content Accessibility Guidelines version 2.0 (WCAG 2.0) AA international standards for web content accessibility was assessed using automated tools and manual assessment strategies.

Results: The CUODW from all the universities had WCAG 2.0 AA conformance errors. The mean number of errors identified by each tool were: AChecker (18, SD = 15), Web Accessibility (15, SD = 16), and WAVE (12, SD = 14). The mean automated and manual contrast errors identified were 6.5 (SD = 5.4) and 1.5 errors (SD = 2.1) respectively. Most CUODW used appropriate colour combinations.

Violations of WCAG 2.0 guidelines relevant to users with visual impairment that utilize screen readers include the absence of alternative text explaining the content of images (guideline 1.1), controls (e.g., a search bar) with input elements lacking text explaining function (guideline 1.3), and <a> (anchor) elements (hyperlinks) with no information regarding where the link navigates to (guideline 2.4) were observed. Other errors include the improper identification of language so that screen readers can dictate text in the correct pronunciation (guideline 3.1), and redundant use of the same element ID, which may confuse screen readers (guideline 4.1).

Conclusion: We encourage Canadian University Ophthalmology programs to improve their webpage compliance with the WCAG 2.0 guidelines, thus improving digital accessibility to users with visual impairment.

Optic disc appearance in arteritic compared to non-arteritic anterior ischemic optic neuropathy

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Conflict of Interest Statement: All authors declare no conflicts of interest.

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Key Words: Optic neuropathy

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Design and Category: Retrospective review of consecutive patients with AION. Neuro-ophthalmology

Introduction: Anterior ischemic optic neuropathy is the most common acute optic neuropathy, and it is important to differentiate arteritic (AAION) and non-arteritic (NAION) forms. It has been reported that fundus findings differ between AAION and NAION. The goal of this study was to compare the optic disc appearance and other clinical features in consecutive patients with AAION and NAION attending neuro-ophthalmology clinics.

Methods: Consecutive patients with AION were included in the study. Fundus photographs were routinely obtained as part of clinical care for these patients. Clinical data including retinal neve fibre layer (RNFL) thickness, best-corrected visual acuity (BCVA), and visual field mean deviation (VF MD) was retrieved and patients were grouped by etiology.

Results: 112 patients were included in the study (n=100 NAION and n=12 AAION). AAION patients were older than NAION patients (mean = 78±7 years vs. 62 ± 14 years, $p<0.001$). Optic disc edema (ODE) was considered segmental in 50 NAION and 0 AAION patients. Pallid edema was more common in AAION patients (7 of 12) compared to NAION patients (1 of 100). Optic disc hemorrhages were more common in NAION patients (51 in 100) versus AAION patients (6 in 12) whereas peripapillary cotton wool spots were more common in AAION patients. The most common type of hemorrhage was intraretinal in NAION patients and AAION patients. The mode Frisen grade in NAION patients was 2 (IQR: 2-3) compared to 1 (IQR: 1-3) in AAION patients. OCT RNFL thickness was on average 213.96µm in NAION eyes and 165.13µm in AAION eyes ($p=0.117$). The fellow eye optic disc had an abnormality (edema or pallor) in 16 patients with NAION compared to 4 patients with AAION. The cup-to-disc (C/D) ratio was significantly different in the fellow eye of NAION patients compared to AAION patients (0.13 vs. 0.37, $p=0.012$). The presenting visual acuity of the affected eye was worse in AAION patients compared to NAION patients.

Conclusions: There are distinct differences in the appearance of the optic disc edema and fellow eye in NAION and AAION patients. Segmental optic disc edema is more common in NAION patients while pallid edema and peripapillary cotton wool spots are more common in AAION patients. AAION patients are older than NAION patients and the fellow eye has a larger cup-to-disc ratio in AAION. These differences can help in differentiating these two conditions based on the clinical exam.

Bilateral sequential vision loss from giant cell arteritis with persistently low inflammatory markers

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Conflict of Interest Statement: All authors declare no conflicts of interest.
Funding Statement: No funding was received for this work.
Key Words: Giant cell arteritis; Erythrocyte sedimentation rate; C-reactive protein; temporal artery biopsy; vasculitis; anterior ischemic optic neuropathy
Design and Category: Case report. Neuro-ophthalmology.

Introduction: To describe a rare case of sequential vision loss with persistently normal erythrocyte sedimentation rate (ESR) and C-Reactive protein (CRP) separated by 3 months in biopsy-proven giant cell arteritis.

Methods: Chart review.

Results: An 86-year-old woman was referred for left eye vision loss. She had a past medical history of dementia, type 2 diabetes, hypothyroidism, previous stroke and hypertension. She woke up with left eye vision loss two weeks prior to presentation. She denied headache, jaw claudication, scalp tenderness, neck pain, fever, loss of appetite, fatigue or muscle stiffness or pain. Examination reviewed a visual acuity of 20/25 OD and 20/40 OS with a left relative afferent pupillary defect and left optic disc edema. There was a right disc at risk. She was diagnosed with a left anterior ischemic optic neuropathy without any concerning features for GCA based on history. Investigations revealed an ESR of 47mm/hr, C-reactive protein of 4.9mg/L (normal less than 5.0mg/L) and platelet count of 379 (normal 150-400x E9/L). She was diagnosed with left non-arteritic anterior ischemic optic neuropathy (NAION) and a 3 month follow- was arranged. She returned for the 3-month follow-up and her caregiver reported that she had been complaining of headache for the past month and it seemed as if her vision was worse. Her visual acuity was light perception in the right eye and counting fingers OS. She had bilateral tonic pupils and dilated fundus examination showed right diffuse retinal edema, a cherry red spot and significant attenuation of the retinal arterioles OD and left optic disc pallor. Repeat blood work was obtained that day and showed a platelet count of 523 xE9/L, ESR of 25mm/hr and CRP of 1.7mg/L. A temporal artery biopsy was performed and confirmed the diagnosis of giant cell arteritis since there was an inflammatory infiltrate centered on the internal elastic lamina. She was treated with Prednisone 1mg/kg and her caregiver reported that she no longer complained of headaches.

Conclusions: Giant cell arteritis may rarely present with normal inflammatory markers and these may remain normal even months after initial presentation. Platelets may be the only hematological parameter that increases over time. A temporal artery biopsy remains an important diagnostic test to confirm the diagnosis when there are low inflammatory markers but still a reasonable suspicion of GCA.

Development of 3D Printed Eye Models with Normal and Abnormal Red Reflexes

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Introduction: The Red Reflex Exam (RRE) is essential for the early diagnosis of blindness in pre-verbal children. RRE training is insufficient without demonstration of an abnormal red reflex. To the best of our knowledge, there are no 3D eye models that can accurately simulate normal and abnormal red reflexes. This research aims to develop high-fidelity 3D models of the eye that display various ocular diseases and accurately respond to the RRE, with the intention of creating a training tool for a standardized training curriculum.

Methods: 3D digital eye models were created by segmenting MRI scans of eyes with and without retinoblastoma. Models were smoothed and refined using fitting algorithms, complementary patient imaging data, and computer-aided drawing software. Physical eye models were created from the digital models using a combination of casting and 3D printing.

For the first models, the retina, choroid, sclera, iris, and tumour were 3D printed in a mix of soft semi-transparent photopolymer and rigid white photopolymer. We created the corresponding molds for molding clear and smooth cornea and lens. A series of prototypes were created to obtain optically clear cornea and lens.

Prototyping included the use of different 3D printers, printing settings, and polishing techniques. After printing, models were hand painted and assembled. Aqueous humor and vitreous humor simulating liquid were injected into the eyeball.

Results: A patient-derived model with retina, choroid, sclera, iris, cornea, lens, optic nerve and tumour was created. Initial prototypes successfully demonstrated abnormal reflexes, such as leukocoria. Lens and cornea clarity was inadequate early on, but surface smoothness has been improved with recent iterations. There are still some limitations of the initial prototype, including suboptimal retention of intraocular liquid from the model.

Discussion/Conclusion: The 3D physical eye model is showing potential to be a tool to facilitate RRE training and provide a realistic experience to medical students, family doctors and pediatric residents. When a satisfactory prototype is designed, further studies will be performed to validate the 3D models and assess their impacts on the learning outcomes of medical students/physicians.

Lina Chen Research Fellow Poster #13

Decreased cone density in circular retinal regions at the outer edge of full thickness macular hole edema in adaptive optics imaging

Purpose: To introduce a method for analyzing adaptive optics (AO) imaging data on the full thickness macular hole (FTMH) and compare the cone density at the corresponding retinal regions surrounding the outer edge of para-macular hole edema (OEME) between the eyes with the FTMH versus the contralateral non-pathological eye within individual patients.

Method: Twenty-two patients (n=22) between the ages 53 and 73 years were recruited at the Kensington Eye Institute, Toronto. Each patient had one eye diagnosed with FTMH and the contralateral eye with no pathology. The AO images from 44 eyes were captured using rxt1 AO retinal camera. Nine images of each retina was overlapped covering 8ºX8º central retina. The raw fragments of 4ºX4º images were aligned to create a montage with developer-provided software. ImageJ was used for creating a grid. On the FTMH montage, a circle outlining OEME, and two perpendicular lines from diagonal meridians by 45º crossing the center of the macular hole were drawn. On the montage of the contralateral eye, a circle delineating the foveal avascular zone (FAZ), two lines with the same features as those on FTMH montage crossing the center of FAZ were drawn. The grid was created by overlaying the two lines from each montage. The created grid was overlaid on each montage. And the region of interest (ROIs) were sampled and compared with the orientation of the grid.

Results: Of raw images from 22 eyes with FTMH, montage creation failed in 15 eyes (15/22, 68%), which was remarkably higher than contralateral eyes (P=0.01). The shifted fragment images were found in 38.8 % of total images taken from the eyes with FTMH, which was significantly higher than contralateral eyes (7.7%) (P=0.001). The cone density in 4 quadrants by OEME was decreased significantly than the contralateral corresponding retina (p=0.0004). Furthermore, the negative correlation between cone density and spacing at same regions was found in FTMH. (r=0.553, CI 95% [-0.79,-0.16], P=0.009).

Conclusion: The method of grid overlaying on the montage image was applicable to analyzing the AO imaging acquired from eyes with FTMH. Utilizing the grid, we found the cone density in circular retinal regions at the outer edge of ME was significantly decreased in adaptive optics imaging, which indicated that disturbance of the cones may occur outside OEME.

Postoperative dry eye symptoms and secondary healthcare utilization in patients prior to, during, and after the COVID-19 pandemic

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Introduction: Dry eye symptoms (DES) continue to be a significant side effect of cataract surgery affecting quality of life and satisfaction of patients postoperatively. The primary objective of this study is to compare DES in patients following uncomplicated cataract surgery prior to, during, and after the COVID-19 pandemic. Our secondary objective was to identify risk factors associated with postoperative dry eye symptoms.

Method: Data from consecutive patients who underwent uncomplicated cataract surgery in November 2019, 2020, and 2021 in a surgical centre in Ontario, Canada was extracted. Patients included were 18 years or older with preoperative Dry Eye Questionnaire 5 (DEQ5) scores (range: 0-2=none, 3-8=mild, 9-15=moderate, 16-22=severe DES). Sample size calculation based on previous studies was done, and 131 patients were included in each group. Preoperative DEQ5, prophylactic treatment, and presence of DES risk factors (ocular comorbidities, systemic diseases, use of glaucoma medications, intravitreal anti-VEGF injections, OPD mires suggestive of dry eye, previous corneal treatments) were recorded. Number of postoperative visits due to DES concerns were calculated. Odds ratios (OR) of risk of postoperative DES based on preoperative DEQ5 or prophylactic treatment were determined. DES risk factors were analyzed using multivariate regression.

Results: Preoperative DES prevalence and DEQ5 scores pre, during and post-COVID-19 decreased (mean±SD: 6.2±5.5, 3.4±4.4, 2.3±3.4, respectively, $p<0.01$). While the number of total follow-ups has decreased during and post-COVID-19, the percentage of follow-ups attributed to DES has increased (26%, 50%, 40%, respectively). Percentage of patients receiving prophylactic treatment preoperatively did not differ significantly between the groups (41.9%, 37.4%, 35.9%, respectively). In the during and post-COVID-19 groups there was a higher risk of postoperative DES with increasing preoperative DEQ5 score (OR=1.13, 95%CI 1.03-1.24 and OR=1.18, 95%CI 1.03-1.35, respectively). No other risk factors predicted DES, and there was no DES risk reduction in patients receiving preoperative treatment, regardless of DEQ5 score or group.

Discussion/Conclusion: There has been an increase in postoperative DES during and after the COVID-19 pandemic despite a decrease in DES preoperatively. Preoperative DES treatment does not seem to reduce the burden of postoperative DES. More research is needed on DES treatment adherence to determine protective measures.

Post-procedural endophthalmitis visual outcomes by microorganism: A systematic review and meta-analysis

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Introduction: Endophthalmitis is a procedural complication that can lead to complete loss of vision. Understanding the visual outcomes by causative organism can help predict visual prognosis and guide treatment recommendations. The purpose of this study was to compare visual outcomes of endophthalmitis following intravitreal injections (IVI) and cataract extraction (CE) by causative organism.

Method: Searches in Cochrane Central Register of Controlled Trials, MEDLINE, and Embase databases identified articles reporting visual outcome by causative organisms in post-IVI and CE endophthalmitis cases from January 2010-February 2022. Risk of bias was assessed using the Hoy et al. tool. Results were pooled using a random-effects meta-analysis determining visual outcome, and comparing outcomes by culture and gram status. We followed MOOSE guidelines for reporting.

Results: Out of 3317 retrieved studies, 101 were included. The most reported gram-positive organisms in endophthalmitis cases following CE (n=1810) were coagulase-negative staphylococci (CONS, n=282), streptococci (n=81), and enterococci (n=78), and the most common gram-negative organisms were *Pseudomonas* species (n=147), *Burkholderia* species (n=35), and *Stenotrophomonas maltophilia* (n=34). In post-IVI cases (n=599), the most common gram-positive organisms were CONS (n=147), other staphylococci (n=80), and streptococci (n=79) and the most common gram-negative ones were *Citrobacter* species (n=19), *S. maltophilia* (n=10), and *Escherichia coli* (n=9). The highest rates of good visual outcome (≥20/40) were seen in CONS cases for both post-CE (39.60%, 95%CI 24.90, 54.99) and post-IVI (8.49%, 95%CI 2.33, 16.87) endophthalmitis, followed by *Stenotrophomonas maltophilia* (37.02%, 95%CI 17.96, 57.75) and other staphylococci (29.92%, 95%CI 4.59, 61.79) for post-CE cases, and other staphylococci (8.61%, 95%CI 0.00, 35.95) and streptococci (1.12%, 95%CI 0.00, 10.60) for post-IVI cases. For post-IVI endophthalmitis, gram-positive cases showed more VA improvement than gram-negative cases (MD: 1.34, 95%CI 0.53, 2.15; P=0.001, I^2=0%). Gram-negative cases were also more likely to have a poor visual outcome than gram-positive ones (RR: 1.63, 95%CI 1.06, 2.51; P=0.03, I^2=0%) in post-IVI endophthalmitis.

Discussion/Conclusion: CONS had the highest rates of good visual outcomes, and culture negative cases were more likely to achieve a good visual outcome than culture positive cases in post-CE and IVI endophthalmitis. Gram-negative cases had worse visual outcomes than gram-positive cases in post-IVI endophthalmitis.

Computerized Simulation of Retinoblastoma Treatment Using Focused Ultrasound

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Introduction: Retinoblastoma is the most prevalent pediatric eye cancer worldwide and is fatal without appropriate treatment. Current therapies are effective at preventing death but carry risk of complications, including blindness and adverse off-target effects. Furthermore, current therapy options are often limited to small tumors (laser therapy). Focused Ultrasound (FUS) may be a minimally invasive therapeutic strategy for retinoblastoma with limited side-effects. We created anatomically accurate 3D *in-silico* models of the globe and orbit to simulate FUS therapy for retinoblastoma.

Methods: Imaging data for retinoblastoma patients seen at The Hospital for Sick Children between 2001 and 2022 were reviewed. Patients were eligible if evaluated for leukocoria or diagnosed with unilateral or bilateral retinoblastoma at SickKids. Representative patients were selected, and magnetic resonance imaging (MRI) scans were collected for 3D *in-silico* model construction. Using segmentation software (3D Slicer, slicer.org), structures of the eye and orbit were segmented. Each anatomical structure was then assigned acoustic and thermal properties (e.g., speed of sound, specific heat capacity) from literature. A preliminary simulation of the acoustic pressure field was computed for one model, with and without the orbital bones.

Results: 148 patients had eligible data. From these, 14 patients (28 eyes) were selected for segmentation. Fourteen of 28 eyes have been fully segmented. Segmentations were exported as voxel grids and tissue-specific speed of sound values were assigned to each voxel. The first simulation of FUS therapy for retinoblastoma revealed an important consideration for future simulations; *in-silico* eye models with and without orbital bone have differences in the acoustic pressure fields.

Conclusion(s): Preliminary simulations indicate that including the orbital bone in FUS treatment simulations is important for simulating accurate FUS outcomes. For our next steps, we will run simulations on segmentations with various stages of retinoblastoma and different FUS parameters to determine optimal treatment parameters. We will then create polyacrylamide hydrogel-based FUS phantoms based on the segmented *in-silico* models and apply FUS to validate the simulation results. These results will facilitate future animal studies depending on safety and feasibility factors of FUS therapy seen in the phantom and simulation studies.

Fowad Daud Undergraduate Poster #17

Combined versus Sequential Pars Plana Vitrectomy and Phacoemulsification for Macular Hole and Epiretinal Membrane - A Systematic Review and Meta-Analysis

Topic: To compare the efficacy and safety between combined and sequential pars plana vitrectomy and phacoemulsification for macular hole (MH) and epiretinal membrane (ERM).

Clinical Relevance: The standard of care for MH and ERM is vitrectomy, but this increases the risk of developing a cataract. A combined phacovitrectomy surgery eliminates the need for a second surgery.

Methods: Ovid MEDLINE, EMBASE, and Cochrane CENTRAL were searched in May 2022 for all articles comparing combined versus sequential phacovitrectomy for MH and/or ERM. The primary outcome was mean best-corrected visual acuity (BCVA) at 12-month follow-up. Secondary outcomes included refractive error from target, and complications. Meta-analysis was conducted using a random effects model. Risk of bias was assessed using the Cochrane RoB 2 tool for randomized controlled trials (RCTs) and ROBINS-I tool for observational studies. (PROSPERO, registration number, CRD42021257452)

Results: Of the 6470 studies found, 2 RCTs and 8 non-randomized retrospective comparative studies were identified. Total eyes for combined and sequential groups were 435 and 420, respectively. Meta-analysis suggested no significant difference between combined and sequential surgery for 12-month BCVA (combined = 0.38 logMAR, sequential = 0.36 logMAR; mean difference (MD) = +0.02 logMAR; 95% CI = -0.04 to 0.08; p = 0.51, I2 = 0%, n = 4 studies, 398 participants), as well as absolute refractive error (p = 0.76, I^2 = 97%, n = 4 studies, 289 participants), risk of myopia (p = 0.15, I^2 = 66%, n = 2 studies, 148 participants), MH non-closure (p = 0.57, I^2 = 48%, n = 4 studies, 321 participants), cystoid macular edema (p = 0.15, I^2 = 0%, n = 6 studies, 526 participants), high intraocular pressure (p = 0.09, I^2 = 0%, n = 2 studies, 161 participants), posterior capsule opacification (p = 0.46, I^2 = 0%, n = 2 studies, 161 participants), posterior capsule rupture (p = 0.41, I^2 = 0%, n = 5 studies, 455 participants) and retinal detachment (p = 0.67, I^2 = 0%, n = 6 studies, 545 participants).

Conclusion: The results suggest there is no significant difference detected between combined and sequential surgeries for visual outcomes, refractive outcomes, or complications. Given that most studies were retrospective and contained a high risk of bias, future high-quality RCTs are warranted.

Validation of Preloaded DMEK Donor Tissues: A Laboratory Based Study on Endothelial Cell Viability

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Descemet membrane endothelial keratoplasty (DMEK) has emerged as the preferred surgical treatment for Fuchs endothelial corneal dystrophy (FECD) and other causes of endothelial dysfunction leading to bullous keratopathy. Advances in DMEK tissue preparation including eye bank prepared donor tissue that is prestripped, prestamped and preloaded, have helped to reduce intraoperative complications related to tissue preparation as well as avoiding implanting upside down grafts and iatrogenic primary graft failure. With these advances in DMEK donor tissue preparation, it is important to assess the viability of the donor tissue for transplantation by assessing endothelial cell loss and tissue integrity. Laboratory based studies, where tissues are analyzed for endothelial cell density, endothelial cell viability and denuded areas, are an integral part of this tissue validation process. **Purpose**: This study aims to investigate endothelial cell loss (ECL) associated with prestripped, prestained, prestamped, and preloaded DMEK donor tissues with a Geuder tube. **Study design**: Laboratory based study. **Methods**: Donor tissues that failed screening criteria for non-tissue quality relation reasons were included in this study. Donor tissues were prepared by an experienced technician at the Eye Bank of Canada. Briefly, the DMEK donor tissues were stripped, marked with Gentian violet dye applied as an F-mark, trephined, stained with trypan blue and then preloaded into a Geuder tube. The Geuder tube was then capped and placed in an Optisol-GS filled vial. DMEK grafts were unfolded and stained in 3.12 µM calcein AM in 1.7% hyaluronic acid for 15-45 minutes to determine endothelial cell viability after 1 or 5 days. The DMEK donor tissues were imaged using an Incucyte at 4x magnification. The percentage of ECL was determined by 2 independent observers by calculating the surface area of denuded areas compared to total tissue surface area using the Fiji software's Trainable Weka Segmentation plugin. **Results**: Preloaded DMEK tissues analyzed at 1 day displayed an average ECL of 11.9% ± 4.5 (N=8). Preloaded DMEK tissues analyzed at 5 days displayed an average ECL of 9.9% ± 4.2 (N=9). No significant difference in ECL was found between preloaded DMEK tissues after 1 and 5 days of storage. **Conclusions:** Preloaded DMEK donor tissues results in an acceptable range of ECL after 1 and 5 days of storage, and is suitable for transplantation. This may help reduce operative room time required for tissue preparation by the surgeon.

Anatomical and Functional Outcomes of Short-Term DensironXTRA Heavy Silicone Oil for Rhegmatogenous Retinal Detachments: A Comparative Case Series

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Purpose: To assess the safety and efficacy of short-term DensironXTRA tamponade for repair of complicated rhegmatogenous retinal detachments (RRD).

Methods: This is a retrospective consecutive case series of patients undergoing pars plana vitrectomy (PPV) with intravitreal DensironXTRA and a comparator group with gas (sulfur hexafluoride (SF_6) or perfluoropropane (C_3F_8)) tamponades by a single surgeon between January 2017 and November 2020 at a tertiary care centre.

Results: A total of 121 eyes with DensironXTRA and 81 comparator eyes with a gas tamponade were included. The DensironXTRA group had a significantly higher number of cases with inferior breaks (82% vs. 48%; p<0.0001) and a history of previous PPV for RRD (64% vs. 12%; p<0.0001). DensironXTRA was removed after a median period of 70 (IQR: 48.5-105.5) days. There was similar anatomical success in both the comparator gas tamponade and DensironXTRA groups (98.8% versus 97.5%, p=0.6506). Although both groups experienced a significant improvement in visual acuity, this change was significantly higher in the comparator gas tamponade group versus DensironXTRA group (p=0.0017). There was no significant change in IOP in the DensironXTRA group (mean difference -0.7; 95% CI -1.753-0.331, p=0.1785). The rates of complications were low and not significantly different between the two groups. There was no evidence for central macular thinning with DensironXTRA compared to the contralateral eye without RRD as well as with DensironXTRA in situ versus after its removal.

Conclusion: DensironXTRA is a promising short-term tamponade agent with good anatomical and functional outcomes and low rates of complications for the repair of complicated RRDs.

Victoria Romero Fresno Fellow Poster #20

GCC changes in wet AMD patients treated with intravitreal injection according to treat and extend protocol in comparison to non-treated dry AMD.

Introduction : Age-related macular degeneration (AMD) is one of the leading causes of irreversible vision loss and blindness among elderly persons. AMD is a progressive degenerative disease that affect the outer retinal layers of the retina. Recently there have been a few publications studying the effect of repeated intravitreal injection which is the gold standard treatment for wet AMD on the ganglionic cell complex (GCC) of the retina. Such changes can limit the visual outcomes expected from treatment.

Previously reported study found a decrease in the thickness of GCC and RNFL in patients receiving intravitreal injection. Very few studies reported no detectable changes in the GCC thickness.

Previous studies have also found a higher incidence of glaucoma in patients receiving intravitreal injections.

Methods : Objective To detect any GCC thickness change from baseline (0) to end point (Year 2). This will be measured by comparing the OCT images taken at 0, 6months,1 year, 18 months and 2 years intervals.

Prospective observational study cross-sectional study. Patients will be divided into 2 groups 23 eyes in each group.

Group 1: wet AMD being treated with intravitreal injection for 3 years or more following treat and extend protocol.

Group 2: dry AMD who are observed with no treatment for 3 years or more.

For every patient following information will be collected:

- Demographics – age, gender and ethnicity / race.
- Medical and medication history
- Visual acuity
- Intra ocular pressure (IOP).
- Number of intravitreal injections and drug administered

A special pictures obtained by a machine called Spectral domain optical coherence tomography (SD OCT) of each patient will be reviewed as well by the investigator to record the GCC and Retinal nerve fiber layer (RNFL) thickness in all 4 quadrants (superior, inferior, nasal and temporal) of the macula.

Visual field examination with Humphrey visual field analyzer 24-2 program will be done at 6 monthly intervals for 2 years

OCT angiography of macula and optic disc in all 4 quadrants (superior, inferior, nasal and temporal) will be done at 6 monthly intervals for 2 years.

3. Results : Pending

4. Discussion/Conclusion : Pending

Surgical drainage methods during pars plana vitrectomy for rhegmatogenous retinal detachment: a meta-analysis

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Conflicts of Interest: MMP: Financial support (to institution) – PSI Foundation, Fighting Blidness Canada. PJK: Advisory board – Novartis, Alcon, Bayer, Roche, Allergan, Novelty Nobility; Financial support (to institution) – Bayer, RegenXBio, Roche, Novartis; Financial support – Novartis, Bayer, Roche, Boehringer Ingelheim, Pfizer, Zeiss; Equity owner – ArcticDx. RHM: Advisory board- Bayer, Novartis, Allergan, Roche; Financial Support (to institution)- Bayer, Novartis.

Category/ Type of Research: Medical Student Paper/ Meta-Analysis

Introduction: Rhegmatogenous retinal detachment (RRD) is primarily treated with pars plana vitrectomy (PPV); however, there remains no consensus regarding optimal drainage methods. Post-operative efficacy and safety outcomes of different subretinal fluid drainage methods during PPV for RRD were compared in this meta-analysis.

Methods: A systematic search strategy was conducted on OVID MEDLINE, EMBASE, Cochrane CENTRAL, and Google Scholar of studies published between January 2000 and October 2022. Included studies reported on either the safety or efficacy of two or more subretinal fluid drainage methods during PPV for patients with RRD. Risk of bias was assessed using the Cochrane Risk of Bias 2 and Risk of Bias in Non-Randomized Studies – of Interventions tools.

Results: Two randomized and five observational studies consisting of 1524 eyes were included.
There were no significant differences in final best corrected visual acuity (BCVA) (p=0.06), primary reattachment rate (p=0.29), risk of external limiting membrane (ELM) discontinuity (p=0.33), and risk of ellipsoid zone (EZ) discontinuity (p=0.20) between posterior retinotomy (PR) and perfluorocarbon liquid (PFCL). The risk of ERM formation was significantly lower in PFCL compared to PR (RR=0.70, 95% CI=[0.59, 0.83], p=<0.01, I^2=0%). The risk of an abnormal foveal contour was significantly greater in PFCL-treated eyes relative to PR (RR=1.56, 95% CI=[1.13, 2.17], p=<0.01, I^2=0%). Pre-existing retinal breaks (PRB) versus PR revealed no significant differences in final BCVA (p=0.12), primary reattachment rate (p=0.91), risk of ELM discontinuity (p=0.93), and risk of EZ discontinuity (p=0.71). The risk of ERM formation was significantly lower in eyes treated via PRB relative to PR (RR= 0.70, 95% CI=[0.60, 0.83], p =<0.01, I^2=0%). There were no significant differences in final BCVA (p=0.11), primary reattachment rates (p=0.59), risk of ERM formation (p=0.58), risk of ELM discontinuity (p=0.18), and risk of EZ discontinuity (p=0.12) between PRB and PFCL. PFCL compared to non-PFCL demonstrated no significant differences.

Conclusions: There was a higher risk of ERM formation following PPV with drainage via PR compared to PRB or PFCL, and a higher risk of an abnormal foveal contour with PFCL relative to PR. There remains limited information on the topic and additional research is justified.

FUNCTIONAL CHARACTERIZATION OF OPTIC PHOTOTAXIS BEHAVIORS IN *LYMNAEA STAGNALIS* – *A NEW IN VIVO MODEL FOR VISUAL PHOTOTRANSDUCTION*

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TYPE OF RESEARCH/ CATEGORY: Basic Research/Retina

The human visual system is anatomically and functionally complex. Diverse vertebrate models have been used to understand how vision systems function under physiological or pathophysiological states. However, current knowledge on the cellular and molecular mechanisms of photoreceptor regeneration following optic nerve injury remains inadequate, and identification of new animal models for study of the fundamentals of vision is critical. While *in vivo* models of invertebrate vision and light sensitivity have been indispensable to assessing the diversity of visual behaviors in animals and mechanisms for retinal regeneration, few have been developed. The freshwater pond snail *Lymnaea stagnalis* has critical anatomical features of the visual system, including pigmented photoreceptor cells in its retina, and exhibits positive light sensitive locomotion. These phototactic behaviours are driven by photoreceptor activation in the retina, downstream signalling via a phototransduction pathway, and CNS integration of light information to elicit a motor response. In this study, we have taken advantage of these valuable features of *L. stagnalis,* as well as our recent genomic and transcriptomic work as a part of the international *L. stagnalis* sequencing consortium, to establish for the first time a new platform assessing visual system function via analysis of phototaxis behaviors and the underlying molecular basis. To understand visual light perception, we first implemented machine learning-based pose estimation to create a novel *in vivo* model of mollusk phototaxis using DeepLabCut software. We established a robust pipeline for extrapolating features of *L. stagnalis* phototaxis locomotion (i.e., trajectory length, speed, acceleration, and tortuosity) and uncovered that most animals in a cohort exhibiting positive phototaxis behaviors. To better understand the distribution of photoreceptor cells implicated in light-sensitivity, we next conducted thorough histological screens of *L. stagnalis* retinal layers and rhodopsin-positive tissues. Finally, to elucidate the molecular basis of phototransduction, we conducted the first detailed phylogenetic assessment of *L. stagnalis* rhodopsin and other proteins essential to visual phototransduction, highlighting the deep conservation of this signalling pathway. Taken together, we have established for the first time a high-throughput experimental model to characterize phototaxis using machine-leaning approaches and demonstrated that the *L. stagnali*s visual system has the fundamental machinery for visual processing, and thus is an excellent *in vivo* model for assessing the fundamentals of visual phototransduction. We anticipate that this model will serve as an exciting opportunity for research into photoreceptor regeneration in invertebrates, with direct clinical implications for addressing visual diseases.

Combined anti-vascular endothelial growth factor and steroid treatment compared with standalone anti-vascular endothelial growth factor treatment for macular edema secondary to retinal vein occlusion: a meta-analysis

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Keywords: dexamethasone, triamcinolone acetonide, ranibizumab, bevacizumab, aflibercept

Conflicts of Interest: MMP: Financial support (to institution) – PSI Foundation, Fighting Blindness Canada. RHM: Advisory board- Alcon, Bausch + Lomb, Bayer, Novartis, Allergan, Roche; Financial Support (to institution)- Bayer, Novartis, Roche. PJK: Advisory board – Novartis, Alcon, Bayer, Roche, Allergan, Novelty Nobility; Financial support (to institution) – Bayer, Roche, Novartis; Financial support – Novartis, Bayer, Roche, Boehringer Ingelheim, Pfizer, Zeiss; Equity owner – ArcticDx.

Study Design: Systematic review and meta-analysis

Purpose: This meta-analysis aims to compare the safety and efficacy of combined intravitreal steroids and anti-vascular endothelial growth factor (anti-VEGF) agents with anti-VEGF monotherapy in treating macular edema (ME) secondary to retinal vein occlusion (RVO).

Methods: A systematic search strategy from January 2005 to October 2022 on Ovid MEDLINE, EMBASE and Cochrane Library was conducted. Randomized clinical trials (RCTs) reporting on patients treated with either a combination of steroid and anti-VEGF agents or anti-VEGF monotherapy were included if they reported on I) best-corrected visual acuity (BCVA) at last study observation or change in BCVA, or II) retinal thickness (RT) at last study observation or change in RT. A random effects meta-analysis was conducted.

Results: This review included six RCTs and 271 eyes at baseline. Anti-VEGF combined with steroids and anti-VEGF monotherapy achieved a similar change in BCVA by last study observation (p=0.48). Combined anti-VEGF and steroid agents were associated with a significantly better BCVA at last study observation in four RCTs relative to anti-VEGF monotherapy (WMD=0.09 logMAR, 95% CI=[0.03,0.15], p=0.003, I^2=0%). Intravitreal anti-VEGF agents and combined anti-VEGF and steroid agents were not significantly different in the incidence of IOP and cataract-related adverse events.

Conclusion: Our meta-analysis of six RCTs found that combined anti-VEGF and steroid treatment achieved a significantly better BCVA at last study observation than anti-VEGF monotherapy. Optical coherence tomography (OCT) parameters and adverse events were similar between treatment modalities at final follow-up.

Efficacy and safety of anti-vascular endothelial growth agents for the treatment of polypoidal choroidal vasculopathy: a systematic review and meta-analysis

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Conflicts of Interest: MMP: Financial support (to institution) – PSI Foundation, Fighting Blindness Canada. RHM: Advisory board- Alcon, Bausch + Lomb, Bayer, Novartis, Allergan, Roche; Financial Support (to institution)- Bayer, Novartis, Roche. PJK: Advisory board – Novartis, Alcon, Bayer, Roche, Allergan, Novelty Nobility; Financial support (to institution) – Bayer, Roche, Novartis; Financial support – Novartis, Bayer, Roche, Boehringer Ingelheim, Pfizer, Zeiss; Equity owner – ArcticDx. DTW: Consultant –AbbVie, Alcon, Apellis, Bayer, Bausch Health, Biogen, Boehringer Ingelheim, Novartis, Ripple Therapeutics, Roche, Topcon, Zeiss. Research grants from Novartis, Roche.

Abstract

Purpose: There remains limited agreement regarding the efficacy and safety of different anti-VEGF agents for the management of polypoidal choroidal vasculopathy (PCV). Herein, we report on a meta-analysis comparing different anti-VEGF agents for the treatment of PCV.

Study Design: Systematic review and meta-analysis.

Methods: Ovid MEDLINE, EMBASE, and Cochrane Library were systematically searched from January 2000 to July 2022. We included articles comparing the efficacy and safety of different anti-VEGF agents, specifically bevacizumab (BEV), ranibizumab (RAN), aflibercept (AFL) and brolucizumab (BRO), for patients with PCV. We excluded non-comparative studies, non-English studies, literature reviews, and studies reporting on less than 10 eyes. A random effects meta-analysis was conducted.

Results: 10,440 studies underwent title and abstract screening, 122 studies underwent full-text review and ultimately six studies were selected for inclusion. Overall, one study was a randomized trial and the remaining six were observational studies. RAN and AFL were associated with a similar BCVA at last study observation in three observational studies (WMD=5.54 ETDRS letters, 95% CI=[-1.08, 12.15], p=0.10, I^2=78%). Retinal thickness was not significantly different between these two comparators in two observational studies (p=0.85). One observational study comparing BEV vs RAN found comparable outcomes for final BCVA (p=0.89), retinal thickness (p=0.74) and polypoidal regression (p=0.92). One randomized trial on BRO vs AFL found comparable outcomes for improvement in BCVA, while anatomical outcomes favoured BRO.

Conclusions: There is a paucity of evidence comparing different anti-VEGF agents for the treatment of PCV and further investigation is warranted. The available evidence suggests that final BCVA is comparable across anti-VEGF agents.

SNAP-25 but not SNAP-23 is essential for photoreceptor function and survival in mice

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Design and Category: Basic, Retina

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. In photoreceptors, SNARE-mediated vesicular transport is considered to play critical roles in the exocytosis of neurotransmitters and the delivery of photopigments. Synaptic changes and failure to replenish photopigments commonly precede photoreceptor degeneration and can result in blindness.

SNARE-mediated fusion involves three core proteins, a syntaxin and SNAP protein found on the target plasma membrane, along with a VAMP protein found on the vesicle. Recent studies have identified that syntaxin-3 is the unique syntaxin isoform that is essential for photoreceptor survival and function, however, its partner SNAP protein remains in question. We hypothesize that syntaxin-3 along with this undefined SNAP protein plays a role in photoreceptor vesicle release. Using photoreceptor-specific conditional knockout (cKO) mice, we investigate the role of candidate proteins SNAP-23 and SNAP-25 in photoreceptor vesicle transport.

Despite finding SNAP-23 mRNA present in photoreceptors, removal of SNAP-23 led to no noticeable phenotype in SNAP-23 cKO mice. We find that the level of SNAP-25 mRNA was developmentally regulated in photoreceptors with the strongest expression occurring at neonatal ages, and accordingly, removal of SNAP-25 led to rapid retinal degeneration. The degeneration observed comprised of structural abnormalities paired with a complete loss of visual functioning demonstrated by electroretinograms and visual acuity.

Using this study, we uncover that the other target plasma membrane SNARE protein required for vesicle fusion in photoreceptors is SNAP-25. Conditional removal of SNAP-25 from photoreceptors phenocopied what was observed in syntaxin-3 cKO mice. Therefore, together with syntaxin-3, SNAP-25 is the essential isoform for photoreceptor survival and function.

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Quantifying the Availability of Social Determinants of Health Data in the Electronic Health Record of Pediatric Ophthalmology Patients

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Abbreviations and Acronyms: Social Determinants of Health (SDOH), SickKids Department of Ophthalmology and Vision Sciences (DOVS), Electronic Health Record (EHR), Forward sortation area (FSA), International Classification of Diseases 10th Revision (ICD-10), Postal Code OM Conversion File Plus (PCCF+)

Key words: Ophthalmology, Social Determinants of Health, Health Inequities, and Electronic Health Record
Type of Research: Clinical Research
Category: Epidemiology/ Public Health

Correspondence

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Human Subjects: Human subjects were included in this study. Research Ethics Board SickKids approval was provided to this project. All research adhered to the tenets of the Research Ethics Board of the Hospital for Sick Children. The requirement for informed consent was waived. No animal subjects were used in this study.

Objective: The conditions in which we are "born, live, learn, work, play, worship, and age," are known as the Social Determinants of Health (SDOH). SDOH have been shown to impact the development and treatment of eye conditions in pediatric populations. Electronic health records (EHRs) offer a potential source of SDOH information, however missing and misplaced data are known limitations of EHRs. We aimed to quantify the availability of SDOH data in the EHR of patients managed in the SickKids Department of Ophthalmology and Vision Sciences (DOVS) and characterize the population by SDOH.

Methods: A retrospective cohort study design was implemented with study dates between June-1st-2018 through May-23rd-2022. Study subjects were eligible if they: (i)were primarily managed in the SickKids DOVS; (ii)had at least one encounter within SickKids DOVS, and (iii)resided in Ontario. Data collected from the EHR included: Medical-Record-Number, sex, modified date of birth (MM-YYYY), ethnic group, preferred language, interpreter needed, postal code, guardians listed, legal guardian status, public insurance status, and diagnosis data (ICD-10-CM). Postal code was used to deduce neighborhood income quintile, geographic location, and urban/rural status using CHASS Canadian Census Analyzer along with PCCF+, and the first/second digits of the FSA of postal codes, respectively. Summary statistics were used to determine the proportion of study subjects with available data for each SDOH variable, and characterize the total study population using the available data.

Results: Our study population consisted of 26,102 patients. Data on sex, age, postal code, insurance status, and guardians listed were available for 99% of patients, respectively. The legal guardian status and preferred language was available for 85%. Ethnic group was available for 0.14%, non-English preferred language for 9.3% and use of language interpreter for 0%. The study population was 52.5% male and 47.5% female. Most participants (44.6%) were 5-13 years of age at time of data collection. The most prevalent preferred language was English (75.9%). Most study subjects (99.09%) were registered with the Ontario Health Insurance Program and resided in urban areas (92.95%). Central Ontario was the most common geographic location (48.92%). The most common neighbourhood income quintile among participant families was the highest quintile (21.7%). Lastly, study subjects had 31,288 unique eye-related diagnoses representing 57 unique ICD-10 definitions.

Conclusions: Our study demonstrates that the coverage of SDOH was highly variable, with large amounts of data from variable groups such as ethnic group, preferred language, use of language interpreter and legal guardian status missing.

Human Placental Tissue and Cell derived HLA-G+ Extracellular Vesicles for the Treatment of Corneal Injury and Corneal Transplant Rejection

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Type of research/ Category: Basic research/ Cornea

Introduction: In response to significant injury, the cornea's immune tolerance is ablated, resulting in inflammation, scarring, and subsequent vision loss. Currently, there are no effective therapies to reduce or reverse corneal scarring. The only way to restore vision is through corneal transplant. However, this comes with the risk of transplant rejection.
The human placenta also displays immune tolerance, largely mediated by the immunomodulatory and anti-inflammatory molecule human leukocyte antigen-G (HLA-G). Extracellular vesicles (EVs) containing HLA-G (HLA-G+ EVs) are secreted by the placenta during development and are involved in the placenta's immune tolerance. As HLA-G has also been detected in the cornea, and is hypothesized to be involved in its immune tolerance, HLA-G+ EVs have potential to restore immune tolerance in the cornea following injury.

Objectives: 1) To isolate HLA-G+ EVs from human placenta tissue and trophoblast cells (HTR-8 cell line), and 2) To study the therapeutic potential of placenta-derived HLA-G+ EVs to reduce corneal transplant rejection and corneal scarring.

Methods: Human placental villi were placed in culture media for 48 hours at 37˚C. HTR-8 cells were incubated in culture media for 24, 48 or 72 hours at 3% or 20% O_2. Conditioned media from placenta or HTR-8 cells was collected and enriched for EVs with aqueous two-phase separation (ATPS). ATPS reagent (polyethylene glycol and dextran) was added to the conditioned media, centrifuged and the EV-enriched dextran phase collected. To confirm enrichment of HLA-G+ EVs, the conditioned media before and after ATPS was analyzed by nanoscale flow cytometry in triplicate. Isolated EVs were stained with anti-HLA-G antibodies or their isotype controls. A gating strategy was used to quantify events (events/μL) similar in size and complexity to EVs, that were also positive for HLA-G.

Results: HLA-G+ EVs were detected in the conditioned media of all 5 placentas (gestational ages: 5-10 weeks) with a mean concentration of 1194±420 events/μL, which was significantly more compared to the controls ($p<0.05$). HLA-G+ EVs were detected in HTR-8 cell conditioned media ranging from 506-2457 events/μL. The mean enrichment of placenta-derived HLA-G+ EVs with ATPS was 9.8-fold (n=3 placentas).

Discussion/Conclusion: We have identified and enriched HLA-G+ EVs in conditioned media from human placentas and trophoblast/HTR-8 cells. Our future aim is to enhance HLA-G+ EV production in trophoblast/HTR-8 cells through lentiviral transduction, and to evaluate the ability of these HLA-G+ EVs to treat corneal transplant rejection, inhibit neovascularization and enhance wound regeneration in corneal cell lines and animal models.

Outer Retinal Hyperreflective Dots, A Potential Biomarker In Rhegmatogenous Retinal Detachment

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Introduction: To investigate the relationship between hyperreflective dots (HRDs) on optical coherence tomography (OCT) in primary rhegmatogenous retinal detachments (RRD) with preoperative clinical characteristics and assess their potential as a prognostic imaging biomarker for postoperative outcomes.

Methods: This retrospective study reviewed 1,768 consecutive primary fovea-off RRDs referred to St. Michael's Hospital, Toronto, Canada between January 2012-September 2022. Patients with gradable OCT at presentation were included. Exclusion criteria included re-detachments or any prior macular pathology. Visual acuity (VA) was obtained at baseline, 3, 6 and 12 months. Baseline foveal OCT scans were graded for the presence of HRDs in the outer retina, morphological stage of RRD in the parafovea (according to Melo et al. 2022) and foveal photoreceptor integrity. Epiretinal membrane (ERM) and cystoid macular edema (CME) were graded on post-operative OCT.

Results: A total of 353 consecutive patients were included, of which 30 were fovea split, and 323 were fovea-off RRDs. The proportion of patients in Stages 1, 2, 3a, 3b, 4 and 5 was 2%(n=7), 13%(n=45), 15%(n=54), 35%(n=124), 23%(n=82) and 12%(n=41), respectively. The presence of HRDs was associated with reduced VA at 3, 6 and 12 months ($p<0.001$) after excluding patients with visually significant cataracts. HRDs were also associated with the height of foveal detachment, duration of central vision loss, and RRD extent ($p<0.001$). Increasing stage of RRD was also associated with HRDs ($p <0.001$). This finding was also significant whilst focusing only on the integrity of foveal photoreceptors ($p <0.001$). HRDs were neither associated wbith ERM formation post-operatively nor with its severity ($p=0.278$). However, they were associated with CME at 3 and 6 months postoperatively ($p=0.018$; $p=0.006$).

Conclusions: HRDs have been hypothesized to consist of intraretinal inflammatory cells. We have found that HRDs were significantly associated with the morphologic stage, extent, duration, and height of the RRD preoperatively and with reduced VA and CME postoperatively. Our results suggest that HRDs are associated with outer retinal degeneration, as long-standing and extensive RRDs are more likely to present with HRDs. The association of HRDs with CME provides some insight on the possible importance of inflammatory processes in RRD pre and postoperatively.

Systemic Arterial and Venous Occlusions Associated with Anti-VEGF Injections: A Meta-Analysis

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

Abstract

Purpose: In this meta-analysis, we aimed to compare the risk of systemic arterial and venous thrombotic events between ranibizumab, bevacizumab, aflibercept, brolucizumab, and sham injections.

Methods: This was a random effects meta-analysis. A systematic search was performed on Ovid MEDLINE, EMBASE, and Cochrane Controlled Register of Trials from January 2005 to September 2021. Inclusion criteria included published randomized clinical trials (RCTs) reporting on systemic arterial and thrombotic adverse events for standard dose intravitreal anti-VEGF agents for any indication. Non-randomized, non-comparative, and non-English studies were excluded.

Results: Nineteen randomized clinical trials reporting on 10,486 eyes were included. In total, there were 60/1638 (3.6%) arteriovenous events in the bevacizumab group and 68/1643 (4.1%) in the ranibizumab group. Across all studies if considering only arterial events, there were 50/1799 (2.8%) events in the bevacizumab group, 66/1809 (3.6%) in ranibizumab, 98/3213 (3.1%) in aflibercept, and 12/730 (1.6%) in brolucizumab. There was no significant difference in the risk of any thrombotic events between bevacizumab 1.25 mg and ranibizumab 0.5 mg (RR= 0.78, [0.40-1.53], p=0.47). There was also no significant difference between bevacizumab and ranibizumab when restricting to arterial thrombotic events (RR=0.75, [0.47-1.19], p=0.21) or venous thrombotic events (RR=1.61, [0.50-5.20], p=0.43) as separate cohorts. The risk of arterial thrombotic events was similar between aflibercept and bevacizumab (RR = 1.26 [0.65, 2.47], p=0.49), between aflibercept and ranibizumab (RR = 0.69 [0.43, 1.11], p=0.13), and between brolucizumab and aflibercept (RR= 0.67 [0.32, 1.38], p=0.27). Finally, compared to sham injections, ranibizumab did not present a significant increased risk for arterial thrombotic events (RR= 1.40 [0.89-2.19], p=0.14).

Conclusion: Overall, there was a similar risk level for systemic arterial and venous thrombotic adverse events between different anti-VEGF agents and between ranibizumab and sham injections. Our results reinforce previously demonstrated safety afforded by these treatments and reveals equivalent safety in terms of post-injection arterial and venous thrombotic events.

Optical coherence tomography biomarkers as potential predictors for visual function and response to intravitreal therapy in diabetic macular edema: a review

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Introduction
Diabetic macular edema (DME) is one of the most common causes of vision loss in patients with diabetes and Optical Coherence Tomography (OCT) is our modern-day gold standard for diagnosing and following DME. The aim of this study was to synthesize a broad range of OCT biomarkers and their association to 1) visual acuity (VA) 2) response to intravitreal therapy (both corticosteroids and anti-VEGF) in DME.

Methods
A qualitative literature search of OVID Medline was conducted to identify studies from 2017-2022 that investigated OCT biomarkers in relation to visual function and response to treatment in DME. All quantitative study types were included and review articles were excluded. In total, 31 studies were included, through which 23 OCT biomarkers were included.

Results
Disorganization of the inner retinal layers (DRIL), presence of epiretinal membrane (ERM), ellipsoid zone (EZ) and external limiting membrane (ELM) continuity were the most reported biomarkers. Absence of baseline DRIL/ERM, as well as preserved ELM/EZ continuity was associated with a better final VA and improved response to all IVI in most studies. Lower choroidal vascular index (CVI) was associated with a favorable response to anti-VEGF and a poorer response to corticosteroids. Studies reporting hyper-reflective dots (HRDs) showed mixed results.

Degradation of the RPE, increased central retinal thickness (CRT), and foveal eversion were all associated with poor visual outcomes and poor response to both anti-VEGF and corticosteroid IVI.

While all studies reported similar trends in biomarker levels post anti-VEGF and corticosteroids, certain biomarkers (DRIL, HRD, NLR and CRT) were found to be more responsive to global cytokine suppression using corticosteroids than anti-VEGF.

Conclusion
The absence of DRIL/ERM and preserved EZ/ELM continuity are widely reported to be associated with more favorable visual outcomes. Fewer data was reported on CVI, RPE continuity, NLR, CRT, and HRDs. With advancement in modern OCT imaging technology, further prospective studies and findings on OCT imaging biomarkers may be helpful in developing more targeted and personalized treatments for patients with DME.

The impact of eyewear insurance coverage on utilization of eye care providers in a publicly funded healthcare system

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Type of research/ Category: Clinical/ Epidemiology / Public Health

Introduction: Eye exams by an optometrist or ophthalmologist (termed "eye care providers" (ECPs)) are required to obtain prescription eyewear (eyeglasses and contact lenses), which can be expensive and are not usually publicly funded. In 2004, government-funded routine eye exams were delisted for Ontarians aged 20-64 leaving coverage only for those aged ≤19 and 65+. We assessed whether eyewear insurance impacts the utilization of ECPs in Ontario.

Methods: We analyzed data from Ontarians aged 12+ responding to the Canadian Community Health Survey in 2003, 2005, and 2013/2014. We compared the utilization of ECPs by eyewear insurance status, eligibility for government-funded eye exams, and sociodemographic factors, using univariate analyses and adjusting for confounding effects using multivariable analyses. Only respondents without diabetes were included as diabetic eye care was insured for all age groups in all survey years.

Results: The utilization of ECPs was significantly higher in Ontarians aged 12+ with eyewear insurance than those without (42.1% vs 37.4% in 2003, 42.4% vs 37.5% in 2005, and 44.0% vs 35.9% in 2013/2014; $p<0.05$ for all). This higher level of utilization was seen in age groups with (12-19 and 65+) and without (20-64) government-funded eye exams (Figure 1). The difference between individuals with and without eyewear insurance was particularly evident among those aged 20-64 in 2013/2014, when this group no longer had government-funded eye exams (34.9% vs 19.9%, a gap of 15.0%, $p<0.05$ among 20-39-year-olds and 43.4% vs 32.9%, a gap of 10.5%, $p<0.05$ among 40-64-year-olds). In comparison, the gap difference was 5.6% (51.9% vs 46.3%, $p<0.05$) among those aged 12-19 and 7.5% (66.4% vs 59.1% , $p<0.05$) among those aged 65+ in 2013/2014. Adjusting for confounding effects, the likelihood of utilizing an ECP was greater among individuals with eyewear insurance than those without (adjusted prevalence ratio (aPR) of 1.41 for those aged 20-64, and 1.10 for those aged 65+; $p<0.05$ for both). Males, individuals from households with less than secondary school education, and individuals from households below mid-level income were less likely to utilize ECPs (aPR 0.84, 0.91, and 0.84, respectively; $p<0.05$ for all).

Conclusions: Lack of insurance coverage for prescription eyewear negatively impacts the utilization of ECPs, even among those eligible for government-funded routine eye exams (12-19 and 65+). This result suggests that the cost of eye exams may not be the only financial barrier influencing the individual decision to undergo vision assessment.

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

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Purpose: There is currently a lack of validated patient-reported outcomes (PROMs) to evaluate treatment outcomes of corneal anesthesia (CA), retinoblastoma (RB), and strabismus (SB) patients. 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 ≥ 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). 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 content of FACE-Q was comprehensible and relevant to CA, RB, and SB patients. After round 1, some modifications, including expanding recall periods, removing concepts that were not relevant 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 to improve the comprehensiveness, were made. In round 2, participants indicated that these modifications were relevant and acceptable and that the modified FACE-Q was more relevant, comprehensible, and comprehensive compared to the original version.

Discussion/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. Next steps include validation and psychometric evaluation of the modified FACE-Q.

Amyotrophic Lateral Sclerosis Mice Eyes Reveal Retinal Nerve Fiber Layer Changes Over Time: An *In Vivo* Imaging Study

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Purpose: Amyotrophic Lateral Sclerosis (ALS) is a disease characterized by degeneration of motor neurons without any cure. An accessible and non-invasive biomarker for ALS is urgently needed for clinical trials. We recently discovered axonal spheroids in the retinal nerve fiber layer (RNFL) in post-mortem eyes of ALS patients which are comparable to spheroids seen in motor neurons of ALS patients[1]. We conducted a longitudinal *in vivo* imaging study to determine whether similar retinal changes can be detected in a commonly used ALS mouse model.

Methods: *In vivo* eye imaging of ALS mice (ALS mouse model $SOD1^{G93A}$, 2 months old, n=12, 6M, 6F) and age-matched control mice (C57BL/6J, n=12, 6M, 6F) was performed biweekly for 12 weeks. Spectralis (Heidelberg Engineering) with Confocal Scanning Laser Ophthalmoscope (cSLO) with infrared (IR, 815 nm) and Blue Reflectance (BR, 488 nm) modalities and Optical Coherence Tomography (OCT, 870 nm) were used for each imaging session. The fundus was observed with cSLO, and OCT was used to validate puncta location in the RNFL. Retinal fundus puncta localized in the RNFL by OCT were counted in both retinas in a masked fashion. Body weight and ALS clinical motor scoring were performed weekly. IOP of each eye was measured in week 1 and week 12 of the experiments. Changes in the number of puncta over time were analyzed using a Generalized Linear Mixed-Effect Model (GLMM, RStudio).

Results: OCT imaging of the ALS mouse eyes revealed discrete hyperreflective puncta within the RNFL. Compared to age-matched controls, a significant increase in the number of hyperreflective puncta was observed at all time points and increased significantly from 2 months to 5 months ($p=0.023$). By week 12, ALS mice showed 8 ± 8.4 puncta in both retinas compared to age-matched control mice which showed 0.25 ± 0.62 ($p<0.001$). The results from the GLMM showed that both ALS mutation ($p<0.001$) and gender ($p=0.003$) significantly affected hyperreflective puncta growth over time. Female ALS mice also showed a significant increase in IOP in both eyes ($p=0.02$).

Conclusion: The findings of discrete hyperreflective puncta in the retinal nerve fiber layer of the ALS mice with increasing age, and their significant association with both ALS mutation and female gender point to new understandings of this ALS biomarker of axonal degeneration.

1. Sharma, K. *et al.* Retinal Spheroids and Axon Pathology Identified in Amyotrophic Lateral Sclerosis. *Invest. Ophthalmol. Vis. Sci.* **61**, 30 (2020).

Analysis of the Electroretinogram with Machine Learning to Identify Patients with Retinal Disease

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ABSTRACT

We analyse ERG responses at three hierarchical levels: indi- vidual signal (1), single test (2), set of tests (3). At the first (1) level, six standard ISCEV responses are analysed indepen-dently: DA 0.01, DA 3, DA 10, DA 3 OPs, LA 3, LA 30Hz Flicker. We aim to discover informative implicit topological features of each type of waveform to effectively cluster the traces. Such features include first and second order derivatives etc. At the second (2) level, we investigate whether character- istics of different responses within a single test are correlated.At the third (3) level, a full-field ERG test is considered in context of the whole population.

METHODSPre-processing

Extraction and transformation pipeline (ET) was developed to retrieve patient test data from a secure digital storage. Weonly extract the aggregated (arithmetically averaged) traces from the binary test file, ISCEV standards for full-field ERGtesting mandate 5 and recommend 1 waveform responses to different light intensities and retinal adaptation state. Age andgender of a subject as of test day are saved. Having applied the ET procedure to multiple database records, six datasets are generated. Each dataset contains multiple waveforms of asingle type (there are six types of waveforms in the full-fieldERG test).

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 foreach waveform.

WAVEFORM LABELING

Clinical reports prepared by an electrophysiogist (TW) and stored in Microsoft® Word format, were parsed Line-by-lineto identify and extract the waveform labels. They are then assigned to the corresponding entries in the six datasets.

SAMPLE SIZE

1850 full-field ERG tests are involved in the research (11100waveforms in total). Around 3% of the tests contain unreliable data or the waveform labels cannot be identified.

RESULTS

Binary classification exercise was performed for each of the six full-field ERG waveform types. The accuracy scores are reported in Table 1.

DA0.01	DA3	DA10	DA3 OPs	LA3	LA 30Hz
90	91	90	93	90	93

Table 1. ROCKET - binary time series classification accuracy, %.

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Evaluation of Pars Plana Vitrectomy with and without Supplemental Scleral Buckle for the Repair of Rhegmatogenous Detachment due to Inferior Retinal Breaks: A Systematic Review

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Abstract:

Title: Evaluation of Pars Plana Vitrectomy with and without Supplemental Scleral Buckle for the Repair of Rhegmatogenous Detachment due to Inferior Retinal Breaks: A Systematic Review

Purpose:

To investigate the efficacy of scleral buckle (SB) with pars plana vitrectomy (PPV) compared to PPV alone in eyes with rhegmatogenous retinal detachment (RRD) due to inferior retinal breaks (IRB).

Methods:

MEDLINE, Cochrane Library, and EMBASE were systematically searched (2000-2022) for randomized clinical trials (RCTs) and observational studies comparing PPV versus PPV/SB for patients with RRD secondary to IRB. The primary outcome was final best corrected visual acuity (BCVA, logMAR), while secondary outcomes included single surgery anatomic success, final anatomic success (FAS), and complications. Results were reported using descriptive statistics.

Results:

Amongst four studies collectively examining 696 eyes, three studies demonstrated that there was no significant difference between PPV and PPV/SB for final BCVA, while one study reported better BCVA with added SB ($p=0.021$). PPV/SB yielded comparable single surgery anatomic success and final anatomic success in three studies relative to PPV alone, however one study reported better single surgery anatomic success with added SB ($p=0.036$). When further stratifying by lens status, the benefit of PPV/SB for single surgery anatomic success was specifically seen in phakic eyes ($p=0.046$). There were no significant differences in the risk of complications between treatment groups.

Conclusion:

Across a limited set of studies, PPV and PPV/SB were associated with similar functional outcomes and risk profile, while single surgery anatomic success may be improved with PPV/SB in phakic eyes with RRD due to IRB.

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

A data-driven model for simulating longitudinal visual field tests in glaucoma.

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Conflict of Interest: All authors claim no conflict of interest.

Purpose: Accurate visual field (VF) progression detection remains one of the most challenging tasks in glaucoma management due to the absence of the ground truth status for VF progression. To this end, this study develops and validate a data-driven model to simulate longitudinal VF data with known progression rates.

Methods: Longitudinal VF tests of 1008 eyes from 755 glaucoma patients were used to learn the statistical features of VF progression and construct a unified pool of noise templates [1] that account for spatially correlated noise in the VF measurements. The learned non-parametric statistical features and known anatomical correlations between VF test points [2] were used to automatically generate progression maps that are consistent with the VF defect pattern in any baseline test of glaucoma patients. Then, VF sequences were constructed by adding spatially correlated noise templates with random sampling to the generated progression maps. In evaluation, the two one-sided tests (TOST) procedure was used to analyze the equivalence between simulated data and data from glaucoma patients. The equivalence bounds used in TOST tests were derived according to clinical conventions. Moreover, we compared the detection rates of VF progression between the simulated VF data and glaucoma patients using mean deviation (MD), cluster, and pointwise trend analysis.

Results:VF global indices (MD and Pattern Standard Deviation), MD linear regression slopes, and progression detection rates (using global, regional, and pointwise trend analysis) for the simulated and patients' data were all practically equivalent (TOST $P < 0.01$). Specifically, in glaucoma patients, the detection rates in 7 years using MD, cluster, and pointwise trend analysis were 24.4%, 26.2%, and 38.4%, respectively. In the simulated data, the mean detection rates (95% confidence interval) for MD, cluster, and pointwise trend analysis were 24.7% (24.1%–25.2%), 24.9% (24.2%–25.5%), and 35.7% (34.9%–36.5%), respectively. Qualitative examples demonstrated that the simulated VF sequences with different progression rates could also be used as predictors of progression status for the actual VF data.

Conclusions: A novel simulation model generates glaucomatous VF sequences practically equivalent to longitudinal VFs from glaucoma patients. Therefore, large sets of VF sequences with controlled progression rates can be simulated to support the evaluation and optimization of methods to detect VF progression. In addition, the simulated VF sequence with different progression rates can provide guidance for interpreting longitudinal VF data and estimating possible progression rates.

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Combinatorial expression of the proneural genes Ascl1 and Neurogenin2 restricts retinal progenitor cells to an amacrine cell fate

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Type of Research & Category: Basic Research & Retina

Abstract:

According to the competence model, multipotent retinal progenitor cells (RPCs) undergo identity transitions to give rise to all seven retinal cell types in a defined temporal order. Despite their multipotency, expression-profiling studies have shown a great deal of molecular heterogeneity between RPCs, even at the same developmental time point. Further investigating the link between RPC heterogeneity and cell fate determination is thus important, not only for understanding cell fate diversification in the retina, but also for informing the development of future repair strategies for retinal damage. In the present study, we report that the coexpression of two proneural transcription factors, Ascl1 and Neurogenin2 (Neurog2), define a population of progenitors restricted to an amacrine cell fate. Using transgenic lines expressing different fluorescent reporters at embryonic day (E) 16.5, we sorted proneural negative, Neurog2$^+$ and Ascl1$^+$ single positive and Ascl1$^+$/ Neurog2$^+$ double positive RPCs for transcriptomic comparisons. Principal component analysis (PCA) of the bulk RNA-seq data revealed that each of these RPC pools are transcriptionally different and identified 7145 differentially expressed genes (DEGs) in double positive RPCs that were classified into eight distinct clusters. Amongst the DEGs, amacrine cell fate specification and differentiation genes were enriched in double$^+$ RPCs. To examine the fate of Ascl1$^+$/Neurog2$^+$ RPCs, we employed a split-Cre lineage tracing system in which the N-terminus of Cre was knocked into the *Neurog2* locus and the C-terminus of Cre was knocked into the *Ascl1* locus. Lineage trace studies revealed that the progeny of double positive RPCs included a majority of amacrine cells. We experimentally interrogated this fate bias by selectively ablating double$^+$ RPCs using the split-cre system to drive the cre-dependent expression of diphtheria toxin subunit A (DTA). Strikingly, in split-cre;DTA animals, there was a significant loss of amacrine cells by P0. Taken together, these findings therefore identify Ascl1$^+$/Neurog2$^+$ RPCs as a unique pool of RPCs that are lineage-restricted and no longer multipotent.

Pars plana vitrectomy with or without internal limiting membrane peel for macular hole and epiretinal membrane: a systematic review and meta-analysis

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Keywords: internal limiting membrane peel, macular hole, epiretinal membrane, pars plana vitrectomy
Conflicts of Interest: MMP: Financial support (to institution) – PSI Foundation, Fighting Blindness Canada. RHM: Advisory board- Alcon, Bausch + Lomb, Bayer, Novartis, Allergan, Roche; Financial Support (to institution)- Bayer, Novartis, Roche. PJK: Advisory board – Novartis, Alcon, Bayer, Roche, Allergan, Novelty Nobility; Financial support (to institution) – Bayer, Roche, Novartis; Financial support – Novartis, Bayer, Roche, Boehringer Ingelheim, Pfizer, Zeiss; Equity owner – ArcticDx.
Financial Support: None.
Study Design: Systematic review and meta-analysis.

Purpose: Our study aims to compare the safety and efficacy of pars plana vitrectomy (PPV) with and without internal limiting membrane (ILM) peeling for macular hole (MH) and epiretinal membrane (ERM), excluding eyes receiving simultaneous phacoemulsification to minimize the influence of combined cataract surgery on visual prognosis.

Methods: A systematic literature search was conducted on Ovid MEDLINE, Embase and Cochrane Library from January 2000 to January 2023 for comparative studies reporting visual and anatomical outcomes for patients with MH or ERM, receiving PPV with or without ILM peeling. Primary outcomes included BCVA at last study observation and change in BCVA from baseline. Secondary outcomes included retinal thickness (RT) outcomes, rates of macular hole reopening or epiretinal membrane recurrence, as well as the need for repeat surgery, and adverse events. A random effects meta-analysis was performed on Review Manager 5.4. Risk of bias of randomized controlled trials (RCTs) was assessed using the ROB2 tool of observational studies using the ROBINS-I tool.

Results: Two RCTs and six observational studies reporting on 689 eyes were included for meta-analysis. PPV with and without ILM peel achieved a similar BCVA at last study observation (p=0.87) and change in BCVA from baseline (p=0.52). This was consistent in eyes with ERM (p=0.36, n=5 studies), although PPV without ILM peeling achieved a significantly better BCVA at last study observation in eyes with MH (WMD=0.09 logMAR, 95%CI=[0.02, 0.15], p=0.01, n=2 studies). Eyes in the ILM peel and non-ILM peel groups had a similar RT at last study observation (p=0.35). However, the non-ILM peel group had a significantly lower RT at 6 months (WMD= 22.07 µm, 95%CI=[1.84, 42.29], p=0.03) and 12 months (WMD=23.06 µm, 95%CI=[3.12, 43.01], p=0.02). PPV with ILM peel had a significantly lower incidence than PPV without ILM peel of MH reopening (RR=0.20, 95%CI=[0.08, 0.48], p=0.0004), repeat MH surgery (RR=0.05, 95%CI=[0.01, 0.35], p=0.003), and ERM recurrence (RR=0.09, 95%CI=[0.02, 0.38], p=0.001).

Conclusion: PPV with and without ILM peel offer similar improvements to visual acuity in patients with MH or ERM. Both treatment modalities achieved a similar BCVA and RT at last study observation. Nevertheless, patients treated with PPV and ILM peel had a lower reopening of MH and recurrence of ERM. We recommend that future RCTs evaluate the safety and efficacy of PPV with and without ILM peel in diverse patient populations to allow for more nuanced treatment decision-making.

Performance of an Artificial Intelligence Chatbot for Ophthalmic Knowledge Assessment: a Cross-Sectional Study

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Keywords: artificial intelligence, natural language processing, ophthalmic knowledge assessment program
Financial Support: None.
Conflicts of Interest: MMP: Financial support (to institution) – PSI Foundation, Fighting Blindness Canada. RHM: Advisory board- Alcon, Bausch + Lomb, Bayer, Novartis, Allergan, Roche; Financial Support (to institution)- Bayer, Novartis, Roche.
Study Design: Cross-sectional study.

Objective: ChatGPT is an artificial intelligence chatbot that has significant societal implications. Artificial intelligence training curricula are being developed in medicine and the accuracy of chatbots in ophthalmology has not been characterized. We aimed to assess the accuracy of ChatGPT in answering practice questions for board certification in ophthalmology.

Methods: We took a consecutive sample of text-based multiple-choice questions provided by the OphthoQuestions OKAP/WQE free trial. Only text-based questions were included. Our primary outcome was the accuracy of ChatGPT for answering practice board certification examination questions. Our secondary outcomes were the proportion of correct and incorrect questions for which ChatGPT provided additional explanations, the mean length of questions answered correctly and incorrectly, and the mean length of ChatGPT's responses to questions answered correctly and incorrectly.

Results: Of 166 available multiple-choice questions, 125 (75.30%) were text-based and analyzed by ChatGPT from January 9th, 2023 to January 16th, 2023. ChatGPT answered 58 questions correctly, achieving an accuracy of 46.40%. ChatGPT's accuracy was greatest in the category general medicine (78.57%) and poorest in retina and vitreous (0%). The proportion of questions that ChatGPT provided explanations and additional insight for was similar between questions answered correctly (65.51%) and incorrectly (59.70%) (difference=5.82%, 95%CI=[-11.04%,22.01%], $\chi 2$=0.45, df=1, p=0.51). The mean length of questions was similar between questions answered correctly and incorrectly (difference=21.40 characters, SE=36.81, 95%CI=[-51.47,94.27], t=0.58, df=123, p=0.22). The mean length of responses was also similar between questions answered correctly and incorrectly (difference=-80.01 characters, SE=65.43, 95%CI=[-209.53,49.51], t=-1.223, df=123 p=0.224). ChatGPT selected the same multiple-choice response as the most common answer provided by ophthalmology trainees on OphthoQuestions 43.71% of the time.

Conclusion: ChatGPT answered less than half of the questions correctly in the OphthoQuestions free trial for OKAP/WQE examinations. It is important for medical professionals and students to appreciate the advances of artificial intelligence in medicine, while acknowledging the limitations of ChatGPT at the current time. Future research should continually evaluate the accuracy of chatbots in medicine, predictors of poor accuracy, and progression of performance with time.

Disparities in Cataract Surgical Training at Kensington Eye Institute Based on Sex and Medical Graduate Type

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Type of Research/ Category: Clinical Research/Cataract

Introduction: Research has shown that female ophthalmologists perform fewer cataract surgeries compared to male ophthalmologists with these differences starting as early as residency training. This study aimed to assess differences in cataract surgical training volumes based on sex and medical graduate type at the University of Toronto.

Methods: Cataract surgical logs of ophthalmology resident graduates from the University of Toronto from 2015 to 2020 were reviewed to evaluate potential differences in cataract surgical experience by sex and medical school graduate type (Canadian medical graduate [CMG] vs international medical graduate [IMG]). Data was analyzed using descriptive statistics.

Results: 35 (54.3% female) ophthalmology residents completed their PGY-4 and 5 years during the study period. 24 (13 (54.3%) female) were CMGs and 11 (6 (54.5%) female) were IMGs. The mean number of cataract cases attended was similar between the sexes; 1,349.3 for female vs 1,333.7 for male trainees. Female ophthalmology residents had a slightly lower proportion of complete cataract procedures performed (34.4% vs 37.9%) and a higher proportion of observed cataract cases (56.8% vs 54.4%) compared to male residents, respectively. Figure 1 shows the average number of complete cataract cases during training. Female residents completed on average 40.6 (8.4%) fewer complete cataract cases compared to male residents at the end of their training. Differences were greater when comparing by medical school graduate type with IMGs having a lower proportion of complete cataract procedures performed (31.1% vs 38.1%) and a higher proportion of observed cases (59.4% vs 54.1%) compared to CMGs, respectively. The sex differences were also seen within the medical graduate type where the proportion of complete cataract cases were 40.0% vs 36.5% for male vs female CMGs respectively and 33.0% vs 28.4% for male vs female IMGs respectively. At the end of training IMGs completed on average 110.0 (22.8%) fewer complete cataract cases compared to CMGs and female IMGs had the greatest difference with an average of 136.5 (26.2%) fewer complete cases than CMGs.

Discussion/Conclusion: Female residents and IMGs completed fewer complete cataract cases compared to male residents and CMGs, respectively. The greatest disparity was found with female IMGs who completed on average 136.5 (26.2%) fewer complete cataracts than CMGs. Further studies are necessary to better understand the reasons for these differences and potential implications on resident perception of surgical competence and future practice choices.

Gender-Based Disparities in OR Resources, Cataract and Teaching Volumes at the University of Toronto's Eye Institute

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Type of Research/Category: Clinical Research/ Cataract

Introduction: Female ophthalmologists perform fewer cataract surgeries compared to males with these differences starting early in residency training. This study aimed to assess number of operating room (OR) days and case volumes by staff gender. Also, teaching volumes by staff and resident gender were compared.

Methods: Cataract surgical logs of ophthalmology residents from KEI between 2015-2020 were reviewed. Distribution of OR days and number of cases were compared. Teaching volumes were compared between staff and resident gender at each stage of training. Descriptive statistics were used.

Results: Forty-nine (30.6% female) staff cataract surgeons operated during the study period. Female staff had slightly more OR days at KEI (15.2 vs 13.7 days per male staff/year). The median number of cases per OR day was also slightly higher for female (14.1) vs male (13.5) staff.

Thirty-five residents (45.7% male) operated during the study period. Residents attended 72.5 vs 67.3 cataract cases per female vs male staff per year, respectively. For female staff, more cases were attended by male compared to female residents at early surgical training (median 107.5 vs 84), however this difference no longer existed by senior stages (median 98.5 vs 98). In contrast for male staff, more cases were attended by female residents compared to male residents at early training (median 162 vs 143.5), however by senior stages the opposite was true (median 204 vs 271.5).

The proportion of complete cataract cases for all residents overseen by female staff was greater throughout most stages of training compared to male staff. At the earliest level, female staff gave more complete cataract cases to all residents (8.9% vs 5.3%), female residents (4.8% vs 4.3%), and male residents (10.2% vs 5.9%) compared to male staff. At the most senior level of surgical training, male staff gave more complete cataract cases to male residents compared to female residents (64.1% vs 58.3%), while female staff gave an equal proportion of complete cases (49.8% male vs 48.9% female residents).

Discussion/Conclusion: Our study is imitated by data collected only from resident logs at one teaching site and may not reflect full OR distribution, cataract and teaching volumes. Male and female staff involved in teaching at KEI had fairly equal OR days and volumes. Female staff provided a greater proportion of complete cataract cases to all residents. These results suggest that female staff may take on a greater role in teaching compared to male staff.

An Orbital Differential Diagnosis Spreadsheet

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Introduction

Diagnostic challenge represents a significant source of delay in treatment and morbidity in medicine. While artificial intelligence electronic differential diagnosis support systems have been developed and found to be helpful in many branches of medicine, they have not been studied in orbital diseases. We propose a probability-weighted scoring system based differential diagnosis spreadsheet to offer potential diagnoses in cases of orbital pathology.

Methods

Using a probability-weighted scoring system algorithm, features on history, physical exam, lab testing and imaging were gathered and deemed to be important in diagnosis of orbital pathology. These features were then given weighting based on probability and prevalence for many orbital pathologies and integrated into a spreadsheet to create the orbital differential diagnosis spreadsheet (ODDS). 16 cases from an orbital textbook were then entered into ODDS and a list of 10 differential diagnoses were compiled and analyzed.

Results

The ODDS was able to determine the correct diagnosis in the top ten differentials in 9/16 cases (56.25%). Among these cases, the median position of the diagnosis was second. Cases without a correct diagnosis were pathologies that were quite rare and signaled a need to update the database of the spreadsheet.

Conclusions

The ODDS shows promise in aiding diagnoses in standard orbital pathology. Optimization for more rare pathology is required. Further work will look into comparing results with artificial intelligence electronic differential diagnosis support systems such as Isabel.

Grading System for Choroidal Effusion Following Glaucoma Surgery Using Fundus Photographs

Introduction

Serous choroidal effusions result from abnormal accumulation of fluid in the suprachoroidal space. In the absence of disease, there is a balance of fluid movement into the suprachoroidal space from the choroidal capillaries and the RPE pump, and fluid movement out through the sclera and emissary channels. A disruption to hydrostatic and osmotic gradients results in fluid accumulation and ciliochoroidal effusion or detachment. One of the most common causes for choroidal effusions is hypotony following glaucoma surgery. This study aims to develop a grading system for choroidal effusion, which is a common complication following glaucoma surgery.

Purpose

The purpose of this study is to develop a grading system for choroidal effusion

Method

This was a prospective non-interventional case series. A total of 30 eyes with choroidal effusion were included in the study. Fundus photographs were taken of each patient, and four vitreoretinal surgeons graded the choroidal effusion independently using a proposed grading system. The grading system included clock hours (0-12), quadrants (superior, inferior, nasal, temporal), choroidal grade (1-4), and choroidal extension (A-D).

Results

The proposed grading system showed high inter-rater reliability. The grading system showed good discriminative ability. A series of photographs of serous choroidal effusion and its grading using the proposed grading system will be shared during the poster presentation.

Conclusion

The proposed grading system for choroidal effusion using fundus photographs and independent raters is reliable, simple and reproducible. This grading system could be a useful tool for clinical assessment and management of patients with choroidal effusion, especially to assess progression or improvement objectively.

Biallelic Variants in *IFT57* May Cause BBS-like Ciliopathy with Retinal Dystrophy

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Type of research: Basic Research **Category:** Retina
Conflict of Interest: None

Primary cilia are critical components of most cells, as they are involved in many cell signalling pathways that regulate cellular and organ development. When this process goes wrong, patients develop ciliopathies, which are a genetically and clinically heterogenous group of diseases that cause a wide range of morbidities. The connecting cilium of the photoreceptor is a homologous structure of the primary cilia, therefore they share proteins and pathways.

A 29-year old male presented to the clinic with rod-cone degeneration which led to legal blindness. Clinical features including polydactyly and a fatty liver were suggestive of a BBS-like ciliopathy. Following negative clinical genetic testing, genome sequencing was performed on the proband and his family, and filtering identified biallelic variants in *trans* in *IFT57* and presumed to be disease-causing. The variants included a deletion in exon 6 that causes a frameshift and loss of function, and a c.1190T>A; p.(Val397Glu) missense variant in exon 11. IFT57 is part of complex B of the anterograde intraflagellar transport IFT proteins. *IFT57* variants have not yet been associated with human retinal degeneration.

In silico analyses suggest that our variants are highly conserved, and that *IFT57* Val397Glu is predicted to be pathogenic and is not found in the population. Immunofluorescence done using patient skin fibroblasts revealed lower cilia count/percentage and abnormal cilia. Collaborators showed that Val397Glu rescues the cilia phenotype in IMCD3 but not RPE1 *IFT57* knockout cell lines, indicating that the cell line plays a role in how the *IFT57* phenotype manifests. The role of *IFT57* could be different in retinal cells than in other cell types. A cycloheximide chase assay showed faster degradation of the missense protein compared to the wild-type, suggesting instability. Taken together, these results suggest that the Val397Glu missense variant in *IFT57* is more unstable than the wild-type protein, and consequently it acts as a hypomorph and together with the knockout variant causes the observed ciliopathy phenotype in our patient.

Utilization of Enface OCT and Deep Learning-Based Automated Segmentation to Quantify Area of GA: ECLIPSE study

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Clinical Research: Retina

Competing Interests Statement: Netan Choudhry is a consultant with research support from Optos PLC and Topcon. This project was completed at the Vitreous Retina Macula Specialists of Toronto. Jonathan Oakley and Daniel Russakoff are employees of Voxeleron LLC with patent on layer segmentation. Samantha Orr and John Golding have no conflicts of interest to disclose.

Introduction: Clinical trials for dry age-related macular degeneration therapeutics track geographic atrophy (GA) area as a primary endpoint—it would be valuable to fully automate this measurement using optical coherence tomography (OCT) rather than the commonly employed fundus autofluorescence. We investigated the accuracy of a GA segmentation algorithm for OCT, comparing the relative performance of different enface views, a critical factor to delineate choroidal hyperreflectivity.

Methods: Patients diagnosed with GA at our centre were retrospectively identified and 50 OCT volume scans were extracted with no exclusions. Scans were manually segmented, delineating GA area in the enface view using custom software. Different enface views and OCT B-scans were used to determine GA boundaries, with enface views generated based on automated layer segmentation. Using this ground truth, we applied a deep learning segmentation algorithm trained on the graded images and the four automatically generated enface images created via three different methods of integrating in the axial direction:

1. Entire volume
2. ILM to Bruch's membrane
3. Bruch's to an offset to the choroid.
4. 335 μm slab 65 μm below RPE Fit

Statistical analysis with DICE coefficient was done to gauge overlap area of test images, and Pearson's coefficient was used to describe correlation of reported areas.

Results: Average OCT image quality was 61/100 (STD=8). For each, a U-Net segmentation architecture used 5-fold cross validation that left our 10 images as a test set at each fold; 6 images were used for validation leaving 34 images for training. Methods 1 and 4 produced the highest DICE coefficients (0.81), followed by method 3 (0.78) and method 2 (0.51). The highest correlation was found using method 1 (0.82), followed by methods 4 (0.72), 3 (0.66), and 2 (0.57).

Conclusions: Fully automated segmentation of GA areas in OCT data can yield accurate results. However, the method of enface image generation can dramatically change the appearance of the choroidal reflectivity and thus the GA area measured. A consensus approach would be advisable in comparison to FAF images.

Figure 1. Example of GA OCT analyzed via 4 different methods. Enface OCT view generated according to methods 1, 2, 3, and 4 (A, D, G, J respectively). The ground truth mask associated with each enface image show (B, E, H, K) and representation of the deep learning segmentation (C, F, I, L).

Novel Features of Degenerative Retinoschisis Identified Using Ultra-Widefield Multicolor Channels: A Review of 139 Eyes

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Clinical Research: Retina

Competing Interests Statement: Netan Choudhry is a consultant with research support from Optos PLC and Topcon. This project was completed at the Vitreous Retina Macula Specialists of Toronto.
Samantha Orr and Amin Hatamnejad: no conflicts of interest to disclose.

Introduction:

To utilize ultra-widefield pseudocolor, green-separated, red-separated, autofluorescence, and OCT images (Optos, PLC Edinburgh) to describe characteristics of degenerative retinoschisis. We aim to describe novel findings on pseudocolor and green separated images to improve detection and diagnosis of this condition and further explore the clinical utility of color-separated images.

Methods:

This is a single center, retrospective, noncomparative case series conducted at the Vitreous Retina Macula Specialists of Toronto. Consecutive cases of degenerative retinoschisis from 2013 to 2022 with quality imaging were included. In addition to clinical information, ultra-widefield Optos pseudocolor, green-separated, red-separated, and autofluorescence images were captured in primary gaze with additional eye-steered images. Peripheral OCT of retinoschisis was acquired at the discretion of the technician. In unilateral retinoschisis, images from the contralateral eye were also analyzed.

Results:

139 eyes of 91 patients with degenerative retinoschisis were included in our analysis. In this group, approximately 70% of patients were managed with observation only. The remaining patients received laser retinopexy, most commonly due to inner retinal holes. A hyporeflective reticular pattern of variable size appears to be associated with areas of schisis. This pattern was seen on pseudocolor images in 39% of eyes (54 eyes), but was visible in 53% of eyes (73 eyes) on the green separated image, which analyses the neurosensory retina. Fine hyperreflective dots were also observed over the area of schisis or at its anterior edge in 50% (70 eyes) of cases. In 27% (37 eyes), retinoschisis was correlated with OCT. Peripheral OCT imaging of the reticular pattern correlated with the schisis cavities and the hyper-reflective dots correlated with scattered hyperreflectivities between the inner and outer retina.

Conclusions:

Ultra-widefield imaging with pseudocolor and green-separated images is a useful adjunct in the diagnosis and characterization of degenerative retinoschisis. Features that may be subtle or not visible on pseudocolor images appear clearly on green-separated images, which provide a detailed view of the neurosensory retina. This was particularly true with the reticular pattern described. Hyperreflective dots were typically visible on pseudocolor and green-separated images and may indicate an otherwise subtle retinoschisis. With use of ultra-widefield OCT, these findings can be further corroborated and confirm the presence of degenerative retinoschisis.

Optical Properties, Dimensions, and Pigment Concentrations in the Pediatric Eye: A Scoping Review

A.

B. ***Rahma Osman[1], Jane Walter[1], Rishabh Johri[1], Aditya Damani[1], Stephanie Rizza[1], Michael Wan[1,2], Asim Ali[1,2], Tos TJM Berendschot[3], Jessie Cunningham[1] , Ashwin Mallipatna[1,2]***

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1.

2. Abstract

Introduction: The optics of the healthy adult eye are well established, however, normative optical property data for the pediatric population is scant. A scoping review was conducted to define the optical properties, pigment concentrations, and dimensions of components of healthy pediatric eyes.

Methods: This scoping review was developed in two stages: a pilot review and final review. The pilot review was designed to build a robust search string and identify gaps in the review's inclusion/exclusion criteria. Electronic databases Medline, Scopus and Web of Science were searched with help from an information scientist. Of the identified articles, 10% underwent an initial title and abstract screening for quality control. A team of five reviewers identified articles that did not fit the scope of the review. A larger multidisciplinary group evaluated results of the pilot review, refining the search string and inclusion/exclusion criteria. Title and abstract screening was then repeated for 10% of the revised search results**.**

Results: The initial search string included the concepts of [anatomical structures and pigments] AND [optical properties OR optical dimensions]; [optical pigments] AND [pigment concentrations]. This search retrieved 15,000 articles, from which 8,501 unique articles were identified. Of these, 10% were subject to the pilot review (850 articles) which resulted in 25 articles being approved for full text review. Based on the results of the pilot review, the exclusion criteria were revised to eliminate articles measuring optical properties in adults and animal models OR pathological properties without a normal control population. The inclusion criteria were revised to only include English language publications measuring one or more of the optical properties from the search list in a pediatric population. The revised search yielded 6,110 unique articles, 603 of which were included in the trial screening. Of these, 163 (27%) were approved for full text review.

Conclusions: A scoping review will be conducted using the revised search string and criteria. A team of independent reviewers will conduct a two-stage literature screening process, data extraction, and quality appraisal. This scoping review aggregates information on the healthy pediatric eye and provides a foundation for developing pediatric-specific optical technologies.

Deciphering the role of Pten in maintaining Müller glia in quiescence in the mouse retina

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Retinal-degenerative diseases, such as age-related macular degeneration (AMD) and retinitis pigmentosa (RP), are caused by the loss of photoreceptor cells that eventually leads to blindness[1,2,3]. Currently, there are no curative strategies to replace lost photoreceptors and restore vision in individuals with these disorders. One endogenous repair strategy is activating the stem cell properties of Müller glia, which are glial cells in the retina that can replace lost cells in regenerative species such as zebrafish[4,5]. However, Müller glia in mammals are deeply dormant and while briefly activated post-injury, there is a rapid return to quiescence. In satellite stem cells in skeletal muscle, mTORC1 is required to push stem cells into a primed G_{ALERT} phase, ready to respond to injury. Here we asked whether mTORC1 signaling also controls the G_0 (deeply dormant) to G_{ALERT} transition in mammalian Müller glia. For this purpose, we created a conditional knock-out (cKO) of Pten, a dual-specificity phosphatase. Specifically, we used a tamoxifen-inducible Müller glia specific Cre driver (*Sox9*^{CreERT2}) to generate *Pten* cKOs using *Pten* floxed mice. We confirmed that in the absence of the Pten function, mTORC1 signaling was activated. We analyzed adult retinas at 1, 7, 21, and 100-days post tamoxifen induction and showed that *Pten* cKO Müller glia nuclei delaminate into the outer nuclear layer, where photoreceptors reside, remaining in this ectopic site up to 100 days post-tamoxifen. We further found an upregulation of mTORC1 and mitochondrial activity in *Pten* cKO Müller glia and hypothesize that these cells have entered a metabolically active step, akin to the G_0-G_{ALERT} transition in adult skeletal muscle stem cells. Future transcriptomic studies will identify *Pten*-regulated genes that control Müller glia latency. Furthermore, to assess Müller glia's trans-differentiating capacity, I will use Cre-based lineage tracing with a Rosa-zsGreen reporter line to determine whether other retinal cells (i.e., amacrine, ganglion, bipolar, horizontal, cone, rod) are derived from *Pten* cKO Müller glia. Together, this study will better position the field to design gene therapies to activate Müller glia for retinal repair.

The Causes of Optic Disc Edema in Patients Presenting with Significantly Compromised Vision: A Retrospective Study

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Keywords: optic disc edema, visual acuity, NAION, AAION, optic neuritis, idiopathic intracranial hypertension, papilledema, VKH
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Purpose: Optic disc edema (ODE) may be caused by a multitude of causes and is one of the most common reasons for referral to neuro-ophthalmology. The goal of this study was to evaluate the most common causes of ODE in patients with significantly compromised vision (initial best-corrected visual acuity (BCVA) of 20/400 or worse) at presentation.

Methods: This was a retrospective chart review over a 5-year period of consecutive patients presenting to tertiary neuro-ophthalmology clinics at the University of Toronto.

Results: A total of 656 patients with ODE were included and 51 patients (7.77%) had an initial BCVA of 20/400 or worse. There were 57 eyes (35 female, 22 male) included at baseline and 50 eyes at final follow-up. The mean age at first visit across patients was 56 ± 20.3 years. Female (n=31) patients were significantly older than male (n=20) patients ($p < 0.05$). The causes of ODE were optic neuritis (ON) (38.6%), non-arteritic anterior ischemic optic neuropathy (NAION) (38.6%), arteritic anterior ischemic optic neuropathy (AAION) (8.8%), uveitis-related (7%), papilledema from idiopathic intracranial hypertension (IIH) (5.3%), and Vogt-Koyanagi-Harada disease (1.8%). The initial BCVA was not significantly different between ON and NAION groups ($p = 0.52$); however, final BCVA was significantly better in the ON group ($p < 0.0001$). The mean initial BCVA was worst in the AAION group (2.62 ± 0.54 logMAR). The most common cause in patients <40 was ON (76.9%) whereas the two most common causes in patients >80 were NAION (60%) and AAION (40%). In patients between the ages of 60-80, NAION (100%) was the only cause.

Conclusions: Patients with ODE and poor vision represent a minority of cases seen in neuro-ophthalmology clinics (<10%). Optic neuritis and NAION are the two most common causes of ODE with poor vision at presentation. Improvement over time is an effective way to differentiate these two causes.

The Use of Preoperative Visual Acuity Thresholds in Pars Plana Vitrectomy for Epiretinal Membrane: A Systematic Review

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

Ethics Approval: This study was conducted in accordance with the Declaration of Helsinki.

***Introduction*:** The purpose of this systematic review was to examine postoperative outcomes in patients with epiretinal membrane (ERM) undergoing pars plana vitrectomy (PPV) in studies in which a preoperative visual acuity threshold was defined as a criterion for inclusion.

***Methods*:** The literature was systematically searched using EMBASE, Ovid MEDLINE, and Cochrane Library from January 2000 to October 2022. Studies which used a preoperative visual acuity threshold as an inclusion criterion in PPV for ERM were included. Primary outcomes were final best-corrected visual acuity (BCVA) and change in BCVA relative to baseline. Secondary outcomes included the risk of intraoperative and postoperative complications. Results were presented using descriptive statistics.

Results: In total, 639 eyes from 7 studies were included. The mean age was 68.1 years and there were a greater proportion of female patients (53.8%). The most liberal preoperative visual acuity threshold across studies reporting on PPV for ERM was 20/28.5 or worse whereas the most conservative threshold was worse than 20/60. The mean preoperative BCVA across all studies was 0.55 logMAR (~20/70) and the mean postoperative BCVA at last follow-up was 0.35 logMAR (~20/45). In general, the visual acuity improved relative to baseline in all studies, regardless of the preoperative visual acuity threshold chosen. The smallest improvement in visual acuity pre- to postoperatively was observed in a study for which the preoperative visual acuity to consider surgery was liberal (20/30 or worse), whereas the greatest improvement in visual acuity was observed in a study that employed a relatively conservative preoperative visual acuity threshold (worse than 20/60). The risk of cataract formation and/or progression ranged from 41.3 – 75% (n = 2 studies), and ERM recurrence was noted in 4.5% of patients (n = 2 studies).

Conclusion: The greatest improvement in BCVA following PPV or ERM was observed in studies that used a conservative preoperative visual acuity threshold. The decision to operate in patients with ERM should involve a patient-centered approach with a thorough discussion of the risks and benefits associated with PPV, irrespective of the preoperative visual acuity threshold that is used.

Tracing connections of the inner retina to identify circuits resilient to photoreceptor degeneration

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Introduction: A common form of hereditary vision loss occurs due to degeneration of the light-sensing photoreceptors (PRs), but we know little about how downstream circuits in the retina change. Understanding whether inner retinal cells maintain their connections is important for designing therapies to reactivate circuits to restore sight. Here we use *rd* PR degeneration mouse models to study the structure and synaptic connectivity of inner retinal circuits following PR degeneration, focusing on the well-characterized direction-selective (DS) circuit. Its main components are the DS retinal ganglion cells (DSRGCs) which receive inputs from starburst amacrine cells (SACs).

Methods: I am using antibody markers and RNA *in situ hybridization* to identify subtypes of DSRGCs that are affected or resilient in degeneration. To analyze the connectivity of this circuit in *rd* retinas, I am using a toolkit developed by our lab that detects retinal cell-cell interactions and connectivity. Our system (TRACR) reports on trans-synaptic interactions by inducing transcription of a fluorescent reporter gene in the postsynaptic cell (Figure 1B).

Results: In my characterization of the SA interneurons in *rd1* and *rd10* mice, I found that these cells remain intact in *rd* models, but are affected in terms of density and possibly protein expression (Figure 1A). Using several approaches, we demonstrated that TRACR reliably identifies known neural circuits in the mouse visual system (Figure 1C and D). I will present ongoing work on applying TRACR in *rd* mice to analyze the connectivity of the DS circuit following degeneration, as validated by expression of the TRACR readout with molecular markers of DS neurons. Together, these results will identify changes in retinal circuits in degenerative disease, as well as circuit-specific resiliencies to degeneration.

Validation of patient-reported outcome measures in adolescent patients with Inherited Retinal Diseases

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Type of Research: Clinical
Category: Retina

Introduction

Recent advancements in ophthalmology have resulted in the first Health Canada-approved gene therapy for a specific gene variant of inherited retinal disease (IRD). IRDs refer to a group of hereditary disorders of the retina, which can lead to progressive photoreceptor degeneration and eventual vision loss, potentially resulting in blindness, among other complications. To assess the efficacy of therapies in the IRD population, measures of vision structure and function are commonly used, but the impact of the condition on patients' daily lives has not been adequately explored. Patient-reported outcome measures (PROMs) are questionnaires designed to measure health outcomes from the patient's perspective and can bridge this gap. Recently, PROMs were developed for adult IRD patients, such as the Michigan Retinal Degeneration Questionnaire (MRDQ) and the Michigan Vision-related Anxiety Questionnaire (MVAQ). However, no PROMs have been tailored to adolescents with IRD, even though clinical trials are increasingly including adolescents as early intervention can enhance the efficacy of these therapies. This study aims to validate the MRDQ and MVAQ questionnaires in adolescents with IRD.

Methods

Adolescent patients (aged 13 to <18 years) diagnosed with IRDs were recruited from the Hospital for Sick Children (University of Toronto) and the Kellogg Eye Center (University of Michigan) and were given the MRDQ, MVAQ, and the Patient Health Questionnaire-4 (PHQ-4). Adolescent responses were analyzed for response distribution, measurement precision, known-group validity, and differential item functioning, as well as compared to adult data from the original MRDQ and MVAQ studies to ensure response consistency.

Results

The results of the study demonstrate that the MRDQ and MVAQ questionnaires are appropriate for assessing the impact of IRD on activities of daily living in adolescents (n=91). The questionnaires showed no floor or ceiling effects, and test-retest reliability was established for each domain, with moderate to strong correlation (r=0.73–0.86). Differential item functioning analysis did not result in any items being excluded. The study found that the domain and trait associations with visual acuity and IRD phenotypes were similar between adolescents and adults.

Conclusion

The validation of the MRDQ and MVAQ questionnaires in adolescents with IRDs confirms their usefulness in assessing the impact of IRD on the activities of daily living of affected individuals. The implementation of these tools in clinical practices and studies can enhance the patient-centered approach to the evaluation and management of adolescent patients with IRD.

Disclosure

E.H. is consultant for Novartis, Janssen, and on a DSMB (for Sanofi Atsena). A.V. is a consultant for Novartis and Adverum Biotechnologies, Inc. D.C.M. is a consultant for Editas Medicine, Inc.

Anemia and Idiopathic Intracranial Hypertension: a Prospective Study

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Conflicts of Interest: None

Financial Disclosures: None

Category: Neuro-ophthalmology

Introduction: Anemia has been temporally associated with idiopathic intracranial hypertension (IIH) in retrospective studies; however, this relationship is uncertain due to lack of prospective studies and as patients with IIH do not routinely have complete blood counts (CBC). Therefore, CBCs may have only been available in patients with significant comorbidities, higher risk factors or symptoms from anemia. In addition, both IIH and anemia are common in young women with obesity, which creates further challenges in establishing an association between IIH and anemia.

Methods: This was a prospective cross-sectional study. Consecutive patients with IIH referred to three neuro-ophthalmology centres between March 2021 and September 2022. Inclusion criteria included presence of papilledema, normal neurologic exam excluding cranial nerve abnormalities, normal neuroimaging, age $\geq$18 years, and complete blood count available within 6-months of presentation. Anemia was defined as mild (110-120 g/L), moderate (80-109 g/L) and severe (<80 g/L).

Results: A total of 143 patients were included, 113 patients had normal hemoglobin (Group-1) and 30 patients had anemia (Group-2). In Group-2, the anemia was defined as mild (15/30, 50.0%), moderate (11/30, 36.7%) and severe (4/30, 13.3%). The anemia was most often microcytic (15/30, 50%) and normocytic (15/30, 50%). There was no difference in female sex (105/113 vs 29/30, p=0.453), age (31.5±9.2 vs 28.5±10.3, p=0.144), and BMI (35.2±6.9 vs 38.0±8.1, p=0.111). Group-1 and Group-2 did not differ in logMAR visual acuity (0.04±0.09 vs 0.07±0.14, p=0.377), RNFL thickness (174.5±68.4 vs 206.5±97.0, p=0.098), mean deviation (-3.2±3.1 vs -3.9±3.4, p=0.367), and the need for medical (34/113 vs 8/30, p=0.715) and surgical treatment (3/113 vs 3/30, p=0.074). Patients with moderate-severe anemia were significantly more likely to require surgical therapy compared to patients with normal hemoglobin (2/15 vs 3/113, p=0.045).

Conclusion: Approximately one out of every five patients with Idiopathic Intracranial Hypertension has anemia and this is severe in over 10% of patients. Patients with moderate and severe anemia may require more invasive surgical treatment. Given the high incidence of anemia and the availability of a complete blood count, we recommend this test be obtained for all patients with suspected idiopathic intracranial hypertension.

Antivirals versus antivirals and steroids for treatment of Herpes-Zoster related ophthalmoplegia: A case series and systematic review

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Conflicts of Interest: None

Financial Disclosure: None

Category: Neuro-ophthalmology

Introduction: Herpes zoster infection is caused by varicella zoster virus. It occurs in individuals who were exposed to the virus, either through natural infection or vaccination. Some patients with herpes zoster develop herpes zoster ophthalmicus (HZO), which involves reactivation of the virus in the ophthalmic division of the trigeminal nerve. Up to 1/3 of patients with Herpes Zoster Ophthalmicus (HZO) may develop ophthalmoplegia. While zoster-related ophthalmoplegia (ZO) is typically treated with antiviral agents, there is controversy regarding the therapeutic role of systemic steroids.

Methods: This was a retrospective case series and case-based systematic review. For the case series, participants were recruited from tertiary neuro-ophthalmology clinics. Eligible participants were those who developed cranial nerve palsies (CNP) within one month of HZO diagnosis. The systematic review followed PRISMA guidelines. MEDLINE, EMBASE and Cochrane CENTRAL were searched from inception to February 2022 for original studies reporting on adults with ZO who were treated with antivirals or steroids only, or combination therapy. Main outcomes were initial presentation, investigations, neuroimaging, treatment regimen and final outcomes of ophthalmoplegia. Research ethics board approval was obtained, and this study follows the Tenets of the Declaration of Helsinki.

Results: Eleven immunocompetent patients with ZO were included. The most common CNP was CN III (5/11), followed by CN VI (2/11) and CN IV (2/11). One patient had multiple CNPs. All patients were treated with antivirals and four were also treated with a short course of oral steroids. At six-months follow-up, 75% of patients treated with combination therapy and 85.7% of patients treated with antivirals alone had complete recovery of ZO. The systematic review identified 63 studies consisting of 76 cases of ZO. When comparing patients treated with antivirals to those treated with antivirals and steroids, patients on combination therapy had more severe ocular findings, including complete ophthalmoplegia ($p<0.001$). Age was the only significant predictor of complete recovery of ophthalmoplegia on multi-variable logistic regression ($p=0.037$).

Conclusion: The rate of complete recovery in immunocompetent patients with ZO was similar in patients treated with antivirals alone versus those treated with antivirals and oral steroids. The systematic literature review affirmed these findings. However, age may influence recovery of ophthalmoplegia.

Yield of Investigations in Young Patients Presenting with Transient Monocular Vision Loss

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Introduction: Transient monocular vision loss (TMVL) in older patients warrants thorough work-up including investigation for potential embolic sources with imaging of the carotid circulation and cardiac evaluation. In young patients with lower risk for atherosclerosis, arrhythmias, and cardiac disease it is unclear whether the same approach should be used. The objective of the present study was to evaluate the yield of investigations in patients under 45 years old presenting with TMVL.

Methods: This was a retrospective cohort study of patients with TMVL presenting to a university-affiliated neuro-ophthalmology clinic. Data was collected on demographics, ophthalmologic exam, neuroimaging, and cardiac investigations.

Results: Twenty participants with TMVL were included in the study. The mean age was 33.1 ± 8.2 years and 80.0% (16/20) were women. The most common finding on past medical history was migraines, at 25.0% (5/20). Ophthalmic examination revealed abnormal findings in 20.0% of participants, including visual field defects and ganglion cell loss. None of the patients demonstrated carotid stenosis on angiography, however one patient had evidence of fibromuscular dysplasia of the ipsilateral internal carotid artery. Seventeen percent (2/12) of participants had diffusion restriction on MRI. ECG findings were abnormal in 20% (3/15) of cases, demonstrating left atrial enlargement and sinus bradycardia. Two of 12 patients had abnormal Holter monitor. Fifteen percent (2/13) of patients who completed echocardiogram had abnormal findings, including mitral regurgitation, and left ventricular hypertrophy. Following bubble study, 2 out of 6 cases were found to have a patent foramen ovale. In terms of treatment, one patient with known cardiomyopathy received an implantable cardioverter defibrillator, while four other patients, including the patient with fibromuscular dysplasia, were started on Aspirin therapy.

Conclusion: In our cohort of young patients presenting with TMVL, 1 of 12 patients that underwent carotid imaging showed evidence of fibromuscular dysplasia and 2 of 6 patients demonstrated patent forman ovale on echocardiogram. There may be rationale to workup young patients for transient monocular vision loss to prevent poor visual and cerebrovascular outcomes.

A dual role for the RGMc protein in retinal angiogenesis

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Introduction: Angiogenesis, the formation of new vessel sprouts from pre-existing vasculature, is responsible for vascularization and generation of specialized structures for the retina during development. Additionally, manipulating angiogenic mechanisms is a promising therapeutic strategy for diseases like cancer and diabetic retinopathy. We uncovered that a protein produced by the liver and muscle tissue known as Repulsive Guidance Molecule C (RGMc) has a dual role on angiogenic activity. Our study demonstrates that RGMc secreted by the liver acts as a pro-angiogenic factor, while RGMc from the muscle acts as a suppressor of angiogenesis in the developing retina. We further show that liver- and muscle-derived RGMc are differentially modified, which likely accounts for the different effects of these proteins. We aim to establish that these modifications may result in preferential binding to RGMc receptors, Neogenin (NEO1) and Bone Morphogenic Protein (BMP), providing insights into the underlying mechanisms through which these proteins modulate angiogenesis.

Methods: Using mouse models with liver and muscle RGMc knockouts ($RGMc^{fl/fl\text{-}\Delta Alb\text{-}Cre}$ and $RGMc^{fl/fl\text{-}\Delta Acta\text{-}Cre}$), we studied the *in vivo* function of these proteins in the developing retina (P6-P11) using whole mount staining protocols for angiogenic markers. The tube formation assay was used to assess if these effects can be replicated *in vitro*.

Results: Assessment of the retinal vascular layers at critical stages of development showed a decrease in angiogenic activity in $RGMc^{fl/fl\Delta Alb\text{-}Cre}$ mice while $RGMc^{fl/fl\Delta Acta\text{-}Cre}$ showed the opposite effect. These findings were replicated in our in vitro tube formation assay, where endothelial cells treated with RGMc protein derived from muscle or liver cells displayed a decrease or increase in vascular formation and growth, respectively. Through western blot analysis, we discovered that muscle derived RGMc lacks the ability to undergo cleavage at its autocatalytic site. Furthermore, we generated an uncleavable mutant RGMc construct and found that it acts to inhibit angiogenesis regardless of whether it is muscle or liver derived.

Discussion/Conclusion: The proposed research uncovers a novel role for RGMc on regulating CNS vascularization during development. We will further examine the mechanisms behind this phenomenon by investigating the interaction of RGMc and its receptors and their effects on developmental angiogenesis of the retina. This research should expand current knowledge in this field by providing insights on the mechanisms that underlie angiogenic processes, which can inspire new therapeutic options. Moreover, this research will explain how different organ systems influence CNS angiogenesis, providing a broader foundation for clinical intervention.

Directed Evolution Enables Simultaneous Controlled Release of Multiple Therapeutic Proteins from Biopolymer-Based Hydrogels

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Introduction: With the advent of increasingly complex combination strategies of biologics, independent control over their delivery is the key to their efficacy; however, current approaches are hindered by the limited independent tunability of their release rates. To overcome these limitations, directed evolution was used to engineer highly specific, low affinity affibody binding partners to multiple therapeutic proteins with applications to retinal degenerative diseases. Affibody proteins, which are small antibody-like proteins, were used to control release rates of insulin-like growth factor1 (IGF-1) and pigment epithelium derived factor (PEDF) independently and simultaneously.

Methods: As a proof-of-concept, specific affibody binding partners for (IGF-1) and pigment epithelium-derived factor (PEDF) are identified using yeast surface display technology. After iterative rounds of magnetic activated and fluorescence activated cell sorting, unique clones for both proteins of interest were discovered. Protein–affibody binding interactions specific to these target proteins were quantified using biolayer interferometry. Subsequently, affibodies were covalently bound to the backbone of multiple biopolymers using click chemistry and release of the therapeutics was quantified over the course of 7 days by ELISA. The system was injected intravitreally into C57BL/6J mice to assess bioactivity of released protein from the vehicle.

Results: Equilibrium dissociation constants (K_D) between IGF-1 and PEDF and their respective binding partners were determined to be between 10^{-7} and 10^{-8} M. Affibody proteins demonstrated high specificity to their respective binding partner. Sustained, independent, and simultaneous release of bioactive IGF-1 and PEDF was achieved over 7 days. After intravitreal injection into C57BL/6J mice in vivo, affibody-controlled release of IGF-1 results in sustained activity when compared to bolus IGF-1 delivery.

Discussion/Conclusions: Affibodies show great promise in addressing the limited tunability of release rates in biologics, which are essential for treating retinal degenerative diseases. This work demonstrates a new, broadly applicable approach to tune the release of therapeutic proteins simultaneously and independently and thus the way for precise control over the delivery of multicomponent therapies is paved.

Characterization of *Spalt*, the *Drosophila* homolog of the vertebrate *SALL* genes, in the developing fly visual system

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Type of Research/Category: Basic Research/Neuro-Ophthalmology

The SALL family of zinc-finger transcription factors plays an important role in mammalian eye development and disease. The *SALL* genes are expressed in the developing vertebrate retina and have been implicated in developmental defects such as retinal coloboma in humans as well as cone photoreceptor and horizontal cell specification in mice, yet little is known about their upstream genetic regulators and downstream targets. My work investigates the role of the *SALL Drosophila* homolog, *spalt* (*sal*), in the developing medulla, which is the largest structure in the fly visual system. With the developmental, genetic, and structural similarities shared between the fly medulla and vertebrate retina, this work will assist in the identification of novel genetic regulators and targets of the *SALL* genes in the developing vertebrate retina.

The *Drosophila* medulla mediates colour and motion processing and is comprised of over 100 cell types. Medulla neural stem cells integrate spatial (Optix/Six3, Vsx1/Vsx2, and Rx/Rx) and temporal (Hth/Meis1, Ey/Pax6, and D/Sox2) inputs to generate neural diversity. Thus, each medulla neuron type is ascribed a unique birth address based on the spatio-temporal identity of the progenitor from which it was born. Surprisingly, it has been observed that neurons with identical spatio-temporal addresses assume different fates based on whether they are generated by dorsal or ventral neural stem cells. This observation suggests that an additional spatial patterning mechanism confers unique identities to dorsal versus ventral medulla progenitors.

Using a cell extraction technique to collect fluorescently labelled dorsal and ventral medulla neural progenitors as inputs for RNAseq, I have identified *sal* as a dorsally enriched patterning gene. Based on immunohistochemistry analysis, *sal* is exclusively expressed in dorsal progenitors at all stages of neurogenesis. Through complimentary loss- and gain-of-function experiments I demonstrate that Sal maintains dorsal stem cell identity via reciprocal cross-repression with the ventral patterning transcription factor, Disco. Furthermore, I show that establishing dorsal-ventral progenitor identity through *sal* and *disco* expression at an early developmental stage is required for ventral medulla development at later stages. The above data suggest that *sal* is a key regulator of medulla stem cell identity along the dorsal-ventral axis. The single-cell ATAC+RNAseq experiments currently underway will uncover the gene regulatory mechanisms that underly how *sal* confers this identity to medulla neural progenitors. We anticipate that these findings will contribute to our understanding of why mutations in the vertebrate *SALL* genes affect the specification of ventral horizontal cells in the mouse retina.

Applications of Artificial Intelligence for Diabetic Retinopathy Screening: An analysis of the Toronto Tele-Retinal Screening Program.

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Objective: The EyeArt (Eyenuk, Inc., 106 Los Angeles, California) artificial intelligence (AI) algorithm is a Food and Drug Administration (FDA) and Health Canada approved system with reliable results in diabetic retinopathy (DR) screening. Herein, we aimed to study the diagnostic accuracy of EyeArt system software for DR screening in an ethnically diverse population, as part of the Toronto Tele-Retinal Screening program.

Study Design: Retrospective Study.

Methods: All consecutive adult patients (age of 18 or older) with diabetes previously enrolled in the Toronto Tele-Retinal Screening program between July 2022 to May 2023 were included. The diagnostic accuracy of EyeArt for detection of DR and referrable disease amongst patients who had 2-field fundus images (macula centered, disc centered) was determined against the same images previously graded by a retina specialist as the reference standard.

Results: A total of 200 participants (400 eyes) were included in the analysis. The prevalence of DR was 10% amongst eyes graded by the retinal specialist. Eight percent (16) of fundus images of eyes included in the analysis were deemed to be ungradable by the EyeArt system. EyeArt graded the DR severity with a 75% agreement to the retina specialist gradings. Presence of diabetic macular edema (DME) agreeability between retina specialist and EyeArt was 96%. Sensitivity and specificity of the EyeArt for detecting referable DR was 83.3% (95% CI: 58.6-96.4%) and 84.8% (95% CI: 78.3-89.9%), respectively. Additionally, the positive predictive and negative predictive values were 37.5% (95% CI: 28.4-47.6%) and 97.9% (95% CI: 94.3-99.2%), respectively.

Conclusions: The findings from this study demonstrate that EyeArt AI system has good accuracy for detecting presence of DR and identifying referable disease amongst an ethnically diverse patient population in the Toronto Tele-Retinal Screening program when compared to a retina specialist. The EyeArt AI system can potentially serve as a point-of-care DR detection tool and help address the diabetic eye screening burden.

Acquired focal choroidal excavation secondary to pachychoroid choroidal neovascular membrane following central serous chorioretinopathy.

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Introduction: To demonstrate a case of acquired conforming type of focal choroidal excavation (FCE) secondary to pachychoroid choroidal neovascular membrane (pCNVM) following central serous chorioretinopathy (CSR) with rate of progression.

Methods: Case report discussing a 54-year-old Asian male who had spontaneous resolution of CSR in the right eye presented with pCNVM and FCE one year after initial diagnosis of CSR.

Results: The patient was initiated on intravitreal anti-vascular endothelial growth factor (aflibercept 2mg/0.05mL) injections over a course of 6 months, resulting in improvement of subretinal fluid and intraretinal hemorrhage, and followed for FCE progression for three years. No recurrence of subretinal fluid was noted. He was followed regularly with serial optical tomography coherence (OCT) imaging and measurements of the progression of FCE at the subfovea and at the initial location of the CNVM for three more years was obtained. The rate of excavation progression was 74.75µm per year at the subfovea and 70.75µm per year at the initial location of the CNVM.

Conclusions: Acquired FCE may occur secondary to CSR and pCNVM. The pathogenesis may be from focal choroidal ischemia, choroidal vascular collapse, and fibrosis leading to choroidal excavation. Also, this case highlights progression of the spectrum of pachychoroid disorders from CSR, pCNVM, and subsequent acquired confirming type of FCE. Further research is needed to assess other diseases leading to acquired FCE and determine the underlying mechanism.

Investigating the role of epithelial to mesenchymal transition (EMT) regulators TCF4 and TGF-β in Fuchs endothelial corneal dystrophy

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Research Type /Category: Basic/ Cornea

Introduction: Fuchs endothelial corneal dystrophy (FECD) is a complex ocular disease characterized by the progressive decline and morphological changes of corneal endothelial cells (CECs) that leads to corneal edema. The most common mutation in FECD is a trinucleotide CTG repeat expansion in the third intron of the transcription factor 4 (TCF4) gene. Studies on the effects of CTG repeats on TCF4 gene expression in FECD have shown inconsistent results, but recent evidence supports increased TCF4 isoform expression. Similarly, increased levels of transforming growth factor-β (TGF-β) 1 and 2 in FECD patients have been reported. Both TCF4 and TGF-β are involved in regulation of EMT and have been implicated in FECD pathogenesis. However, the interplay between TCF4, TGF-β and EMT in FECD remains to be elucidated. This study aims to determine whether TCF4 overexpression and TGF-β stimulation are sufficient to cause a FECD-like phenotype in normal CECs.

Methods: We generated stable corneal endothelial cell lines derived from normal donors or FECD patients that overexpressed different TCF-4 isoforms (-A, -B, -C). Western blot was performed to probe for EMT markers. Filamentous-actin staining was used to examine morphological changes. Scratch assay was performed to measure wound closure rates.

Results: We found that overexpression of TCF4 isoforms, even in the context of increased TGF-β1/-β2, did not increase EMT markers (fibronectin, ZEB1), change morphology or alter wound closure rates in normal cells. However, overexpression of TCF4-B isoform, but not TCF4-A or TCF4-C isoforms, in FECD cells resulted in increased cellular migration speeds compared to controls ($p<0.05$).

Conclusions: Overexpression of TCF4 in the presence of increased TGF-β1/-β2 is insufficient to induce a FECD-like phenotype in normal cells, suggesting that additional dysregulated pathways are likely required to induce FECD. In contrast, dysregulation of TCF4 in FECD cells led to altered cellular migration. Future studies will investigate the mechanistic link between TCF4-B and cell migration and provide further insight into FECD pathogenesis.

A Systematic Review of Toxicities of Densiron-68 in the Surgical Management of Retinal Detachment

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Purpose: Use of heavier-than-water intraocular tamponades may be helpful in managing complicated inferior retinal detachments (RD). Densiron-68 is a heavy silicone oil with the potential to promote chorioretinal adhesion and provide retinal support in the upright and supine positions. The full spectrum of possible complications of Densiron-68 is unclear. This systematic review aimed to summarize the published literature regarding toxicities of Densiron-68 in RD surgery.

Study Design: Systematic review.

Methods: A search strategy was designed on Ovid MEDLINE, EMBASE, and the Cochrane Library. Primary studies evaluating the toxicities and reversibility of Densiron-68 toxicities in RD management in adults between January 2000 to May 2022 were included. Studies involving retinal conditions other than RD, non-English studies, secondary studies, non-peer-reviewed articles, or those that included less than 5-eyes were excluded. The primary outcome was reported toxicities associated with Densiron-68. The secondary outcome was the reversibility of these toxicities.

Results: 28 studies were included, which collectively reported on 1078 eyes. Mean follow-up time was 41.9 weeks (IQR 32.4-52.0 weeks). The weighted mean pre-operative and post-operative BCVA was 1.38 ± 0.64 logMAR (20/500 Snellen) and 0.86 ± 0.55 logMAR (20/150 Snellen), respectively. Intraoperatively, the most common complication was Densiron-68 in the anterior chamber (AC, n=2). Postoperatively, 38 toxicities were identified. Of all postoperative toxicities, the three most common were raised IOP (n=249 eyes), emulsification of Densiron-68 (n=158 eyes), and intraocular inflammation (n=145 eyes). Of the studies that reported toxicity reversibility, 91% of raised IOP (203/222 eyes), 56% of emulsification (10/18 eyes), and 100% of intraocular inflammation (67/67 eyes) cases resolved. The length of time for reversal ranged from 2 days – 2 months for raised IOP and 7-35 days for inflammation.

Conclusions: Across 28 studies that assessed the use of Densiron-68 in surgically managed cases of retinal detachment, there was an overall improvement in BCVA. A total of 38 unique post-operative toxicities were identified. Of the 3 most common toxicities, toxicity reversibility was achieved in most cases.

Relationship between Disease and Treatment Factors in Diabetes Mellitus with Vision Difficulty in the National Health Interview Survey: A Cross-sectional, Population-Based Analysis

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Introduction: Vision difficulty is common in individuals with diabetes. The relationships between disease and treatment factors in diabetes with vision difficulty at a population level remain unknown. The objective of this cross-sectional, population-based analysis study was to investigate the relationship between disease and treatment factors in diabetes and self-reported vision difficulty.

Methods: The National Health Interview Survey (NHIS) is an annual population-based survey based on the U.S civilian non-institutionalized population age 18 and older. It provides self-reported data on demographic characteristics, socioeconomic factors, health status, and health care access. The 2021 iteration of the NHIS consisting of data collected from January to December 2021 was used. Adult participants of the NHIS that responded to the vision difficulty question "Do you have difficulty seeing, even when wearing glasses or contact lenses?" were included in this analysis. Univariable and multivariable logistic regression analysis were performed for each diabetes-related factor of interest with the outcome of vision difficulty. Multivariable analysis controlled for confounding sociodemographic variables.

Results: Of the 29,464 included participants, 45.37% were male and 54.63% were female. Univariable logistic regression showed there was an increased odds of self-reported vision difficulty among participants with diabetes (OR 2.14; 95%CI, 1.94-2.37; p<0.001), prediabetes (OR 1.95; OR 95%CI, 1.78-2.13; p<0.001), or gestational diabetes (OR 1.54; 95%CI, 1.28-1.86; p<0.001) compared to healthy participants. In participants with diabetes, those who reported taking insulin had higher odds of vision difficulty (OR 1.62; 95%CI, 1.37-1.92; p<0.001), as did those who had taken less insulin to save money within the past year (OR 1.87; 95%CI, 1.13-3.09; p=0.01, or reported an overwhelming level of stress related to managing their diabetes (OR 2.14; 95%CI, 1.77-2.58; p < 0.001). Multivariable analysis confirmed an association of vision difficulty with a diagnosis of diabetes (OR 1.19; 95%CI, 1.05-1.34, p=0.005), prediabetes (OR 1.31; 95%CI, 1.18-1.45, p<0.001), gestational diabetes (OR 1.35; 95%CI, 1.11-1.64, p=0.003), and those who experienced diabetes-related stress (OR 1.80; 95%CI, 1.46-2.21, p<0.001) adjusting for relevant confounding factors. Participants who had a blood sugar test within the past year additionally had a higher risk of self-reported vision difficulty (OR 1.15; 95%CI, 1.05-1.27, p=0.04), adjusted for confounders.

Conclusion: Multiple disease and treatment-related factors in diabetes are associated with self-reported vision difficulty across a large sample of the U.S civilian population. Increasing vision difficulty was found in diabetic participants who had stress related to their condition, as well as those who required insulin but had inadequate management.

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