ISVER
האגודה הישראלית לחקר העין והראיה
Israel Society For Vision & Eye Research
ARVO
CHAPTER AFFILIATE

הכנס השנתי של
האגודה הישראלית לחקר העין והראיה
27.2.2025
יום חמישי | מלון דניאל, הרצליה

PROGRAM & ABSTRACTS
45th Annual Meeting
Daniel Hotel, Herzliya
February 27th 2025

תכנית מדעית ותקצירים
הכנס השנתי ה- 45 של
האגודה הישראלית לחקר העין והראיה
מלון דניאל, הרצליה
27 בפברואר 2025

יו"ר האגודה:
פרופ' מיכל קרמר

הוועדה המדעית:
ד"ר סאמר ח'טיב, פרופ' רובי שלום-פוירשטיין, ספיר שלום

שיפוט תקצירים:
ד"ר סאמר ח'טיב, פרופ' רובי שלום-פוירשטיין, ספיר שלום
ד"ר קלאודיה יהלום, פרופ' שירי סודרי

ארגון התכנית המדעית:
ד"ר קלאודיה יהלום, פרופ' דינה צור, ד"ר הדס בן-אלי

הפקת הכנס:
IN STYLE

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תודותינו והערכתנו לחברות התומכות בכנס:

PLATINUM

Roche

GOLD

BAYER

Dexcel pharma

LAPIDOT GROUP

לראות
העמותה לחקר בריאות העין ומניעת עיוורון בישראל (ע"ר)

SILVER

abbvie

אלפא נט בע"מ
Alpha Net Ltd

Blueprint Genetics

DiagnosTear

DTY Optical
flexible solutions you can trust

אלדן
קבוצת ניאופרם

G.S Optixx
ג.ש אופטיקס

IOS
האיגוד הישראלי לרפואת עיניים
ISRAELI OPHTHALMOLOGICAL SOCIETY

MEDIFISCHER Engineering & Science

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Time	Session and Location	
	Exhibition Area	
08:00-08:30	Welcome Reception & Registration	
	Plenary Hall - *Poseidon*	
08:30-08:40	Opening Remarks	
	Parallel Sessions - Posters "Rapid Fire" Presentations	
08:40-09:50	Plenary Hall - *Poseidon*	Daniel Hall
	Pediatrics	Anterior Segment
	Retina	Neuro-Ophthalmology, Glaucoma
	Genetics & Basic Science	Oncology-Oculoplastics
	AI	
	Uveitis	
	Plenary Hall - *Poseidon*	
10:00-10:40	Bringing data to life - From trial and error to predictable medicine **Prof. Shai Shen-Orr, Technion**	
	Exhibition Area	
10:40-11:30	E-posters over Coffee	
	Parallel Sessions	
11:30-12:10	Plenary Hall - *Poseidon*	Daniel Hall
	Retina	Pediatrics
12:10-12:55	Genetics & Basic Science	Oncology-Oculoplastics
12:55-13:50	Lunch – At Hotel Restaurant	
	Plenary Hall - Poseidon	
13:50-14:00	Grants Awards	
14:00-14:35	Drug repurposing for retinal neuroprotection **Prof. Francine Behar-Cohen**	
14:35-15:45	Anterior Segment	
	Exhibition Area	
15:45-16:05	E-posters over Coffee	
	Plenary Hall - *Poseidon*	
16:05-16:45	Neuro-Ophthalmology, Glaucoma	
16:45-17:20	AI	
17:20	Closing Remarks	

יושבי ויושבות הראש של האגודה הישראלית לחקר העין והראיה
CHAIRPEOPLE OF THE ISRAEL SOCIETY FOR VISION AND EYE RESEARCH

Prof. Elaine Berman	1979-1982	פרופ' איליין ברמן ז"ל
Prof. Michael Belkin	1983-1985	פרופ' מיכאל בלקין
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Prof. Shabtay Dikstein	1990-1993	פרופ' שבתאי דיקשטיין
Prof. Fabian Abraham	1994-1996	פרופ' פביאן אברהם ז"ל
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Prof. Eyal Banin	2010-2012	פרופ' איל בנין
Prof. Avi Solomon	2012-2015	פרופ' אבי סלומון
Prof. Dror Sharon	2015-2018	פרופ' דרור שרון
Prof. Itay Chowers	2019-2021	פרופ' איתי חוברס
Prof. Shahar Frenkel	2021-2024	פרופ' שחר פרנקל
Prof. Michal Kramer	2024	פרופ' מיכל קרמר

חברי וחברות ועד האגודה הישראלית לחקר העין והראיה
BOARD MEMBERS OF THE ISRAEL SOCIETY FOR VISION AND EYE RESEARCH

Prof. Michal Kramer - Chairperson	פרופ' מיכל קרמר - יו"ר
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Dr. Reut Ifrah	ד"ר רעות יפרח
Prof. Ruby Shalom-Feuerstein	פרופ' רובי שלום-פוירשטיין
Treasurer - Dr. Samer Khateb	גזבר - ד"ר סאמר ח'טיב
Association's auditor - Prof. Haim Levi	מבקר העמותה – פרופ' חיים לוי

מלגות לחוקרים צעירים

מענקי מלגות השתתפות ב ARVO למחברי העבודות המצטיינות 2024,
ניתנו באדיבות עמותת "לראות" והאיגוד הישראלי לרפואת עיניים

1st Prize - Maxim Bez
Department of Ophthalmology, Tel-Aviv Sourasky Medical Center, Tel-Aviv
Fabrication and characterization of 3D-printed, stem cell-derived tri-layered retinal implants

2nd Prize - Natan Lishinsky-Fischer
Ophthalmology Department, Hadassah Medical Center, Jerusalem, Israel
The presence of subretinal drusenoid deposits as a predictor of cardiovascular disease

3rd Prize – Tamar Azrad-Leibovitch
Life Sciences School of Optometry and Vision Science, Bar-Ilan University, Ramat-Gan, Israel
A new rat model for retinal degeneration: The GCaMP6f+\- RCS-\- Rat

80% ממקרי העיוורון ניתנים למניעה באמצעות איתור מוקדם וטיפול מתאים

עמותת "לראות", הוקמה ב-2006 במטרה למצוא מרפא למחלות עיניים הגורמות לעיוורון ולהקטין את מספר החולים. העמותה פועלת להעלאת המודעות לחשיבותן של בדיקות ראייה סדירות, למניעת התפתחות מחלות עיניים ואיתור פגמים.

בעלי תפקידים בעמותת לראות

נשיא העמותה: פרופ' מרדכי שני; **יו"ר העמותה:** מר אוהד להב;
מנכ"לית העמותה: גב' נדין הולנדר.
יו"ר המועצה המדעית: פרופ' דרור שרון.
חברי הועד המנהל: פרופ' אדו פרלמן, פרופ' איתי חוברס, פרופ' אריה סולומון, פרופ' אירית בכר, פרופ' ענת לוינשטיין, פרופ' חנא גרזוזי, פרופ' יעקב פאר, פרופ' אהוד אסיה, פרופ' דרור שרון, פרופ' יאיר מורד, פרופ' חני ורבין, ד"ר רונית לוינגר, מר מרק עמוס, ד"ר ניר ארדינסט.

פרויקטים נבחרים של עמותת לראות

- **בדיקות עיניים בקהילה ובמקומות העבודה:**

עשרות אלפי קשישים בישראל, מקבלים את הידרדרות ראייתם, לעיתים עד לכדי עיוורון, כגזירת גורל. הם לא מודעים לכך שבמקרים רבים, ניתן להציל ולשפר משמעותית את ראייתם ואת איכות חייהם, בזכות הרפואה המשוכללת והמתקדמת של היום.
עמותת "לראות" מביאה את המרפאה לסביבתם הקרובה של הקשישים: לבתי אבות, למרכזי יום, למתנסי"ם או לביתם הפרטי, שם אנו עורכים ימי בדיקות מרוכזים, בכל הארץ. תוצאות הבדיקה מועברות בטכנולוגיה חדישה ומשוכללת לרופא/ה מומחה/ית, אשר מאבחנים את הבעיה ומצילים קשישים מעיוורון מיותר, פשוט כך .

- **הנגשת מידע ויעוץ רפואי:**

עמותת לראות מחויבת להעלאת מודעות לבריאות העין ומניעת עיוורון. בפורומים המקצועיים שלנו ובקבוצת הפייסבוק, תוכלו לשאול כל שאלה ולקבל תשובה מפי רופא/ה מוסמך/ת. פורומים לדוגמה: מחלות עיניים אצל ילדים, ראיה ירודה, גידולי עיניים ועוד.

- **המטה הישראלי למחקר חדשני בתאי גזע**:

כחלק ממאמץ לאומי לשיפור בריאות העין ומניעת עיוורון בישראל, עמותת לראות מובילה את הקמתו וניהולו של המטה הישראלי למחקר בתאי גזע, אשר משמש כגוף המאגד תחתיו חוקרים מכל התחומים ומוביל מחקר חדשני בתאי גזע.

- **חודש המודעות:**

מדי שנה, בחודש דצמבר, עמותת יוצאת בקמפיין ארצי להעלאת מודעות לבעיות שונות הקשורות בראייה ועיוורון. במסגרת פעילויות חודש המודעות מתקיימות הרצאות, חשיפה במדיה, הפקת מגזין בנושא קידום בריאות העין בשיתוף איגוד רופאי העיניים בהוצאת עיתון 'הארץ' ועוד.

בקרו אותנו:

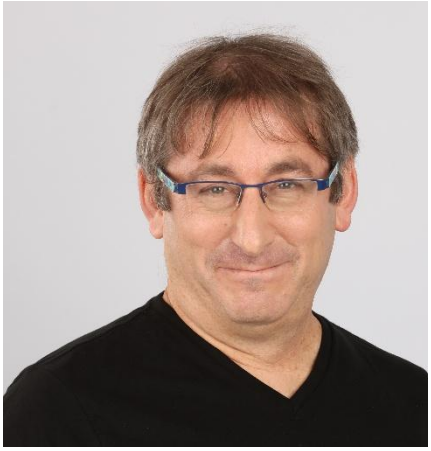
פייסבוק www.facebook.com/Lirot.NGO אינסטגרם https://www.instagram.com/lirot_association

יוטיוב https://www.youtube.com/user/LirotAssociation אתר https://www.eyes.org.il/Home

נדין הולנדר, מנכ"לית העמותה nadine@eyes.org.il

Keynote Speaker

Prof. Shai Shen-Orr



Bringing data to life - From trial and error to predictable medicine

Thursday, February 27th, 2025, at 10:00

Systems Biologist Shai Shen-Orr is an Associate Professor in the Faculty of Medicine at the Technion—where he directs the laboratory of Systems Immunology and Precision Medicine. Shai develops novel analytics for studying the immune system—tools which he applies to study the drivers of immune variation, and their implications for Precision Medicine.

Shai is the Director of the Zimin Institute for AI Solutions in Healthcare and the co-director of Tech.AI, Technion's AI umbrella organization. Most recently he is the founding director of the Technion Healthy Aging Institute and is co-CSO of the global non-profit, the Human Immunome Project.

Based on his academic research Shai co-founded CytoReason, where he serves as Chief Scientist. CytoReason is a PharmaAI company developing a computational disease modeling technology to support the world's largest pharma companies in increasing the probability of phase 2 success.

Keynote Speaker

Prof. Francine Behar-Cohen

Drug repurposing for retinal neuroprotection

Thursday, February 27th, 2025, at 14:00

Current position: Professor of Medicine, Ophthalmology, University Paris city, surgical and medical retina specialist at Cochin hospital AP-HP and at Foch Hospital

Director of the INSERM team Physiopathology of ocular diseases: therapeutic innovations at the Centre de Recherche des Cordeliers, Paris France

Founder of Eyevensys SAS France and of co-founder of Early Sight Switzerland

Scientific Expertise

- Ophthalmology teaching (medical and scientific students and professionals)
- Member of the scientific Inserm evaluation committee in neurosciences (CSS 1), 2007- 2012
- Expert for government institutions : President of group of work on LED at the ANSES (2009-2011), President of group of work on 3D technologies (2010-2015), president of the GT-LED2 (2015-present). Member of the group of work on virtual reality (2018-2021)
- Member of the comité d'expert scientifique at the ANSES (french agency for the security of environment) (2010-2012)
- Member of the scientific council of ANSES (2021-present)
- Member of the Scenihr (2011-2012) (EU committee for the evaluation of security of emerging technologies).
- Member of the Scientific Council of the Fondation pour la Recherche Médicale (2011-2015)
- Member of the Fédération des Aveugles et Handicapés Visuels (2011-present)
- Editorial board member of : Progress in Retinal and Eye Research (IF :11), Molecular Vision, Translational Visual Science and technology, Ophthalmologica, Journal of Ocular Pharmacology.
- Member of the Bayer Vision Academy (2018-present)
- Member of the Bayer Global International Award scientific committee (2018-present)

VALORIZATION

- Inventor of more than 35 family patents
- Founder of Optis France in 1999, now Eyegate Pharma Int (Boston, USA)
- Founder of Eyevensys SAS in 2008
- Founder of EarlySight Switerland in 2016

Président of the Pour la Vision patient Association

[Pour la vision | Association CROhttps://www.pourlavision.org]

Time	#	Abstract Title	Speaker	Hall	Session & Moderators	
08:00	Welcome Reception & Registration			מתחם התערוכה		
08:30	Opening Remarks		Prof. Michal Kramer	מליאה (פוסידון)		
Rapid Fire - Parallel Sessions (08:40-09:50)						
08:40	PP1	validation of the PlusOptix S12C for detecting amblyopia risk factors in a tertiary care pediatric population	Alon Avrahani **AC**	אולם מליאה-פוסידון	ילדים E-posters 3	Rapid Fire יו"ר: פרופ' יוסי מנדל וד"ר רעות יפרח
08:42	PP2	Strabismus without Amblyopia in children: does it affect binocular reading speed?	Guy Barnett-Itzhaki			
08:44	PP3	Botulinum Toxin A for the Treatment of Esotropia in Children- A Tertiary Center's Experience	Anat Bachar Zipori			
08:46	PP4	Comparison of Bilateral Medial Rectus Recession Versus Unilateral Recession Resection as Surgery for Monocular Esotropia without Amblyopia	Eddie Barayev			
08:48	PP5	Equitable healthcare: bridging socioeconomic gaps in amblyopia treatment outcomes based on evidence from a tertiary care center	Konstantin Yaakov Gushansky **AC**			
08:50	PP6	Parents' resolution with their child's diagnosis, parent-child communication about the diagnosis, and the well-being of adolescents and young adults w	Itay Green			
08:52	PP7	Clinical and Genetics Characteristics in a Pediatric Cohort	Rotem Azmon **AC**			

		with Inherited Retinal Diseases				
08:54	RP1	Analysis of Near Infrared reflectance vs. Blue autofluorescence in patients with Geographic Atrophy secondary to AMD	Roee Arnon **AC**			
08:56	RP2	Prolonged use of Acetazolamide for treatment of Central Serous Chorioretinopathy	Wajdi Naamneh			
08:58	RP3	Investigating the effect of electrical pulse configuration on the spatial spread of retinal activation: Parameter optimization for retinal prostheses	Aliza Folger **AC**			
09:00	RP4	The dark-adapted ERG Oscillatory Potentials depends upon activation of the cone system	Aviad Nemet **AC**			
09:02	RP5	Development of a portable electrophysiological system for ex-vivo eyes	Nairouz Farah		**רשתית** **E-posters 4**	
09:04	RP6	Retinal Vascular Occlusion after COVID-19 Vaccination – A Nationwide Cohort Study	Yuval Koslov **AC**			
09:06	RP7	Development of a Simultaneous Combination Therapy for Alternative Multidimensional Etiologies of Subretinal Angiogenesis	Ghadeer Abu-Tair			
09:08	RP8	Patients with age-related macular degeneration have increased susceptibility to valvular heart disease	Natan Lishinsky-Fischer			
09:10	RP9	Transcriptome-wide Association Study Identifies Novel Risk Loci Associated With Age-Related	Michelle Grunin **AC**			

		Macular Degeneration				
09:12	RP10	Prechoroidal cleft characteristics in neovascular age-related macular degeneration	Naama Lippin **AC**			
09:14	RP11	Axial Length Increase Following Combined Pars Plana Vitrectomy and Encircling Scleral Band	Tiran Golani			
09:16	GP1	Clinical and Molecular Characterization of Microphthalmia, Anophthalmia, and Ocular Coloboma in the Israeli population	Shirley Pincovich **AC**		**גנטיקה** **E-posters 5**	
09:18	GP2	Possible Genetic Trochlear Nerve Palsy in One Family	Shir Butnik-Cohen **AC**			
09:20	GP3	A heterozygous LRP1 variant is associated with isolated high myopia in a family of Jewish-Tunisian ancestry.	Ari Biller **AC**			
09:22	GP4	Heterozygous loss-of-function variants in TJP1 (ZO-1) cause microphthalmia and coloboma	Jonathan Eintracht **AC**			
09:24	GP5	Recent identification of four novel genes associated with macular dystrophy in Israeli individuals	Tamar Ben Yosef			
09:26	GP6	Phenotype-Genotype Correlation in a Cohort of Israeli Patients with OCA1 Albinism	Or Shmueli **AC**			
09:28	GP7	Study on the BAF (SWI/SNF complex) subunits BAF155 and BAF170 activities in the development and maintenance of pigmented eye lineages in mammals	Nitay Zuk-Bar **AC**			
09:30	GP8	Cognitive Assessment of transgenic mice	Basel Obeid **AC**			

		with Alzheimer's Disease				
09:32	GP9	An optimized procedure for intracameral injection in rats with low risk of adverse effects	Avital Eisenberg-Lerner			
09:34	GP10	AD-3281 inhibits pathological neovascularization in preclinical models of neovascular AMD (nAMD), suggesting potential as a novel therapy	Batya Rinsky **AC**			
09:36	AIP1	A Data-Driven Natural Language Processing Platform for Clinician-Led Exploration of Retinal Fluid Dynamics and Personalized Management of nAMD	Dinah Zur	**אולם מליאה-פוסידון**	**AI** **E-posters 3**	
09:38	AIP2	Artificial Intelligence-Based Chatbots as Oculoplastic Consultants: Are They Good Enough?	Ofira Zloto			
09:40	AIP3	Validation and Clinical Applicability of Deep Learning Model for Automated Diabetic Macular Edema Segmentation in OCT Scans	Yahel Shwartz **AC**			
09:42	AIP4	Predicting Vision Abnormalities in Pediatric NF1 Using Machine Learning and OCT data	Ayelet Goldstein			
09:44	AIP5	Smartphone-Based Teleophthalmology for Triage of Urgent Ophthalmic Conditions	Shlomit Jaskoll			
09:46	UP1	Gender Influences on Uveitis Etiology: Insights from a Meta-analysis and systematic review	Tom Liba **AC**		**Uveitis** **E-posters 4**	
09:48	UP2	The Impact of Perceived Stress on Uveitis Onset and Flare-ups	Iliya Simantov **AC**			

08:40	ASP1	Reliability of a multifunctional meibography device in normal young participants	Liat Gantz	**אולם דניאל**	**מקטע קדמי** **E-posters 2**	**Rapid Fire** **יו"ר:** **ד"ר נור חטיב** **וד"ר זיו רוטפוגל**
08:42	ASP2	Behavioral and Clinical Indicators for Dry Eye Disease: Preliminary Findings	Reut Ifrah			
08:44	ASP3	The Association Between Blepharitis and Lower Eyelid Ectropion in a Large Cohort of Patients	Lital Smadar **AC**			
08:46	ASP4	Assessing visual performance in presbyopes using dynamic focal sunglasses	Ravid Doron			
08:48	ASP5	Microbiome Profiling of Pterygium	Raz Rubinshtein **AC**			
08:50	ASP6	miR-184/ATF3 axis is required for the maintenance of active limbal stem cell state and corneal homeostasis	Gharam Yassen **AC**			
08:52	ASP7	Characterization of Immune Cell Populations in a Murine Model of Pediatric Penetrating Keratoplasty	Mark Krauthammer			
08:54	ASP8	Intraoperative sensor and alerting system for phacoemulsification	Yoav Nahum			
08:56	ASP9	Designing a Novel Tool for Corneal Foreign Body Removal	Lee Goren **AC**			
08:58	ASP10	Annular Dark Shadow as a Potential Familial Marker for Keratoconus: A Preliminary Investigation	Arige Gideon Abousaid			
09:00	ASP11	Descemet membrane endothelial keratoplasty compared to ultrathin Descemet stripping automated endothelial	Tal Corina Sela **AC**			

		keratoplasty: a meta-analysis				
09:02	ASP12	Effect of Pupil Size and Corneal Spherical Aberrations on Premium Lenses' Optical Performance	Benjamin Stern **AC**			
09:04	ASP13	The effects of corneal flap side-cut angle on flap stability of femtosecond LASIK surgery	Igor Kaiserman			
09:06	NGP1	A Novel Multi-Parameter Point-of-Care Tear Film Test for Diagnosis of Dry Eye Syndrome, Severe Meibomian Gland Dysfunction, and Responsiveness to Therapy	Shimon Gross			
09:08	NGP1	Teprotumumab Exacerbates Damage in a Mouse Model of Optic Neuropathy	Stephen Richard **AC**	**אולם דניאל**	**נוירואופתלמולוגיה + גלאוקומה E-posters 1**	**Rapid Fireיו"ר: ד"ר נור חטיב וד"ר זיו רוטפוגל**
09:10	NGP2	The incidence of subsequent high intracranial pressure in patients undergoing early, open, and wide strip craniectomy for sagittal synostosis	Anat Bachar Zipori			
09:12	NGP3	Alterations in pupil light reflex kineticks in patients with Optic Neuritis	Marian Haiadry **AC**			
09:14	NGP4	Oculomotor dysfunctions among Israeli Defense Force soldiers admitted to an inpatient rehabilitation unit for polytrauma: the impact of co-occurring t	Zohar Treistman Da'ari			
09:16	NGP5	Predicting Structural Reliability in Ophthalmology Using Sequence-Based Analysis of Humphrey Visual Field Test Results	Nir Avisar **AC**			

		in glaucoma patients				
09:18	NGP6	Using Major Vessel Position Measurements to Reduce OCT RNFL False Positives	Lustig Barzelay			
09:20	NGP7	The association between Migraine and Glaucoma: A retrospective cohort study	Matan Bar			
09:22	NGP8	Higher Risk and Earlier Onset Glaucoma in Cushing's Syndrome	Yael Sharon			
09:24	NGP9	Evaluating compliance in glaucoma treatment: big data analysis of prescription patterns and influencing factors	Alon Zahavi			
09:26	NGP11	Objective Quantification of Apathy Among the Cognitive Spectrum Using Virtual Reality: Gaze Metrics and Autonomic Nervous System Responses	Shlomit Zorani **AC**			
09:30	OOP1	The Effect of Posterior Approach Ptosis Surgery vs. Anterior Approach Ptosis Surgery on Signs of Dry Eye Syndrome	Rachel Shemesh **AC**	**אולם דניאל**	**אונקולוגיה ואוקולופלסטיקה** **E-posters 5**	
09:32	OOP2	Congenital blepharoptosis-surgical approach results	Daniella Shalom **AC**			
09:34	OOP3	Association Between Acquired Punctal Stenosis and Ocular Surface Disease: the Egg and the Chicken Story	Yael Barzelay			
09:36	OOP4	High-Risk Histopathological Features Following Primary Enucleation in Bilateral Retinoblastoma	Tehila Shlomov **AC**			

09:38	OOP5	Sebaceous Carcinoma of the Eyelid Metastasis Showing Small Cell Carcinoma-Like Features: a Case Report	Nur Khatib			
09:40	OOP7	Blinking Pattern and Dry Eye: A Videographic Analysis	Roee Arnon **AC**			
09:42	OOP8	Ophthalmologic Abnormalities in Cleft Lip and Palate	Daphna Landau			
09:44	OOP9	Twenty years of Chalazion: Big Data Analysis from the CLALIT HMO	Yogev Giladi			
10:00	Bringing data to life - From trial and error to predictable medicine		Prof. Shai Shen-Orr	**מליאה (פוסידון)**	**מרצה אורח**	
10:40	**E-posters over Coffee**			**מתחם התערוכה**	**E-posters 1-5**	
Parallel Sessions (11:30-12:10)						
11:30	R1	Diet Habits in Israeli Age-Related Macular Degeneration Patients,	Tzippora Greenberg	**אולם מליאה-פוסידון**	**רשתית** **יו"ר:** **פרופ' איתי חוברס** **וד"ר יפעת שר-רוזנטל**	
11:35	R2	Delivery of sub Retinal Soft Mono Layer Retinal Pigment Epithelium Implant	Gilad Rabina			
11:40	R3	Artificial retinal implant composed of 3D scaffold integrated with photoreceptors and retinal pigment epithelium cells	Tamar Yaniv **AC**			
11:45	R4	Small heat shock superfamily of proteins as a retinal defense mechanism against pathogenic amyloid beta	Efrat Naaman **AC**			
11:50	R5	Single cell study of hypothermic effect of retinal survival during ischemia	Eden Buza **AC**			
11:55	R6	Photoreceptor to Retinal Pigment Epithelium Atrophy Ratio and Longitudinal Atrophy Growth in Age-Related	Itay Chowers			

		Macular Degeneration			
11:30	P1	The Objective Scatter Index (OSI) and Cataract Assessment in the Pediatric Population	Hadas Mechulam	**אולם דניאל**	**רפואת עיניים ילדים** **יו"ר:** **פרופ' אירן ענתבי** **ד"ר עלוית וולף**
11:35	P2	Clinical findings, multimodal imaging and electrophysiology of pediatric patients with unilateral perifoveal annular lesion	Miriam Ehrenberg		
11:40	P3	Prospective Open Label Randomized Controlled Clinical Study Evaluating the Efficacy of Perceptual Learning among Patients with Congenital Nystagmus	Sigal Zmujack Yehiam		
11:45	P4	Surgical Outcomes of Patients with Mild to Moderate Exodeviation with and without Combined Superior Oblique Palsy	Dahlia Palevski		
11:50	P5	Evaluation of the G-ROP Model for Retinopathy of Prematurity in the Israeli Preterm Population: A Multicenter Prospective Study	Binyamin Friedman **AC**		
Parallel Sessions (12:10-12:55)					
12:10	G1	A homozygous frameshift mutation in KHDC4 causes syndromic Leber congenital amaurosis in Arab Christian patients	Neta Barnoy	**אולם מליאה-פוסידון**	**גנטיקה** **יו"ר:** **פרופ' ערן פרס** **ד"ר מירי ארנברג**
12:15	G2	Optimization of gRNA for Enhanced RNA Editing of Mutations Causing Inherited Retinal Diseases	Johanna Valensi **AC**		
12:20	G3	Effect of Systemic Immune Status on Disease Progression in the Fam161a Knock-	Rotem Mizrahi **AC**		

		out Mouse Model of Retinitis Pigmentosa			
12:25	G4	PRPF31 heterozygous mutations: effects on cell dynamics and mitochondrial function in iPSC-derived RPE models	Tal Shadi **AC**		
12:30	G5	Suppressor-tRNA mediated translational readthrough of premature termination codon mutations causing Inherited Retinal Dystrophies	Asodu Sandeep **AC**		
12:35	G6	Cell-Free DNA Methylation in Aqueous Humor	Adi Kramer **AC**		
12:10	OO1	Thyroid blood tests and TED management of tobacco consumers and cannabis consumers	Jonathan Kfir **AC**	**אולם דניאל**	**אונקולוגיה ואוקולופלסטיקה** **יו"ר:** **ד"ר מיה אייגר-מוסקוביץ ופרופ' גיא בן סימון**
12:15	OO2	Lacrimal gland volume measurements in normal and thyroid orbitopathy patients using Magnetic Resonance Imaging- ongoing study	Khaled Khalifa		
12:20	OO3	Corneal Pathologies in Patients with Thyroid Eye Disease: Prevalence, Clinical Characteristics and treatment	Shira Shapira-Nass		
12:25	OO4	The differences in clinical characteristics and outcomes of ptosis surgery: a report of 260 cases	Shalev Fried **AC**		
12:30	OO5	Outcomes after multidisciplinary treatment for pediatric and adult orbital rhabdomyosarcoma	Nur Khatib		
12:35	OO6	Impact of high-risk histological features in unilateral retinoblastoma: massive choroidal invasion,	Itay Nitzan **AC**		

		retrolaminar optic nerve invasion, both or none			
12:40		Discussion			
12:55	**Lunch at Hotel Restaurant**			**מסעדת המלון**	
13:50	**Awarding Prizes**			**אולם מליאה-פוסידון**	
14:00	Drug repurposing for retinal neuroprotection		Prof. Francine Behar-Cohen		**מרצה אורחת**
14:35	AS1	PRIMA-1MET inhibits the development of limbal stem cell deficiency in Trp63-mutated ectodermal dysplasia mouse model	Rabea Misherki **AC**	**מקטע קדמי יו"ר: פרופ' אירית בכר פרופ' רובי שלום פוירשטיין**	
14:40	AS2	Point mutation in p63 perturbs limbal stem cell boundary formation and renewal dynamics in vivo	Waseem Nasser **AC**		
14:45	AS3	Mitochondria Transplantation Promotes Corneal Epithelial Wound Healing	Ziv Rotfogel		
14:50	AS4	Proteomic and epitranscriptomic signatures as biomarkers for corneal limbal stem cell deficiency	Yamit Cohen-Tayar **AC**		
14:55	AS5	Bleomycin subconjunctival injection for corneal neovascularization in a rat model	Rita Zlatkin **AC**		
15:00	AS6	Trace Element Analysis in Feline Corneal Sequestrum	Oren Pe'er		
15:05	AS7	Prospective Randomized Controlled Clinical Study Evaluating the Efficacy of Perceptual Learning in Improving Vision among Patients with Keratoconus	Assaf Greenbaum		
15:10	AS8	Copper can be detected in tears of undiagnosed patients with Wilson disease	Yakov Rabinovich **AC**		

15:15	AS9	Detection of Subclinical Corneal Edema in Patients With Fuchs Endothelial Dystrophy Using Galilei Corneal Tomography	Shmuel Kagasov **AC**		
15:20	AS10	Dual therapy with tacrolimus and sodium hyaluronate enhances tear film stability in evaporative dry eye disease: insights from a spontaneous canine large animal model	Lionel Sebbag		
15:25	AS11	Comparing Surgeons' Muscle Properties While Using Standard Surgical Microscope versus an Ophthalmic Exoscope with an Augmented-Reality Headset	Shelly Yacubovich		
15:30		Discussion			
15:45	**E-posters over Coffee**			**מתחם התערוכה**	**E-posters 1-5**
16:05	NG1	Extracellular vesicles from stressed non-pigmented ciliary epithelial cells alter gene expression in trabecular meshwork cells	Elie Beit-Yannai	**אולם מליאה-פוסידון**	**נוירואופתלמולוגיה וגלאוקומה** **יו"ר:** **פרופ' הדס קליש-שטיבל** **ד"ר אלון זהבי**
16:10	NG2	Studying Critical Flicker Frequency Threshold (CFF) in glaucoma subjects: anatomical and Functional Correlations	Ilana Bouzaglo Eden **AC**		
16:15	NG3	Preclinical efficacy of EXOPTEN: a novel exosome-based therapy for acute optic nerve pathology	Gabriella Braun		
16:20	NG4	Acute Optic Neuropathy in Older Adults: Differentiating Between MOGAD Optic Neuritis and Nonarteritic Anterior Ischemic Optic Neuropathy	Hadas Stiebel-Kalish		

16:25	NG5	Seasonal Variation of Idiopathic Intracranial Hypertension	Mai Mizrachy **AC**		
16:30	NG6	Evaluation of the ocular neuroprotective effects of 3K3A-activated protein C using a mouse model of optic nerve crush	Gil Ben-David **AC**		
16:45	AI1	Predictive Model for APOE4 Carriers Using Retinal Imaging and machine learning	Oren Haviv **AC**		**AI** **יו"ר:** **ד"ר אורלי גל-אור** **פרופ' חיים לוי**
16:50	AI2	Near InfraRed Imaging for the Assessment of Geographic Atrophy Using Deep Learning	Aviv Fineberg **AC**		
16:55	AI3	Automatic Identification and segmentation of choroidal vessels on Optical Coherence Tomography, Using AI	Bar Yacobi **AC**		
17:00	AI4	A Behavioral-Based Machine Learning Predictive Model for Myopia in Children	Jonathan Levine		
17:05	AI5	Machine Learning Analysis of Factors Influencing Suboptimal Visual Outcomes Post-Cataract Surgery	Yaacov Cnaany **AC**		
17:10		Discussion			
17:20		**Closing Remarks**	**Prof. Michal Kramer**		

תקצירים

Abstracts

PP1

Validation of the PlusOptix S12C for detecting amblyopia risk factors in a tertiary care pediatric population

Alon Avrahami[1], Hadas Ben-Eli [1,2], Aviya Benyamin[2], Edna Granit[1,2,] Hadas Mechoulam[1], Irene Anteby[1]

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Abstract

Purpose: To evaluate the sensitivity and specificity of the PlusOptix S12C device in detecting amblyopia risk factors (ARFs) in children aged 2-7 years, in accordance with the 2020 Israeli Ministry of Health (MOH) directives the 2021 American Association for Pediatric Ophthalmology and Strabismus (AAPOS) guidelines.

Methods: A cross-sectional, observational study was conducted at a tertiary care hospital. Children approaching for vision test were screened using the PlusOptix S12C device and results were compared with gold-standard cycloplegic refraction and cover test. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for the overall population and subpopulations based on amblyopia risk factors.

Results: A total of 196 children aged 24-84 months were screened (46.4% boys, mean age of 56.94±17.52 months). The PlusOptix S12C demonstrated an overall sensitivity of 85.5% and specificity of 82.3%. Sensitivity for hyperopia was lower (47.7%), while specificity was 81.7%. For strabismus, sensitivity was 67.8% and specificity was 91.1%. The device failed to produce readings in 21.9% of children, primarily those with significant refractive errors or strabismus.

Conclusions: The PlusOptix S12C demonstrated good sensitivity and specificity for detecting amblyopia risk factors, making it effective for large-scale pediatric vision screening, even in very young children. However, due to its lower sensitivity in detecting high hyperopia and strabismus, the key risk factors for amblyopia, children with no result on the device should be referred for a full ophthalmologic refraction test. The device aligns well with the 2021 AAPOS and MOH guidelines but requires supplementary testing for high-risk cases.

BACK TO PROGRAM

PP2

Strabismus without Amblyopia in children: does it affect binocular reading speed?

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Purpose:

Limited research exists on reading speed in strabismus without amblyopia. Our study compares binocular reading speed in children with strabismus without amblyopia versus normal controls.

Methods:

We conducted a prospective study with 81 participants: 35 childhood-onset strabismus without amblyopia and 46 controls. Mean ages were 12.6±1.9 for the strabismus group and 12.8±2.1 years for the control (p=0.82). Inclusion criteria were age 10-17 years, best-corrected visual acuity >20/30 distance, and >J1 near either eye. Exclusion criteria were presence of other eye pathology or neurologic/cognitive conditions. Reading speed was assessed using the International Reading Speed Texts, with each participant reading two passages (3 and 5). Speed was measured in words per minute (WPM).

Results:

Age showed a significant correlation with WPM (r=0.68, p<0.001). A strong correlation between WPM of passages 3 and 5 was found both in strabismic and control children (r=0.99, r=0.98 accordingly, p<0.001).

Mean binocular reading speed for passage 3 for strabismus group was 109.5 WPM and104.7 WPM for the control (p=0.61). Mean binocular reading speed for passage 5 for strabismus group was 111.6 WPM and 108.5 WPM for the control (p=0.88). No correlation between binocular reading speed and stereopsis or near point of convergence was found in both groups.

Conclusions:

Children with strabismus without amblyopia did not have a slower binocular reading speed compared with controls. Further studies with eye tracking may provide more information. Strabismus without amblyopia appears not to affect reading performance in children aged 10-17 years.

BACK TO PROGRAM

PP3

Botulinum Toxin A for the Treatment of Esotropia in Children- A Tertiary Center's Experience

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Background: The use of botulinum toxin A (also known as Botox®) for strabismus was first described and developed in 1980 by the ophthalmologist Alan Scott. Since then, it has been widely accepted around the world as an alternative to conventional strabismus surgery or as an adjunct to strabismus surgery. It has had FDA approval as an alternative to surgical recessions since 1989 for patients twelve years and older.

Purpose: Describe our experience using botulinum toxin A (BTA) extraocular muscle injections to treat pediatric esotropia (ET).

Methods: Retrospective study of consecutive patients younger than 18 years of age, presenting between 2019 and 2024 to the pediatric ophthalmology and strabismus clinic at Tel Aviv Medical Center with esotropia that was treated with BTA injections as a stand-alone treatment or as an adjunct to surgery.

Results: Nineteen children with esotropia were included (9 females, average age 3.2±3.1 years range 0.85-11.8 years). This comprised ten patients with large-angle infantile esotropia who underwent bi-medial rectus recession (BMR) with BTA injection to the 2 medial recti. Two of them required repeated surgery for residual esotropia. Another was considered for a second strabismus surgery due to oblique dysfunction but has not yet undergone an operation. Seven patients presented with acute esotropia and opted for BTA injections to the medial recti as an initial treatment and recovered well, restoring binocularity. Two patients had undergone BTA injections to the medial rectus for various indications, including sixth nerve palsy and sensory esotropia. **Conclusions:** Botulinum toxin A is an effective and safe option for treating children with esotropia. Ocular alignment and binocularity can be restored in acute ET with a single injection. It is also helpful as an adjunct to surgery for large-angle infantile ET.

BACK TO PROGRAM

PP4

Comparison of Bilateral Medial Rectus Recession Versus Unilateral Recession Resection as Surgery for Monocular Esotropia without Amblyopia

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Introduction: Esotropia is a common horizontal strabismus, often requiring surgical correction. In patients with monocular non-alternating esotropia, unilateral recess-resect (RNR) surgery is often performed, as it spares surgery on the better, non-deviating eye. On the other hand, symmetric bilateral medial rectus recession (BMR) surgery is often preferred by surgeons as it is less likely to cause incomitance. However, parents may be reluctant to operate on the non-deviating eye. Few studies compared the outcomes of bilateral versus unilateral surgery in esotropia or addressed cases of non-amblyopic monocular esotropia. This study compared outcomes of unilateral RNR versus BMR in patients with monocular esotropia and near equal visual acuities.

Methods: A retrospective study of all patients with monocular esotropia with similar visual acuities in both eyes undergoing RNR or BMR at our institution. Surgical success was defined as ocular horizontal deviation of 10 prism diopters (PD) or less.

Results: 37 patients were included (17 underwent RNR and 20 BMR). Age was similar in both groups. Follow-up after BMR was significantly longer (36±33.8 months vs. 11±9.7, P=0.005). Preoperative esotropia at near fixation was similar in both groups (RNR, 36.7±11.2PD vs. BMR 35.8±12.2PD, P=0.80). Mean near deviation at the end of follow-up after RNR was 4.9±5.4PD and 8.9±10.6PD after BMR (P=0.17). Surgical success was similar in both groups: (88%, n=15) following RNR and (75%, n=15) following BMR (P=0.30).

Conclusion Unilateral and bilateral surgery have good surgical outcomes in patients with monocular, non-alternating esotropia and similar visual acuities in both eyes. Surgical approach should be tailored based on surgeon discretion and patient or parental preferences.

References

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2. Polling JR, Eijkemans MJ, Esser J, Gilles U, Kolling GH, Schulz E, et al. A randomised comparison of bilateral recession versus unilateral recession-resection as surgery for infantile esotropia. Br J Ophthalmol. 2009;93(7):954-7.

BACK TO PROGRAM

PP5

Equitable healthcare: bridging socioeconomic gaps in amblyopia treatment outcomes based on evidence from a tertiary care center

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Purpose Amblyopia is a leading cause of visual impairment in children, with circumstantial evidence suggesting a correlation between socioeconomic status and treatment outcomes. This study aimed to investigate the association between socioeconomic status and amblyopia treatment success rates in children aged 3–18 years.

Methods A retrospective cohort study was conducted by reviewing electronic medical records of amblyopia patients treated at a tertiary center over 24 years. Participants were divided into two groups: those from impoverished areas (study group) and those from non-impoverished areas (control group). Baseline demographic and clinical characteristics, treatment compliance, and outcomes were analyzed.

Results The study included 102 participants, 50 of whom were from impoverished areas. Both groups had similar distributions of age (6.70±2.75 vs. 6.56±2.90 years, p=0.80), gender (58.0% vs. 63.4% females, p=0.69), and baseline clinical characteristics, except for baseline visual acuity, which was significantly lower in the study group (0.79±0.61 vs. 0.57±0.36 LogMAR, p=0.03). The mean follow-up duration was 34 months.

Both groups showed significant improvement in visual acuity and a reduction in severe amblyopia prevalence (study group: 22% vs. 50%, p<0.01; control group: 17.3% vs. 37.5%, p<0.01). Final visual acuity and amblyopia severity distributions were comparable between groups (0.48±0.57 vs. 0.38±0.40, p=0.31). Treatment success rates, defined by visual acuity improvement (42% vs. 50%, p=0.43) and reduction in severe amblyopia (38% vs. 46%, p=0.55), were also similar.

Conclusions Although children from impoverished areas presented with significantly lower baseline visual acuity, their treatment outcomes were comparable to their peers. This highlights the transformative role of equitable, community-based healthcare services in bridging socioeconomic gaps. Consistent access to quality care can neutralize social disparities, ensuring effective amblyopia treatment across diverse populations and fostering health equity.

BACK TO PROGRAM

PP6

Parents' resolution with their child's diagnosis, parent-child communication about the diagnosis, and the well-being of adolescents and young adults with vision loss.

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Purpose: Rates of mental health problems among individuals with vision loss are high. This study explored the role of the parent-child relationship in the mental health and daily functioning of adolescents and young adults with vision loss. We focused on two aspects of the relationship: parents' resolution with respect to their child's diagnosis and open and positive parent-child communication about the diagnosis. We expected that higher parental resolution would be associated with more open and positive communication and that such communication would be associated with better well-being among legally blind adolescents and young adults.

Methods: Participants were 15 parents of legally blind children (94% mothers, 6% fathers, child age 5-33 years) and 25 legally blind adolescents and young adults (56% male, 44% female, age 18-40). Parents completed the "Reaction to Diagnosis Questionnaire" and "The Child and Parent Perspectives on Communicating about Epilepsy Questionnaire" (CPPCE), adapted to the context of vision loss. The adolescents and adults also completed the CPPCE, as well as several indicators of well-being: their acceptance of their diagnosis, the Self-Esteem Scale, sense of belonging to the visually impaired community, depression, and anxiety symptoms (DASS-21), and daily functioning (the Visual Function Questionnaire, VFQ-25). All questionnaires were filled out online using the ARC-Sheba PROMs Online system.

Results: Parents' higher resolution was correlated with greater openness and positivity in communication with their child. Reports of more frequent and positive communication with their parents were associated with greater acceptance of the diagnosis and a higher sense of belonging to the visually impaired community. In addition, participants with higher self-esteem reported better daily functioning. Communication with parents was not significantly associated with symptoms of depression or anxiety.

Conclusions: These findings highlight the importance of considering parents' resolution with regard to their child's visual impairment and parent-child communication about the impairment in efforts to support the well-being of individuals with visual impairment. Further research with a larger sample is needed to replicate and validate these results.

BACK TO PROGRAM

PP7

Clinical and Genetics Characteristics in a Pediatric Cohort with Inherited Retinal Diseases

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Purpose: Inherited Retinal Dystrophies (IRDs) are a group of rare inherited diseases involving dysfunction or death of the retinal cells. Although its rarity, IRDs are hold as one of the leading causes of vision impairment and blindness among children and working age population. The aim of our study was to characterize main IRDs, causing genes and main clinical manifestations in a pediatric cohort from a national referral center for low vision in children.

Methods: Retrospective study case series of medical charts from children aged 0-10 years with a diagnose of IRD. Data included IRD type, clinical manifestations, demographic details, refractive errors and molecular analysis when available.

Results: We have identified 199 children. Mean follow up was 5.6 years. Retinitis Pigmentosa (RP) was the most common IRD, followed by Achromatopsia and CSNB. All three together consist around 81% of the entire cohort .Genetic testing were performed in 162 cases, with a causing gene detection rate of 77%. The most common causing genes identified were *CNGA3*, *TRPM1* and *CNGB3*. Children with Achromatopsia tended to reach diagnosis earlier, with a significant delay in the diagnosis in children with Blue cone monochromatism (BCM) .The most common clinical manifestation was nystagmus, mainly in RP, Achromatopsia and CSNB .Vision loss was a common first clinical symptom among patients with BCM .

High myopia was in general the most common refractive error at the last visit. Children with BCM and CSNB had progressive myopia. *TRPM1* gene was associated to progressive myopia, *CACNA1F* gene was associated to rather stable myopia. *CNGA3, CNGB3* and *CRB1* were associated with hypermetropia.

Conclusions: The most common IRDs diagnosed during the first decade of life were RP, achromatopsia and CSNB. The most common causing genes were *CNGA3*, *TRPM1* and *CNGB3*. Nystagmus was the most common manifestation and generally presented during the first two years of life. Visual impairment and photophobia are also common early symptoms. The early recognition of IRDs in a family is essential for proper guidance to parents including available support, visual rehabilitation, genetic counseling and gene therapy when possible.

BACK TO PROGRAM

RP1

Analysis of Near Infrared reflectance vs. Blue autofluorescence in patients with Geographic Atrophy secondary to AMD

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Purpose: Geographic atrophy (GA) is an advanced and irreversible form of age related macular degeneration (AMD). Clinical trials define the primary outcome measure of GA area increase by blue autofluorescence (BAF). We aim to i investigate the lesion size overlap between BAF and near-infrared (NIR) imaging in eyes affected byGA through image registration techniques.

Methods: GA images were extracted from patients' charts. Corresponding pairs of NIR and BAF images of the same eye and from the same day were matched. Two retina specialists validated and annotated GA regions using polygonal segmentations to ensure clinical accuracy and consistency across the dataset. Image pairs were aligned through registration, and the polygon annotations of GA were converted into binary masks, to evaluate overlap. Spearman's rank correlation test was used to evaluate correlations between polygonal size for BAF and NIR. Similarity was evaluated using Intersection over Union (IoU) and the Dice coefficient.

Results: 146 pairs of images of 53 eyes from 37 patients were evaluated. The mean IoU was 0.916$\pm$ 0.081 , indicating an average overlap of over 91% between BAF and NIR images. The Dice score was used as a secondary metric, yielding an average of 0.954$\pm$0.048 and a median of 0.968 , confirming the strong agreement between the two modalities (r_s=0.99,$p<0.0001$).The rate of change in GA was similar for BAF and NIR (median 1.08 mm2/year vs 0.97 mm2/year,r_s=0.98,$p<0.0001$)

Conclusions: NIR is of high merit in foveal sparing GA, moreover, we demonstrated high correlation among NIR and BAF overlap in perifoveal GA regions. NIR imaging demonstrates potential as a reliable method for evaluating GA. It allows for accurate identification and assessment of GA, making it a valuable tool for clinicians and possibly serving as an alternative or complement to BAF imaging.

BACK TO PROGRAM

RP2

Prolonged use of Acetazolamide for treatment of Central Serous Chorioretinopathy

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Purpose: Previous studies have indicated that Acetazolamide effectively decreases macular edema associated with various intraocular pathologies. Short-term (four to six weeks) Acetazolamide treatment reduced the time for clinical resolution in patients with Central Serous Chorioretinopathy (CSCR) but had no significant effect on final visual acuity or recurrence rate**.** This retrospective study aimed to assess the efficacy of long-term treatment with Acetazolamide in patients with CSCR.

Methods: Seven males and one female aged 41-60 (mean ± standard deviation, SD: 47 ± 7.9) diagnosed with CSCR were treated with Acetazolamide for 56-627 days (mean ± SD: 262 ± 215). The main outcome measures were sub-retinal fluid volume by OCT and best corrected visual acuity.

Results: All patients presented with significantly reduced sub-retinal fluid and improved best-corrected visual acuity. Six patients experienced full CSCR resolution without recurrence with a mean follow-up of 7.5 months. In one patient, the CSCR was resolved under the macula, but extra-macular sub-retinal fluid accumulation remained. In one patient, the CSCR was not resolved. No significant side effects were observed.

Conclusions: Long-term Acetazolamide may present a viable treatment for CSCR, resulting in sustained improvement in visual acuity and normalization of central foveal thickness. Initial evidence that long-term Acetazolamide may lower recurrence rates is provided.

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RP3

Investigating the effect of electrical pulse configuration on the spatial spread of retinal activation: Parameter optimization for retinal prostheses

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Purpose: Despite the great promise retinal prostheses hold for vision restoration in people with degenerative diseases of the outer retina, the visual acuity they offer is greatly limited. Here we present initial investigations into electrical pulse configuration optimization for eliciting high spatial resolution stimulation of the retina.

Methods: To investigate the electrically induced retinal responses we used WT LE-GCaMP6f and the blind RCS-GCaMP6f animal model recently established by our group. An isolated retina was mounted on a commercially available MEA, with the photoreceptors facing the MEA electrodes. The electrically induced RGCs responses were visualized using an upright microscope equipped with a CCD camera to allow for fluorescent image acquisition at 10Hz. Electrical pulses with varying amplitudes (1-60μA) and widths (100-1000μsec) were injected using two configurations. The first: anodic first biphasic pulses, and the second: anodic first biphasic pulses with cathodic first pulses from neighboring electrodes. Spatial spread of the induced responses was estimated using Z-score mapping and thresholding of the acquired fluorescence data.

Results: our results, obtained from WT retinas, revealed the expected trend wherein increasing current amplitude resulted in the increase of the activated region diameter (e.g. a 300μsec monophasic pulse with a charge injection of 1nC yields an activation diameter of 150μm vs 400μm for 8nC). Moreover, for the shortest pulse (100 μsec) the diameter of the activated region for the same charge injection was larger than for the other investigated pulse durations. Interestingly, the first stimulation configuration resulted in a wider spread of the retina activation at the threshold charge for the same electrode(e.g. 81 μm for a 1ms pulse) as compared to the second configuration(e.g. 65.04 μm for the same pulse width).

Conclusion: We presented a robust model for the investigation of electrical stimulation configuration effects on the induced retinal responses and data in agreement with previous reports. This model, will aid in the optimization of electrical stimulation paradigms for high spatial resolution activation, one of the main limitations of currently available retinal prostheses.

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RP4

The dark-adapted ERG Oscillatory Potentials depends upon activation of the cone system

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Purpose: Determine the importance of a normal functioning cone system for the generation of oscillatory potentials in the dark-adapted electroretinogram (ERG)

Methods: ERG responses were recorded in the light-adapted (LA) state (background of 30cd/m2) and in the dark-adapted (DA) state (20 minutes in darkness) with the Diagnosis E3 system, using Burian-Allen corneal electrodes, following the ISCEV standard for FFERG. ERG responses were recorded from 50 individuals with normal visual function, serving as the control group, 6 patients suffering from achromatopsia, 5 patients suffering from vitamin A deficiency and 4 members of the same family, all diagnosed with GUCY2D-associated autosomal dominant cone-rod dystrophy. ERG analysis was based upon amplitude measurements of the a-wave and b-wave. The oscillatory waves were isolated by filtering the ERG response with a band width filter of 75-300 Hz. Then their magnitude was defined by root mean square (RMS) calculation in a dynamic duration window; from a-wave trough to b-wave peak.

Results: In the control group, the RMS of the OPs of the LA ERG were relatively small and showed minor dependency upon light stimulus strength. In contrast, OPs in the DA state were characterized by strong dependency upon stimulus strength. Patients with achromatopsia had minimal LA ERG responses and the OPs ‘were minimal and could not be measured reliably. Their DA ERG responses were close to normal, but the OPs were considerably smaller than those of the control group. Patients with vitamin A deficiency were characterized by close to normal or normal light-adapted ERG parameters including a- and b-wave amplitudes and OPs RMS. The dark-adapted ERG responses were similar to their LA data, including amplitudes, temporal pattern and RMS. The FFERG responses of the patients suffering from Cone-Rod Dystrophy due to dominant mutation in the *GUCY2-D* gene were similar to our findings in the achromatopsia patients.

Conclusions: These results are consistent with the assumption that normal activation of the cone driven ON- and OFF-pathways is needed for the activation of neural networks in the inner retina, underlying the generation of the OPs, which can then be strengthened by additional inputs from the rod system during dark-adapted conditions.

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RP5

Development of a portable electrophysiological system for ex-vivo eyes

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Purpose: To date, there are no accurate experimental models allowing for the pre-clinical monitoring of disease progression and the development of treatment strategies in degenerative diseases of the retina. Here, we present the development of an electrophysiology portable devise, which is part of the developing of a system used for ex-vivo preservation of the eye.

Methods: Towards this end, we have developed a portable robust system for the recording of ERG signals from the eye. Signal acquisition and visual simulation were controlled using a custom written MATLAB code. ERG signals were recorded from perfused ex vivo porcine eyes using a corneal electrode mounted on the cornea of the isolated eyeball. Eyes were stimulated with light power of 500nW/mm2, with 20 msec pulse duration, 1 sec rest, and a total of 30 pulses. The recorded data was then thoroughly analysed. The average of the 30 repetitions was calculated and the ERG amplitudes were then defined as the difference between the maximal and minimal values of the average signal. Using this system, we monitored the amplitude throughout perfusion until the signal was undisguisable from the noise.

Results: Following perfusion with oxygenated Ringer's solution, we obtained robust ERG signals for up to 3 hours. A slow decay in the ERG amplitude showing a time constant of 0.015 min reaching a plateau, was observed for perfused eyes. In contrast, the non-perfused eyes showed a much faster decay with a time constant of 3.5min.

Conclusion: We have presented a novel device for monitoring ERG in an excised porcine eye model Using this device we measured ERG response for up to at least 3 hours from death in eyes perfused with oxygenated Ringer's solution.

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RP6

Retinal Vascular Occlusion after COVID-19 Vaccination – A Nationwide Cohort Study

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Purpose: The Pfizer–BioNTech BNT162b2 SARS-CoV-2 vaccine, introduced in December 2020, represented a major milestone in combating the COVID-19 pandemic. Despite its proven efficacy, there have been concerns about potential adverse effects, such as retinal vascular occlusion (RVO), particularly as booster doses become widely administered. This study aimed to assess the association between anti-SARS-CoV-2 vaccination and the development of RVO in a large population cohort.

Methods: This retrospective cross-sectional study utilized electronic health records from Clalit Health Services (CHS), the largest healthcare provider in Israel. Individuals with newly diagnosed RVO between December 2017 and January 2023 were matched in a 1:3 ratio with controls who did not develop RVO. Vaccination status, defined by the number of anti-SARS-CoV-2 vaccine doses received (ranging from 0 to 5), was assessed alongside key confounders and comorbidities to examine the potential impact of vaccination on RVO development.

Results: The study included a total of 31,112 subjects, comprising 7,528 RVO cases and 22,584 matched controls. The mean age of participants was 65.04 years, with a slightly higher mean age in the RVO group. Vaccination status was not significantly associated with RVO development ($p = 0.57$). Multivariate analysis revealed no significant increase in RVO risk based on vaccination status, with adjusted odds ratios approximating 1 across models. While RVO cases exhibited a higher prevalence of certain comorbidities, such as hypertension and hyperlipidemia, these factors did not alter the lack of association between vaccination and RVO risk when controlled for in the analysis.

Conclusion: This large cross-sectional study found no evidence of an increased risk of RVO associated with anti-SARS-CoV-2 vaccination, regardless of the number of doses received. These findings provide reassurance regarding the retinal safety of these vaccines, especially as booster doses remain critical in combating the ongoing pandemic. Future research should focus on investigating specific RVO subtypes and use comprehensive diagnostic criteria to elucidate potential vaccine-related risks further.

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RP7

Development of a Simultaneous Combination Therapy for Alternative Multidimensional Etiologies of Subretinal Angiogenesis

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Purpose: Retinal vascular diseases and Age-Related Macular Degeneration (AMD) are the leading causes of visual impairment and blindness. Abnormal neovascularization stemming from the retina and choroid are a sight-threatening complication associated with these diseases. Abnormal vessels characterized by increased permeability and bleeding tendencies, leads to retinal edema, exudates, and eventually atrophy, and fibrosis. Current therapies which block the vascular endothelial growth factor (VEGF) signaling pathway often achieve incomplete treatment effect. We aim to develop a novel combination therapy for multidimensional blocking of downstream key proteins involved simultaneously in various signal pathways of retinal vascular diseases and AMD.

Methods: A comprehensive review of the relevant literature revealed a universal set of key proteins mediating simultaneously different etiologies in the pathophysiology of various retinal vascular diseases. Specific small molecule inhibitors (SMIs) for two selected proteins, Rac1 and RAGE, were screened *in-vitro*, using WST-1 cell proliferation and cell migration assays of human umbilical vein endothelial cells (HUVECs). A 3D choroid sprouting model was used to validate the anti-angiogenic effect, *ex-vivo*, followed by the laser-induced choroidal neovascularization (CNV) model, which imitates neovascular AMD (nAMD), *in-vivo*.

Results: We identified selective SMIs for two non-VEGF target proteins: Azeliragon for the RAGE protein and Ehop-016 for the Rac1 protein, which fundamentally inhibited the proliferation and migration of HUVECs *in-vitro*. Combining both SMIs induced a significantly augmented, synergistic effect compared to each SMI individually (Synergy Score>14.96). A profound anti-angiogenic effect of the combined inhibition was demonstrated using a 3D choroid sprouting model *ex-vivo* (0.41±0.13). The combined formulation was highly efficient in hindering the CNV formation when injected intravitreally in a laser-induced CNV mouse model *in-vivo*, resulting in an effect comparable to that achieved by Aflibercept treatment, which is known to completely abolish the CNV formation in this model.

Conclusions: Simultaneous, multidisciplinary inhibition of non-VEGF mediated pathways using SMI combination therapy against Rac1 and RAGE proteins is highly efficient in suppressing experimental CNV formation in preclinical models. These data establish the basis of a potentially multidisciplinary novel non-VEGF treatment for various retinal vascular diseases and nAMD.

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RP8

Patients with age-related macular degeneration have increased susceptibility to valvular heart disease

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Purpose: Valvular heart disease (VHD) contributes significantly to cardiovascular-related morbidity worldwide. Aortic valve stenosis is the third most common cardiovascular disease in the Western world, following hypertension and coronary artery disease. Recent studies have reported an association between VHD and the presence of subretinal drusenoid deposits (SDDs), a distinct manifestation of age-related macular degeneration (AMD). However, these findings were based on self-reported questionnaires and relatively modest cohort sizes. Our goal was therefore to investigate the putative associations between AMD and VHD and between the presence of SDDs and VHD.

Methods: This is a retrospective case-control study. 945 patients with AMD and 8275 control patients without AMD from a single tertiary center were included in this study. All patients with AMD underwent spectral-domain optical coherence tomography (SD-OCT). The SD-OCT scans were annotated by two, experienced graders. Among the patients with AMD, 547 had drusen and SDDs, and 398 had drusen only with no SDDs. We also extracted data from all 9220 patients' electronic medical records, including demographics and previous heart valve procedures based on ICD-9 codes.

Results: Patients with AMD had a higher prevalence of various VHDs compared to the control group, including increased rates of aortic stenosis (OR: 2.00, 95% CI: 1.40-2.86; p=0.0001), aortic regurgitation (OR: 2.41, 95% CI: 1.49-3.91; p=0.0002), and mitral valve regurgitation (OR: 1.51, 95% CI: 1.13-2.01; p=0.004). Heart valve procedures were also more prevalent among AMD patients including aortic valve replacement (OR: 1.70, 95% CI: 1.08-2.66; p=0.019) and tricuspid valve replacement (OR: 3.99, 95% CI: 1.03-15.46, p=0.03). Moreover, a supervised machine learning model successfully detected the presence of AMD based solemnly on the patient's history of VHD. In the AMD cohort, we found no significant difference in VHD prevalence between patients with non-neovascular AMD and patients with neovascular AMD, or between patients with SDDs and patients without SDDs.

Conclusions: Patients with AMD have a higher prevalence of VHD and are more likely to undergo a heart valve–related procedure compared to patients without AMD, with no difference between patients with SDDs and patients without SDDs in the AMD cohort.

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RP9

Transcriptome-wide Association Study Identifies Novel Risk Loci Associated With Age-Related Macular Degeneration

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Purpose: Age-related macular degeneration (AMD) affects 200 million individuals yearly, with global cost of care of $343 billion. Previous GWAS implicated 34 loci associated with AMD(International AMD Genomics Consortium[IAMDGC]) but identifying effective therapeutic targets remains difficult. The innate immune system, particularly monocytes/macrophages, are suspected to play a crucial role in AMD pathogenesis, although underlying mechanisms remain poorly understood.

Methods: We integrated monocyte eQTL and AMD GWAS data to identify AMD risk genes. We utilized IAMDGC genomic data for 16,108 cases/18,038 controls(15,616/16,723 EUR,207/322 ASN,50/357 AFR,and 235/636 OTH) and imputed to TOPMedv2. Ancestry-specific GWAS analyses with covariates were conducted via REGENIE Firth test and meta-analyzed with METAL. 51,162,741 variants(MAF>0.1,INFO>0.8) were analyzed across ancestries. We combined genetic data from European ancestry controls(n=432) with monocyte expression in states of stimulation(naive, LPS 2h. LPS 24h, and IFN 24h; Fairfax et al. 2014) to develop elastic-net regression models of genetically-regulated expression. After filtering for models with association to gene expression, we performed a transcriptome-wide association study(TWAS) of monocyte expression on AMD in each state using MetaXcan. A second modeling strategy using multivariate adaptive shrinkage (MASH),which borrows information across treatments, was implemented for further TWAS. eQTL genes underwent pathway analysis per treatment via enrichR.

Results: 16 TWAS associations after Bonferroni-correction were identified across the genome, 14 in known AMD loci and 2 novel loci. The top result in LPS stimulated monocytes was PLEKHA1(P=6.13E-107), and the top result in naive monocytes was HTRA1(P=6.90E-78), both in the known HTRA1/ARMS2 AMD-associated locus. BUB3(P=7.24E-10) and NUDT21(P=4.96E-02) were newly associated with AMD. BUB3 is associated with choroidal thickness in a European population. Our second MASH pipeline identified multiple significant novel loci across the genome.

Conclusions: These TWAS results represent genes strongly regulated by known AMD variants, and novel loci. Our results support the role of genetic regulation of monocyte inflammatory processes in AMD, and highlight novel biology underpinning pathogenesis. Validation of these candidate genes may elucidate novel risk genes and therapeutic targets.

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RP10

Prechoroidal cleft characteristics in neovascular age-related macular degeneration

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Purpose: This study aimed to comprehensively characterize the prechoroidal cleft (PCC) in neovascular age-related macular degeneration (nAMD), exploring its spectrum of behavior from a purely mechanical to an exudative phenomenon, and assessing its clinical significance.

Methods: We conducted a retrospective analysis of optical coherence tomography (OCT) images from 81 eyes of nAMD patients with PCC. PCC morphology, size, and relationship to subretinal fluid and neovascularization were analyzed at multiple timepoints.

Results: PCC size correlated with disease activity, demonstrating an increase during active neovascularization and a decrease following anti-VEGF treatment. PCC morphology varied, with distinct features associated with different clinical presentations ranging from purely mechanical to strongly exudative. A biconcave shape was significantly associated with early signs of exudation.

Conclusions: This largest reported series on PCC in nAMD demonstrates a spectrum of behavior, from a benign structural finding to a key indicator of exudative activity. PCC morphology, particularly the biconcave shape, may provide crucial insights into disease pathogenesis and aid in guiding clinical management. Further prospective studies are needed to confirm these findings.

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RP11

Axial Length Increase Following Combined Pars Plana Vitrectomy and Encircling Scleral Band

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Objectives: To evaluate changes in axial length (AL) following combined pars plana vitrectomy (PPV) and encircling scleral band surgery for retinal detachment (RD), with a focus on factors influencing AL progression during the postoperative period. Although previous research has explored changes in ocular measurements following scleral buckle procedures, to our knowledge, this is the first study to investigate the effects of PPV combined with an encircling scleral band.

Methods: This retrospective study included patients who underwent combined PPV and encircling scleral band surgery at a tertiary medical center in Israel from December 2018 to February 2024. Medical records of 45 patients with preoperative and postoperative biometric measurements and a minimum follow-up period of one year were analyzed. Data included AL, anterior chamber depth (ACD), lens thickness (LT), intraocular pressure (IOP), best-corrected visual acuity (BCVA), and lens status. AL progression was assessed using the Wilcoxon signed-rank test, while correlations with clinical parameters were evaluated using Spearman's correlation and linear regression models.

Results: A significant increase in AL was observed postoperatively in the operated eye, with a mean change of +0.69 mm (preoperative AL: 25.37 ± 1.85 mm; postoperative AL: 26.05 ± 2.09 mm, $p < 0.0001$). Postoperative ACD measurements were significantly greater (3.71 ± 1.69 mm) than preoperative values (3.61 ± 0.58 mm, $p = 0.002$), and LT significantly increased from 4.06 ± 1.16 mm preoperatively to 4.29 ± 0.85 mm postoperatively ($p = 0.025$). Eyes with macula-on RD elongated by an average of 0.58 ± 0.35 mm, while those with macula-off RD elongated by 0.79 ± 2.38 mm, although macular status did not significantly influence AL progression. Nor did other factors such as age, IOP, or lens status.

Conclusions: This study demonstrates a significant increase in AL following combined PPV and encircling scleral band surgery, with variations between operated and non-operated eyes, independent of macular status, lens status, or age. These findings suggest that AL changes could impact postoperative lens calculations, potentially affecting visual outcomes in pseudophakic patients. Further research is needed to explore the long-term implications of these AL changes on refractive stability and visual function.

BACK TO PROGRAM

GP1

Clinical and Molecular Characterization of Microphthalmia, Anophthalmia, and Ocular Coloboma in the Israeli population

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Purpose: To clinically and genetically characterize a cohort of Israeli individuals affected with congenital maldevelopment of the eye, including microphthalmia, anophthalmia and ocular coloboma (MAC).

Methods: Study participants diagnosed for anophthalmia, microphthalmia and colobomas and their families were recruited through three medical centers in Israel, under IRB approval after signing an informed consent. Clinical data of family history, demographics, pregnancy, previous genetic screening, development, endocrinological tests and imaging were reviewed. Genetic analysis included whole exome sequencing and Sanger sequencing.

Results: 13 patients from 12 families were recruited to date. Phenotypes included non-syndromic microphthalmia (7 families), non-syndromic coloboma (2 families), syndromic coloboma (1 family) and microphthalmia with coloboma (2 families). Genetic diagnosis was obtained in one family, in which two siblings affected with microphthalmia were found to be homozygotes for a deletion of exon 1 of the *MFRP* gene, leading to start loss.

Conclusions: MAC are rare yet severe conditions, significantly affecting vision and daily living. Researching these conditions addresses a critical gap in medical knowledge and patient care. It has the potential to impact public health and patient care in Israel and beyond, by advancing our understanding of these conditions, leading to better diagnostic, preventive, and treatment strategies.

BACK TO PROGRAM

GP2

Possible Genetic Trochlear Nerve Palsy in One Family Authors: Shir Butnik-Cohen, Sigal Zmujack-Yehiam, Chen Weiner, Alina Kotliar, Eran Pras

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Background: Fourth cranial nerve palsy (4CNP), is a condition characterized by impaired movement of the superior oblique muscle, resulting in vertical diplopia and in some patients a head tilt. While the most common etiology is related to trauma, followed by vascular disease, or tumors, familial occurrences and genetic factors remain poorly characterized.

Aims: to present a family of 8 individuals presenting with 4th CN palsy within two generations, in what appears to be autosomal dominant pattern with incomplete penetrance and to investigate the underlying molecular cause

Methods: A comprehensive clinical and orthoptic analysis was conducted in 8 subjects from one family (2 parents and 6 children). The father and two children presented trochlear nerve palsy with varying degrees of vertical deviation. Blood test for genetic analysis was drawn from both parents and 3 of the children (3 affected and 2 unaffected subjects). A detailed review of their medical histories, clinical presentations, and family structures was performed. Genetic testing by whole exome sequencing is underway.

Results: Among the 6 siblings, two were diagnosed with 4CNP, presenting vertical diplopia and compensatory head tilt . Both underwent surgical corrections. In addition the father had mild symptoms and signs. The inheritance pattern suggested a possible autosomal dominant trait. Genetic analysis was done to one of the brothers, two unaffected siblings and both parents.

Conclusion: We present a unique family with familial fourth nerve palsy. The inheritance pattern is AD with partial penetrance. Molecular studies are underway

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GP3

A heterozygous LRP1 variant is associated with isolated high myopia in a family of Jewish-Tunisian ancestry.

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#Equal contribution *Equal contribution

Purpose: To investigate the genetic cause of high myopia in a family of Jewish-Tunisian ancestry.

Methods: Affected family members underwent a thorough ophthalmologic examination including optical coherence tomography (OCT). High myopia was defined as a spherical equivalent of the refractive error ≤ -7.00 D when ocular accommodation was relaxed. Whole-exome sequencing (WES) for the proband and linkage analysis using 750k SNP arrays for the nuclear family were performed, assuming autosomal dominant inheritance. WES variants that passed a filtering cascade were screened using our in-house database of ethnically matched controls and validated using Sanger sequencing. Results were compared with up-to-date global databases to test prevalence and evaluate pathogenicity.

Results: In a family of Jewish-Tunisian ancestry, four individuals (ages 10-43 years) had refractive errors ranging from -13 to -21 diopters. Fundus and OCT findings and thorough clinical evaluation were compatible with isolated high myopia. Genetic analysis revealed a heterozygous mutation in LRP1 (NM_002332.2: c.12721T>C; p.Ile4080Thr), with a phyloP score of 6 and CADD score of 24.2, segregating within the kindred as expected for dominant heredity.

Conclusions: We report a novel LRP1 variant associated with autosomal dominant isolated high myopia. LRP1 encodes Low-Density Lipoprotein Receptor-Related Protein 1, a multifunctional cell surface receptor involved in various biological processes, regulating lipid metabolism, endocytosis, and clearance of extracellular proteins and lipids. LRP1 also plays a role in cell signaling, influencing cell migration, differentiation, and survival processes. Additionally, it is implicated in neurological functions and diseases, including Alzheimer's disease, by mediating the clearance of amyloid-beta peptides. LRP1 heterozygous variants have also been associated with developmental dysplasia of the hip. In the eye, LRP1 is expressed in retinal cells and influences ocular health by regulating extracellular matrix turnover, lipid metabolism, and inflammation. The LRP1 variant we describe is expected to affect the binding site of LRP1 and TGF-β, a protein whose altered expression levels have been associated with myopia. Furthermore, LRP1 is affected directly by LRPAP1 (LRP-associated protein 1), which acts as a molecular chaperone for LRP1, regulating its proper folding and trafficking to the cell surface, and preventing its premature activation or ligand binding within the secretory pathway. LRPAP1 mutations have been shown to cause high myopia. Thus, we delineate a possible role of LRP1 in the pathogenesis of high myopia, presumably by the same mechanism as LRPAP1, and suggest that genetic evaluation of isolated severe myopia should include analysis for the presence of LRP1 pathogenic variants.

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GP4

Heterozygous loss-of-function variants in *TJP1* (*ZO-1*) cause microphthalmia and coloboma

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Purpose: Microphthalmia, anophthalmia and coloboma (MAC) are a spectrum of developmental eye diseases causing 15-20% of childhood blindness cases worldwide. There can be significant overlap with a mixed phenotype. These conditions are associated with over 100 genes active in ocular developmental pathways. Gene regulatory networks regulate eye morphogenesis, which relies on intercellular communication regulated by tight junctions. Animal models have demonstrated a critical role for TJP1 in vertebrate eye morphogenesis, yet it has never been previously associated with any human eye condition. Here, we report the first pathogenic loss-of-function (LoF) *TJP1* variants causing a MAC phenotype.

Methods: Blood samples were collected from index cases and unaffected family members with informed consent according to ethical standards. Genomic DNA was sequenced using whole exome sequencing and copy number assessed by AFFYMETRIX 750K chip. Fastq files were uploaded to the Genoox pipeline and analyzed using Franklin (Genoox, Israel) or by Chromosome Analysis Suite (ThermoFisher, USA). Variants were verified by Sanger sequencing. GeneMatcher was used to identify other *TJP1* families worldwide.

Results: A cohort of five families with *TJP1* mutations was identified. In family I of Jewish-Georgian heritage, a heterozygous frameshift variant in exon 21 (c.3079_3082delGACA, p.Asp1032fs) was detected with bilateral microphthalmia and iris, optic disc and chorioretinal coloboma. In family II of Jewish Moroccan-Tunisian descent with bilateral coloboma and unilateral microphthalmia, a heterozygous 1.4Mbp deletion on chromosome 15 including *TJP1* was detected. A heterozygous nonsense variant in exon 22 (c.3376C>A, p.Arg1126*) was detected in family III of Colombian heritage with bilateral coloboma and congenital cataracts. In family IV of white British descent, a heterozygous nonsense variant in exon 23 (c.4066C>T, p.Arg1356*) was identified with bilateral coloboma and renal dysfunction. In exon 24, a heterozygous frameshift variant (4734_4735del, p.His1578GlnfsTer7) was detected in family V of white British descent with bilateral coloboma and microphthalmia.

Conclusion: The identification of five MAC families with heterozygous loss-of-function *TJP1* variants suggests it is essential for early eye development. All detected variants lay in exons 21 to 24, indicating certain protein domains may be sensitive to disease-causing but not lethal LoF mutations. Cellular models will reveal novel disease mechanisms due to TJP1 loss. **BACK TO PROGRAM**

GP5

Recent identification of four novel genes associated with macular dystrophy in Israeli individuals

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Purpose: Macular Dystrophies (MDs) are a subgroup of inherited retinal diseases characterized by bilateral, relatively symmetrical macular abnormalities that significantly impair central visual functions. To date, pathogenic variants in over 20 MD-associated genes have been identified. The most common form of MD is Stargardt disease type 1, caused by bi-allelic variants in *ABCA4*. This study aimed to identify the genetic cause of MD in a subset of Israeli patients in whom *ABCA4* was not the causative gene and to characterize their retinal phenotype.

Methods: Study participants underwent a comprehensive ophthalmological evaluation, including best-corrected visual acuity, visual field testing, fundus autofluorescence, optical coherence tomography and electroretinography. Genetic analysis included exome sequencing and Sanger sequencing.

Results: In 10 participants from nine Israeli Jewish families pathogenic variants in four novel MD-causative genes were identified: *SAMD7* (one Yemenite family, onset at 25y), *AP5Z1* (one North African family, onset at 40y), *KATNA1* (two families, Ashkenazi and Yemenite, onset at 8y, 25y and 45y) and *C19orf44* (five families, Ashkenazi and Yemenite, onset at 18-63y). The phenotype associated with *SAMD7* and *AP5Z1* is autosomal recessive MD. The phenotype associated with *KATNA1* is autosomal dominant MD. Mutations in *C19orf44* are associated with a unique autosomal recessive clinical phenotype characterized by patchy perifoveal chorioretinal atrophy, but most patients received an initial diagnosis of MD. While most variants are rare and private, the c.549_550del allele of *C19orf44* is common among Jews of Ashkenazi and Yemenite descent.

Conclusions: While *ABCA4* is the first suspected gene in patients with MD, mutations in other, much less common causative genes are present in many affected individuals. Four novel MD-causative genes have been identified recently, and pathogenic variants in these genes were found in Israeli patients of various ethnicities. This study expands the spectrum of causative genes which should be evaluated in individuals affected with MD.

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GP6

Phenotype-Genotype Correlation in a Cohort of Israeli Patients with OCA1 Albinism

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Purpose: To characterize and compare ocular phenotypes of patients with *TYR* gene mutations.

Methods: A retrospective study of patients affected with albinism due to TYR gene mutations followed between 2009 and 2023 at Hadassah-Hebrew University Medical Center, Jerusalem, Israel. Mutations were detected by a combination of Sanger sequencing, restriction digest, haplotype analysis, and exome sequencing. The primary outcome was best-eye and binocular visual acuities (LogMAR) in the last follow-up. Secondary outcomes included the magnitude of refractive errors, presence of strabismus, nystagmus, foveal hypoplasia, transillumination defects (TID), and severe photophobia.

Results: Preliminary analyses of eighty-nine patients with TYR mutations aged 13.2±12.5 years were performed. The most common genotypes were homozygotes for c.1037-7T>A (IVS2-7T>A) (47 patients), followed by homozygotes for c.140G>A (p.G47D) (11 patients).

The mean Binocular visual acuity (LogMAR) was 0.43±0.23 for c.1037-7T>A homozygotes and 0.65±0.34 for the other genotypes (P=0.005). The mean best eye visual acuity (LogMAR) was 0.47±0.24 for c.1037-7T>A homozygotes and 0.60±0.32 for other genotypes (P=0.047). The mean spherical equivalent was 2.67±3.47 for c.1037-7T>A homozygotes and 2.50±4.25 for other genotypes (P=0.84). Foveal hypoplasia was evident in 92.8% of c.1037-7T>A homozygotes and 91.6% of other genotypes (P=0.84). No differences were found between c.1037-7T>A homozygotes and other genotypes regarding severe photophobia, strabismus, nystagmus, or magnitude of transillumination defects.

Conclusions: Patients affected by albinism due to TYR mutations demonstrated moderate visual impairment on average. Homozygotes for c.1037-7T>A had better vision than other genotypes. On the other hand, homozygotes for c.1037-7T>A did not show lower levels of refractive errors, strabismus, or foveal hypoplasia to account for the difference in vision, however. Further research is needed to explain this phenomenon.

Keywords: *TYR*; genotype-phenotype; vision

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GP7

Study on the BAF (SWI/SNF complex) subunits BAF155 and BAF170 activities in the development and maintenance of pigmented eye lineages in mammals.

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Introduction: Organogenesis of the vertebrate eye depends on different progenitor domains that undergo complex morphogenesis and gradual differentiation in coordinated manner in process which entails activity of multiple signaling pathways and transcription factors (TFs). The roles of chromatin remodelers in the gradual development of neuroectodermal eye lineages is currently mostly unknown.

The BAF (SWI/SNF) chromatin remodeling complexes were shown to play key roles in neural differentiation, directing cell differentiation through lineage specific activity of different alternative assemblies that directly interact with tissue specific TFs. The Baf155 (Smarcc1) and Baf170 (Smarcc2) are the two obligatory scaffold subunits of the BAF complexes. Baf155 is considered to function in progenitor cells in contrast to the Baf170 containing complexes, which primarily function during tissue differentiation.

Purpose: To study the roles of Baf155 and Baf170 and their functional redundency in cells of the pigmented lineage in the eye.

Methods: we have analyzed the phenotype of Baf155 and Baf170 conditional knockout in cells of pigmented lineage: Baf155-cKO; Baf155flox/flox;DctCre and Baf170-cKO; Baf155flox/flox;DctCre compared to control litter mates. The phenotype analysis included ERG, OCT, histology and immunolabeling for detecting of cell specific markers on tissue sections. Furthermore, Geo-seq analysis was performed to characterize the transcriptome of the developing optic stalk.

Results: This analysis revealed partial functional redundancy between Baf155 and Baf170 and importantly exposed a unique role for Baf155 in retinal function in old mice and for the development of the optic stalk and optic nerve head.

Conclusions: Baf155 in pigmented cells of the optic cup is revealed to play key role in formation of the optic nerve and for retinal functions. Current efforts are to further uncover the role of the Baf155 in eye development and possible relation to degenerative eye diseases such as age-related macular degeneration (AMD) and glaucoma.

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GP8

Cognitive Assessment of transgenic mice with Alzheimer's Disease

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Background: Alzheimer's disease (AD) is characterized by accumulation of amyloid-β (Aβ) in the brain, which can also be detected in the eye. Aβ accumulation is difficult to detect by magnetic resonance imaging prior to significant brain atrophy, yet characteristic behavioral changes may be detected earlier. Our study group aims to facilitate early diagnosis of cognitive decline in AD patients by characterizing AD transgenic mice, measuring brain and retinal Aβ accumulation in parallel to cognitive decline, and correlating the findings with imaging modalities. In the present study we characterized behavioral and cognitive deterioration in transgenic AD mice.

Methods: Six transgenic 5XFAD AD mice and 6 wild type controls underwent behavioral assessment using the Morris water maze (MWM) and open field test (OFT) at 9, 11 and 13 months of age. MWM was used to evaluate spatial learning and was performed by calculating time to reach the hidden platform in the water tank. OFT was used to evaluate exploratory behavior and anxiety by analyzing center crossing in a gray lusterless box situated in a dimly lit room. Both OFT and MWM assessments were analyzed using ANY-maze software (Stoelting Co., Wood Dale, IL, USA).

Results: No behavioral differences were detected on 9 and 11 months of age between control and AD mice. At age 13 months, subtle deficits in spatial cognition were shown in the AD group.

Conclusion: 5XFAD AD mice are known to develop AD disease at age 12-15 months,

where there is a 3–4-fold decrease in performance compared to younger ages. The background strain C57BL/6J, can influence the expression of these impairments.

In this study we characterized a gentle cognitive deterioration in the study group at 13 months of age. Future studies will follow further decline, in correlation with neuro imaging and deposition of Aβ in the retina and the brain.

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GP9

An optimized procedure for intracameral injection in rats with low risk of adverse effects

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Purpose: Intracameral injection is a standard administration routine in ophthalmology. Application of intracameral injection in rodents for research is challenging due to the limiting dimensions and anatomy of the eye, including the small aqueous humor volume, the lens curvature and lens thickness. Potential damage during intracameral injections introduces adverse effects and experimental variability. We optimized a procedure for intracameral injection in rats with low risk of adverse effects which allows precision and reproducibility.

Methods: Sprague-Dawley rats were used as experimental models. Since the lens position in rats protrudes into the anterior chamber, injecting from the periphery, as in humans, is unfavorable. We therefore created an incision in the central corneal region using a 31 G 0.8 mm stiletto blade to form a self-sealing tunnel into the anterior chamber. To minimize loss of aqueous humor and shallowing of the anterior chamber, we created the tunnel in an almost flat angle to form a long route. We then inserted a 34 G nanoneedle into the tunnel for injection. This enabled penetration with minimal friction resistance and avoiding touching the lens.

Results: We injected trypan-blue and confirmed by slit microscopy the presence of the dye in the anterior chamber. The depth of the anterior chamber remained intact after injection and no adverse effects developed. To demonstrate that compounds delivered by this method of intracameral injection are bioavailable to the corneal endothelial layer, we injected Hoechst dye, which stains cell nuclei. Corneas were harvested 15 minutes post Hoechst injection and nuclear staining was observed in corneal endothelial cells in fluorescent microscopy.

Conclusion: We implemented a procedure for accurate intracameral injection in rats. This procedure may be used for intracameral delivery of various drugs and compounds in experimental models, increasing the efficiency and reproducibility of ophthalmic research.

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GP10

AD-3281 inhibits pathological neovascularization in preclinical models of neovascular AMD (nAMD), suggesting potential as a novel therapy

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Purpose: Age-related macular degeneration (AMD) is a leading cause of blindness worldwide, with the neovascular form (nAMD) accounting for 90% of vision loss cases (Thomas CJ et al., 2021). While anti-VEGF therapies are the primary treatment, incomplete responses are common, highlighting the need for complementary therapies. We aimed to evaluate the efficacy and safety of a novel small molecule, AD-3281, a METAP2 inhibitor, as a potential treatment for nAMD.

Methods: The effects of AD-3281 were assessed using a choroidal sprouting assay (CSA) and a laser-induced choroidal neovascularization (LI-CNV) model in C57BL/6J mice and Norway rats. Treatments were delivered via intravitreal injection immediately after laser injury. CNV size was quantified using isolectin staining of RPE-choroid flat mounts 7 days post-induction in mice (14 days for rats). mRNA expression of three angiogenesis-related genes was analyzed in retinal and choroidal tissues 7 days post-treatment. Toxicity was evaluated through electroretinogram (ERG) recordings and histological analysis of retinal structure. Additionally, non-GLP 4-week single-dose intravitreal pharmacokinetics (PK) and maximum tolerated dose (MTD) toxicity studies were conducted in Dutch-belted pigmented rabbits.

Results: In the CSA, AD-3281 significantly reduced sprouting area compared to controls. In the LI-CNV model, AD-3281-treated eyes exhibited reduced CNV area compared to vehicle-treated eyes. No significant differences in mRNA levels of angiogenesis-related genes were observed between AD-3281-treated and control mice. ERG analysis showed similar functional responses across groups, and histological evaluation revealed no structural alterations or changes in outer nuclear layer thickness. In the rabbit studies, no treatment-related mortality or adverse effects were observed in clinical observations, body weight, clinical pathology, intraocular pressure, ERG, or imaging assessments.

Conclusions: AD-3281 demonstrates potent anti-angiogenic effects in preclinical models of nAMD, coupled with a favorable safety profile. These findings support further investigation of AD-3281 as a promising novel therapy for nAMD.

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AIP1

A Data-Driven Natural Language Processing (NLP) Platform for Clinician-Led Exploration of Retinal Fluid Dynamics and Personalized Management of Neovascular Age-Related Macular Degeneration (nAMD)

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Purpose: Neovascular age-related macular degeneration (nAMD) requires frequent monitoring and treatment, with highly variable responses between patients. While automated OCT algorithms become widely available, clinicians lack the ability to independently interact with their datasets and utilize the vast amount of fluid data generated to implement in clinical decision making. This project aims to develop the *RETINA-EXPLORER*, a machine learning-driven platform that empowers clinicians to intuitively interact with their nAMD data through a user-friendly natural language processing (NLP) interface and enhance personalized nAMD treatment strategies.

Methods: A comprehensive dataset comprising 5,675 OCT volume scans, 7,262 visual acuity exams, and 11,260 injections from 548 nAMD patients at Tel Aviv Medical Center, with up to four years of follow-up, was utilized. OCT scans were analyzed using a deep learning algorithm (Notal OCT Analyzer, Notal Vision Ltd.), providing quantitative volumetric and topographic fluid data. Categories were developed for responder types, fluid volumes, visual acuity, and treatment patterns to facilitate intuitive data analysis for clinicians. PandasAI, a Python-based tool, was used to simplify data querying. The platform leveraged the OpenAI language model within PandasAI to accurately interpret nAMD terminology in clinician queries. A web interface was developed using Streamlit serves to provide an accessible and interactive environment for clinicians.

Results: The prototype effectively processed large datasets. The NLP interface provided clinicians with rapid access to patient-specific data, allowed identification of trends in retinal fluid dynamics

and treatment response patterns, treatment history, and allowed to ask questions in natural language. The tool provided the users with results as text, tables, or figures. Moreover, clinicians could compare individual cases to similar cohorts, gaining insights into fluid dynamics and response trends. Findings will be showcased, highlighting the platform's potential through real-world case studies and its ability to streamline clinical decision-making.

Conclusions: RETINA-EXPLORER addresses the challenge of data overload in nAMD management by offering a data-driven platform for personalized treatment. Preliminary results demonstrate enhanced clinical efficiency by enabling intuitive data exploration through natural language queries, with outputs tailored to clinician needs. As further validation is conducted, this platform has the potential to become a tool for clinicians to independent data exploration and optimizing nAMD patient outcomes.

Organizations: Tel Aviv Medical Center, Tel Aviv University, Evolution Inc, Notal Ltd

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AIP2

Artificial Intelligence-Based Chatbots as Oculoplastic Consultants: Are They Good Enough?

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Purpose: To compare the responses of ChatGPT and Gemini to a series of questions related to oculoplastic surgery.

Methods: An experienced oculoplastic surgeon developed a set of 16 representative questions, and responses were gathered from two AI generative models: OpenAI's ChatGPT 4o and Gemini Pro. Seven highly experienced oculoplastic surgeons evaluated each response, without knowing the source, and rated them based on three criteria—accuracy, comprehensiveness, and clarity—using a scale from 1 to 5.

Results: GPT-4o received an average overall score of 4.3 ± 0.8, indicating a performance between "Good" and "Very Good." In comparison, Gemini scored an average of 4.0 ± 0.8, generally aligning with a "Good" performance level. These results suggest that, on aggregate, GPT-4o was rated more favorably by ophthalmologists across the evaluated dimensions ($p = 0.021$). When comparing question subtypes (table 1) , ChatGPT provided statistically significantly more comprehensive and clearer answers for eyelid-related questions compared to Gemini (t-test, $p<0.01$) , whereas Gemini performed statistically significantly better in comprehensive and clarity for questions related to the lacrimal system compared to ChatGPT (t-test, $p=0.01$, $p=0.03$, respectively).

Conclusion: This study is, to the best of our knowledge, the first to evaluate the responses of widely used LLM chatbots to common oculoplastic questions. Our findings indicate that both GPT-4 and Gemini provide accurate, comprehensive, and clear answers to these questions, with ChatGPT outperforming Gemini, particularly in eyelid-related topics. These results highlight the potential utility of chatbots, especially ChatGPT, as supplementary tools for addressing common patient inquiries in oculoplastic.

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Validation and Clinical Applicability of Deep Learning Model for Automated Diabetic Macular Edema Segmentation in OCT Scans

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Purpose: To develop and evaluate a deep learning model for automatic OCT segmentation of retina layers and four clinically important pathological diabetic macular edema (DME) features and assess clinical applicability.

Methods: Clinical OCT volumes from eyes with DME were collected from real-world settings, with two expert graders providing pixel-level segmentations for retinal layers, intraretinal and subretinal fluids, microaneurysms, and exudates. A U-Net-based deep learning model was trained and evaluated on sequestered data. Receiver operating characteristic (ROC) curves were analyzed for fluid detection, and clinical applicability was assessed by three retinal experts across 1200 OCT scans from 50 DME patients, covering the full range of severity, and from four points during treatment. Agreement between model and expert graders was quantified using intraclass correlation coefficients (ICC) and Dice similarity coefficients.

Results: The model achieved a mean AUC of 0.93 (±0.04) per slice and 0.88 (±0.07) per volume for all DME features detection. In detecting intraretinal fluid, model-grader agreement was 91%, and intraclass correlations for retinal layers ranged from 0.73 (95% CI, 0.08-0.96) to 0.96 (95% CI, 0.90-0.99). Dice coefficients demonstrated strong alignment between model and graders for detecting intraretinal fluid, microaneurysms, and exudates.

Conclusions We present a fully automated model capable of segmenting, measuring, and providing geometric characterization of DME biomarkers with performance comparable to that of experienced graders. This model holds the potential to enable detailed studies of morphological changes and treatment efficacy in real-world settings. Additionally, it can streamline structured reporting in clinical practice and minimize subjectivity in clinicians' assessments.

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AIP4

Predicting Vision Abnormalities in Pediatric NF1 Using Machine Learning and OCT data

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Background: Neurofibromatosis type 1 (NF-1) is a genetic disorder often presenting with significant ocular manifestations in pediatric patients, which can lead to progressive vision impairment and eventual vision loss. Optical Coherence Tomography (OCT), a non-invasive imaging technique, provides high-resolution views of retinal and optic nerve structures, offering critical insights for diagnostics. However, predicting vision abnormalities in NF-1 pediatric patients remains challenging due to the variability in disease progression and expression.

Purpose: This study proposes a machine learning-based approach for the early prediction of vision abnormalities using OCT data in pediatric NF-1 patients.

Methods: This retrospectivel study analyzed 1108 OCT measurements from 200 pediatric NF-1 patients treated at Hospital Sant Joan de Déu in Barcelona. Various machine learning models, including logistic regression and Light Gradient Boosting Machine (LGBM), were applied to identify predictors of vision abnormalities based on changes in retinal and optic nerve layer thickness.

Results: The analysis revealed significant reductions in the retinal nerve fiber layer (RNFL), the ganglion cell layer (GCL+), and the expanded ganglion cell layer (GCL++) among patients with vision abnormalities. Additionally, patients older than 73 months exhibited a higher risk of vision impairment, with statistical significance ($p < 0.0001$). Among the tested models, the LGBM classifier demonstrated the highest performance, achieving an F1 score of 0.88, Cohen's Kappa of 0.84, and impressive AUC metrics of 0.97 (ROC) and 0.94 (precision-recall). Furthermore, Critical cut-off values for OCT layer thickness were identified using SHAP analysis, providing clinically relevant benchmarks for early diagnosis and personalized treatment planning. These findings suggest that total macular or nerve layer measurements alone can deliver comparable predictive accuracy, streamlining the diagnostic process.

Conclusion: The integration of OCT metrics with advanced machine learning models shows significant potential for improving early detection and management of vision abnormalities in pediatric NF-1 patients. This approach offers a robust framework for facilitating timely intervention and optimizing outcomes for NF-1 patients.

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AIP5

Smartphone-Based Teleophthalmology for Triage of Urgent Ophthalmic Conditions

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Purpose: To assess the accuracy, safety, and efficiency of a remote triage tool combining smartphone-captured bilateral eye images and a structured patient-reported questionnaire. The study focused on evaluating the tool's ability to support clinical decision-making for urgent ophthalmic conditions, ensuring patient safety and optimizing resource allocation.

Methods: Patients were recruited from the emergency department (ED) of Hadassah Medical Center. A total of 89 sequential cases were evaluated. Each patient completed a 27-question questionnaire covering their presenting condition and relevant ophthalmic history. A researcher then used a smartphone camera to capture a standardized set of six photographs for each patient. Two clinicians, blinded to the ED diagnosis, independently reviewed the questionnaires and images. Based on the provided data, the cases were categorized into three pathways: referral to the emergency department, community follow-up, or home monitoring and the referral decisions were compared with in-hospital diagnoses. Agreement rates, safety metrics, and the tool's potential to identify cases that did not require emergency room visits were assessed to evaluate its clinical applicability.

Results: Clinicians demonstrated moderate agreement on referral decisions using the remote tool, with an agreement rate of 71.9% (Cohen’s Kappa = 0.437, p = 3.28 ’ 10!"). Notably, the tool effectively identified 54% of cases as potentially suitable for nonemergency management, reducing unnecessary ED visits. However, 16% of cases were identified as having a potential risk of harm, as the remote referral decisions failed to appropriately recognize the urgency of their condition. These findings underscore the tool's potential to optimize resource utilization while emphasizing the need for ongoing enhancements to strengthen its safety standards.

Conclusions: This study underscores the potential of smartphone-based imaging and structured patient-reported questionnaires to enhance remote medical evaluations. While the tool showed promising accuracy and efficiency, it is currently limited to diagnosing anterior segment and "red eye" conditions due to the sole reliance on smartphone images. Future studies and optimization of this tool may lead to the development of a more accurate, updated questionnaire and the integration of machine learning into a novel teleophthalmology system.

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UP1

Gender Influences on Uveitis Etiology: Insights from a Meta-analysis and systematic review

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Purpose: To evaluate gender-specific differences in the etiology of uveitis through a comprehensive meta-analysis and systematic review, thereby illuminating how sex-based factors may influence disease prevalence, associated conditions, and potential underlying mechanisms.

Methods: the systemic and meta-analysis review conducted following the PRISMA guidelines searching through databases, like PubMed/MEDLINE, Scopus, Central, Web of Science and Google Scholar from January 2014 to January 2024. Our focus was on studies that differentiate between uveitis etiology based on gender. Risk ratios (RR) and 95% confidence intervals (CIs) were estimated using a Mantel-Haenszel random-effects model; heterogeneity was assessed via I^2. Study quality and risk of bias were evaluated using the Newcastle–Ottawa Scale and JBI Critical Appraisal Checklists.

Results: Our analysis revealed pronounced gender-related differences in uveitis etiologies. Females demonstrated a significantly higher risk of uveitis associated with autoimmune conditions, including Systemic Lupus Erythematosus (RR=2.25, p<0.0154), Multiple Sclerosis (RR=2.12, p<0.0015), Sarcoidosis (RR=1.97, p<0.0001), Rheumatoid Arthritis (RR=1.94, p<0.0110), and Juvenile Idiopathic Arthritis (RR=1.87, p<0.0005). Females also showed elevated risk for Vogt-Koyanagi-Harada disease (RR=1.32, p<0.0025) and Toxoplasmosis (RR=1.29, p<0.0458). In contrast, males had increased risk for uveitis linked to conditions such as Diabetes Mellitus (RR=0.29, p<0.0015), Eales Disease (RR=0.30, p<0.0006), Sympathetic Ophthalmia (RR=0.52, p<0.0063), Behçet's Disease (RR=0.56, p<0.0001), and Ankylosing Spondylitis (RR=0.57, p<0.0001).

Conclusions: This meta-analysis highlights significant gender differences in uveitis etiologies, with females more susceptible to autoimmune-associated uveitis and males more prone to uveitis linked to certain systemic conditions. These findings suggest that hormonal, genetic, and immunologic factors may drive sex-based disparities in disease pathophysiology. Recognizing these differences can guide targeted diagnostic approaches, optimize treatment strategies, and ultimately improve patient outcomes.

BACK TO PROGRAM

UP2

The Impact of Perceived Stress on Uveitis Onset and Flare-ups

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Purpose: Psychological stress is acknowledged as a trigger in various inflammatory diseases, such as inflammatory bowel diseases and psoriasis. In this study, we aim to evaluate the impact of stress on the onset and disease flare-ups of uveitis.

Methods: Psychological stress was evaluated using three validated questionnaires assessing perceived stress and traumatic events; the perceived stress scale (PSS), the post-traumatic diagnostic scale-5 (PDS-5), and an additional questionnaire about the type of stressful event. Patients with non-infectious uveitis treated at a tertiary medical center were recruited, after signing an informed consent. Excluded were patients who were unable to fulfill the questionnaire due to the language barrier, and patients with infectious uveitis Additional recorded data included demographics, time of disease onset, type of uveitis, ocular inflammation activity and flare-ups timing, treatment, and ocular complications. Data were analyzed for a correlation between stressful events and uveitis.

Preliminary Results: 124 patients were handed the questionnaires, but only 70 (56.4%) filled them to date. The majority of patients who filled out the questionnaire (92.8%, 65/70) reported 1 or more life events perceived as stressful, and most of them (76.9%, 50/65) had at least one stressful event recognized as traumatic according to the PDS-5 questionnaire. Respectively, most of the participants ranked high stress scores in the PSS questionnaire (72.8%, 51/70). The interval between the stressful event and the disease breakout was reported within 3 months in 38.5% (27/70), between 3 to 6 months in 14.2% (10/70), and between 6 to 12 months in 20% (14/70). Twenty percent (14/70, 20%) of patients reported no proximity (more than 12 months) or relation between any stressful event and uveitis diagnosis or flare-up.

Conclusions: Our findings support the hypothesis that stress may play a role in uveitis, which is a group of multifactorial diseases, similar to other known inflammatory conditions.

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ASP1

Reliability of a multifunctional meibography device in normal young participants

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Purpose: Multi-functional diagnostic devices, such as meibographers, streamline clinical workflows by integrating multiple ocular assessments. Ensuring reproducibility across examiners is vital for accurate diagnosis, and monitoring treatment. This prospective study evaluated the inter-examiner reproducibility (IER), inter-rater reproducibility (IRR), and within-subject variability (WSV) of the multifunctional HRK-9000A meibographer (Huvitz, South Korea(.

Methods: Meibomian glands (MGs) of both eyelids of healthy participants were captured during the same session by Examiner 1 (E1) and Examiner 2 (E2) in a counter-balanced design. The images were rated offline by E1, E2 and an Independent Rater (R1). The inter-examiner reproducibility (IER between E1 vs. E2) and inter-rater reproducibility (IRR between E1 vs. R1 and E2 vs. R1) were determined based on non-parametric Bland-Altman plots, intraclass correlation coefficients (ICCs) and weighted Kappa (κ) values. Within-subject variability (WSV) was determined using ICCs.

Results: 35 participants (mean age:22.0±2.5 years, 19-30) were included in the study. The MG grade for the upper (E1:1.0±0.8, E2:1.2±0.8, R1:0.9±0.8,0.9±0.7) and lower eyelids (E1:1.9±0.9, E2:1.5±1.0, R1:2.1±1.1,1.8±1.0) were significantly correlated for all comparisons ($p < 0.001$). ICCs for repeated measurements of the same participants were all above 0.90 indicating excellent WSV. IRR was moderate (0.43-0.57) with good reliability (ICC range:0.76-0.86) for the upper eyelids and good (0.60-0.65) with good reliability (ICC range:0.85-0.88) for the lower eyelids. The WSV was excellent (ICCs for repeated measurements>0.9).

Conclusions: The Huvitz HRK-9000A meibographer demonstrated excellent reliability with good inter-examiner reproducibility and inter-rater reproducibility, making it a suitable for the meibographic assessment and monitoring of MGD progression or treatment.

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ASP2

Behavioral and Potential Clinical Indicators for Dry Eye Disease: Preliminary Findings

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Purpose: Dry eye disease (DED) is a widespread eye condition affecting millions globally. This study aims to identify behavioral and clinical factors that may predict individuals at risk of developing dry eye, enabling early intervention.

Methods: The following information was collected from the participants: demographic data, visual acuity, invasive and non-invasive tear break-up time (TBUT), tear meniscus height, Schirmer test, lid margin abnormalities, meibography, aberrometry, meibum gland (MG) expressibility and quality, corneal and conjunctival staining, complete and incomplete blinks per minute during a reading task from a monitor, subjective symptoms and habits (Ocular Surface Disease Index (OSDI), MG dysfunction (MGD) questionnaire, and digital eye strain (DES) questionnaire). Dry eye (OSDI≥ 13 and TBUT<10 sec) and MGD (dry eye and MG loss>25%) were diagnosed based on the Tear Film and Ocular Surface Society criteria. Correlations were examined using Spearman's tests, and dry eye vs. non-dry eye as well as MGD vs. non-MGD groups were compared with Mann-Whitney tests.

Results: Of the 56 participants in this preliminary cohort (mean age:21±3 years, range: 18-31), 43% (N=24, mean age:21±2 years, range: 19-27) had dry eye, and 23% (N=13, mean age:22±2 years, 19-27) had MGD. Tetrafoil aberration was significantly positively correlated with dry eye diagnosis (Rho=0.33, p=0.01) and was significantly higher (0.04±0.03 vs. 0.03±0.02, p=0.02) in the dry eye compared with the non-dry eye group. MG expressibility was significantly lower (2.08±0.58 vs. 2.41±0.61, p=0.04) in the dry eye compared to the non-dry eye group. Tetrafoil aberration was higher and approached significance (0.05±0.04 vs. 0.03±0.02, p=0.05) in the MGD compared to the non-MGD group. The lid abnormalities score (LAS) was significantly worse in the MGD vs. non- MGD group (2.00±1.22 vs. 1.11±1.20, p=0.02), and both MG expressibility (1.85±0.55 vs. 2.39±0.58, p=0.006) and quality (2.62±0.51 vs.

2.88.0±0.32, p=0.03) were significantly lower in the MGD compared with the non-MGD group. The MGD questionnaire score and some DES questionnaire items were significantly positively correlated with diagnosis of dry eye and MGD.

Conclusions: In this preliminary study, tetrafoil aberration and MG expressibility emerged as a potential predictors for dry eye. LAS, MG expressibility and quality were potential predictors for MGD. More participants are needed to draw definitive conclusions and identify other risk factors.

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ASP3

The Association Between Blepharitis and Lower Eyelid Ectropion in a Large Cohort of Patients

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Purpose: Blepharitis and lower eyelid ectropion are highly prevalent ocular conditions occurring in 37%-46% and 2-3% of the general adult population, respectively. Blepharitis has multifactorial origins and involves anterior and posterior types of eyelid inflammation. Lower eyelid ectropion results in ocular surface exposure, epiphora and chronic conjunctivitis. This study aims to investigate any possible association between both conditions.

Methods: Medical records of 37,692 consecutive patients examined at a single medical screening center between 2001-2020 were retrospectively analyzed.

Main Outcome Measures: The prevalence of lower eyelid ectropion and of blepharitis, a possible association between the 2, and the relation of each to age and sex.

Results: A total of 35,670 patients were included. Ectropion was diagnosed in 69 patients (0.2%), and blepharitis in 4725 patients (13.2%). Male sex was more prevalent for each pathology (88.4% ectropion, and 85% blepharitis, $P < 0.001$). Older age was associated with each diagnosis (77.3 years for ectropion patients vs. 52.2 years for the general screened population and 60.5 years for blepharitis patients vs 52.2 years for the general screened population $P < 0.001$). The prevalence of ectropion was significantly higher in patients with coexisting blepharitis compared to those without (0.8% vs. 0.1%, respectively, $P < 0.001$).

Conclusions: Ectropion was significantly more prevalent in patients with blepharitis. Both conditions were associated with older age and male sex. This coexistence can aid in decision making of early surgical intervention of lower eyelid ectropion as well as the approach to medical treatment of blepharitis.

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ASP4

Assessing visual performance in presbyopes using dynamic focal sunglasses

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Purpose: Presbyopes, whether emmetropic or contact lens users for distance vision, often switch between reading glasses and sunglasses or use plano multifocal sunglasses for near tasks outdoors. Recent technology has introduced dynamic focal sunglasses equipped with electrically tunable lenses, using Liquid Crystal technology, capable of adjusting from plano to a near correction of up to +2.50 D without mechanical components. This initial clinical study compares basic visual functions using dynamic sunglasses to identical sunglasses with a static correction .

Methods: The study involved seven presbyopic participants: five emmetropes and two contact lens-induced emmetropes. They underwent autorefraction and subjective examinations to ensure emmetropic corrections within ±0.50 diopters (D) SPH and -0.50D CYL, with habitual near correction of less than 0.50D SPH between the two eyes. Participants required a far visual acuity of at least 0.67 decimal for distance and 0.00 LogMar for corrected near vision. Reading correction was measured using both dynamic sunglasses and static correction. Visual acuity (LogMar) and contrast sensitivity (Pelli-Robson chart) at 40 cm, reading acuity (LogMAR), and maximum reading speed (words per minute, WPM) (MNREAD Acuity Charts) were assessed. Tests were conducted randomly with dynamic sunglasses and identical sunglasses featuring static correction under lighting conditions simulating outdoor illumination of 6000 lux. The Mann-Whitney U test was used for statistical analysis for binocular measurements.

Results: The study included four women and three men, with an average age of 50.7±5.4 years. Habitual visual acuities were 0.92±0.12 decimal for distance and 0.42±0.18 LogMAR for near. The average spherical equivalent for distance was -0.17±0.46D, with a near correction of 1.54±0.37D. There were no significant differences between dynamic and static sunglasses in near visual acuity (0.03±0.03 LogMAR, p=0.95) or contrast sensitivity (1.71±0.23 vs. 1.69±0.24 LogMar, p=0.94). Similarly, reading acuity (0.02±0.02 vs. 0.03±0.02 LogMar, p=0.56) and maximum reading speed (154.60±21.70 vs. 154.40±15.35 WPM, p=0.79) showed no significant differences .

Conclusions: Dynamic sunglasses offer visual functions comparable to those provided by similar sunglasses with static correction for near vision. This preliminary study supports the potential of new technologies for near vision adjustment in emmetropic presbyopes. Further research with larger sample sizes could offer more insights into the benefits and limitations of dynamic sunglasses.

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ASP5

Microbiome Profiling of Pterygium

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Purpose: The ocular microbiome plays a crucial role in maintaining ocular health, with imbalances linked to various ocular conditions. Pterygium, a common ocular surface disease characterized by fibrovascular overgrowth of conjunctival tissue, may change the conjunctival microbiome. This study aims to characterize the microbiome composition of pterygium.

Methods: Excised Pterygium tissues were collected from nine patients according to IRB and signature of informed consent. DNA was extracted, purified and amplificated for the 16S rRNA gene using polymerase chain reaction, followed by microbiome profiling.

Results: The main bacterial phyla found in normal conjunctival microbiome are Actinobacteria, Proteobacteria, and Firmicutes. Previous studies investigated ocular surface using 16S rRNA gene reads revealed 115,003 sequences (Dong 2011) to 1,690,427 reads (Zhou 2014). None of these studies explored pterygium - induced changes of the microbiome.

Conclusion: This is the first report identifying microbiome of pterygium tissues excised for bacterial 16S rRNA analysis. We will compare the phyla to normal conjunctival microbiome as reported in the literature.

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ASP6

miR-184/ATF3 axis is required for the maintenance of active limbal stem cell state and corneal homeostasis

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Purpose: Recently we discovered two discrete limbal epithelial stem cell (LSC) populations in the murine cornea. A population of quiescent LSCs (qLSCs) that act a reservoir for wound healing and a population of active LSCs (aLSCs) that are highly proliferative and is essential for corneal cell replenishment. However, very little is known about the genetic regulation of these new cells. This study aims to study the mechanism of regulation of the active limbal stem cell (aLSC) population by miR-184, that its mutations have been linked with congenital corneal pathology.

Methods: We employed knock out (KO) mouse strains that lack miR-184, ATF3 aLSC transgenic reporter K15-GFP. Bioinformatic tools were employed to identify potential transcription factor binding sites within the K15 promoter.. Promoter activity assays and in vitro studies were performed to study the regulatory interactions between miR-184, ATF3, and K15-GFP. Lastly, corneal wound healing assays were conducted to assess the impact of miR-184 and ATF3 ablation on SC/progenitor cell behavior and niche integrity under stress conditions.

Results: Bioinformatic analysis of the K15 promoter predicted that ATF3 is a candidate transcription factor regulating aLSCs. In situ hybridization demonstrated that miR-184 is expressed by LSC and corneal basal progenitor cells but absent in differentiated cells. miR-184- (KO) mice exhibit reduced expression of aLSC markers, including ATF3 and K15-GFP, suggesting impaired aLSC functionality. Promoter assays confirmed that miR-184 positively regulates ATF3, and that ATF3 can activate K15 promoter. ATF3-KO mice displayed reduced expression of aLSC markers, further validating the miR-184/ATF3/K15 regulatory axis in aLSCs. Functional analyses revealed that miR-184 ablation increased aLSC proliferation, corneal turnover, and delayed wound healing.

Conclusions: The miR-184/ATF3 axis is essential for maintaining aLSC identity and function. Understanding the downstream signaling of miR-184 may provide novel therapeutic insights for corneal diseases and advance the broader understanding of stem cell fate decisions.

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ASP7

Characterization of Immune Cell Populations in a Murine Model of Pediatric Penetrating Keratoplasty

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Purpose: Clinical and laboratory data suggest lower corneal transplant survival in pediatric penetrating keratoplasty (PK), but the underlying immunologic mechanisms are not known. The purpose of this study was to quantify antigen-presenting cell and graft-infiltrating immune cell frequencies in a murine model of pediatric PK.

Methods: Corneal buttons were harvested from 10-week-old C57BL/6 mice and transplanted into the eyes of 3.5-week-old (young) or 10-week-old (adult) BALB/c male mice. Grafts were monitored for eight weeks using slit lamp evaluation to assess corneal opacity. At 14 days post transplantation, transplant recipients were euthanized and cell populations analyzed by flow cytometry. The frequencies of CD11c+ antigen-presenting cells (APCs) were assessed in the ipsilateral cervical and submandibular lymph nodes. Corneal grafts were also collected and the frequency of CD45+ leukocytes was quantified, along with the percent of CD45+IFNγ+ (Th1), CD45+IL-4+ (Th2), CD45+IL-17 (Th17) and CD45+CD49b+ (NK) cells.

Results: There was a trend towards lower eight-week graft survival in young mice as compared to adult mice (20% vs. 50%, p=0.276). At 14 days post-transplantation, there was a higher frequency of CD11c+ APCs in the draining lymph nodes of young mice versus adult mice (0.63±0.11% vs. 0.37±0.15%, p=0.029, % of total cells). Young mice exhibited trends toward higher percentages of graft infiltrating NK and Th2 cells compared to adult mice: NK cells: 6.9±3.03% vs. 4.55±0.21% (p=0.38, % of CD45+ cells); Th2 cells: 0.37±0.11% vs. 0.15±0.21% (p=0.22). Similar frequencies of Th1 (9.17±2.59% vs 8.15±1.49%, p=0.66) and Th17 (1.73±0.85% vs. 1.6±0.7%, p=0.86) cells were observed between groups. We observed a 3.3- fold increase in NK cells in young transplant recipient mice and a 1.22-fold increase in NK cells in adult transplant recipient mice compared to age-matched controls (p=0.28).

Conclusions: In a murine model of PK, we observed trends toward lower corneal transplant survival in young mice as compared to adult mice, as well as higher frequencies of APCs and immune cells, in particular NK cells, in young mice. These findings recapitulate the poor outcomes seen clinically in pediatric PK, and suggest further investigation of both the afferent and efferent arms of the lloimmune response in young mice to better understand the underlying immune mechanisms leading to graft failure in pediatric PK.

Support: Research to Prevent Blindness, Alcon Research Institute, Lions Young Investigator Award.

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ASP8

Intraoperative sensor and alerting system for phacoemulsification

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Purpose: To describe the development of an intraoperative sensor and alerting system for phacoemulsification

Methods: A sound-insulated MEMS-based microphone connected to a touchscreen tablet-based console was designed and manufactured. Phacoemusification was performed near it using Alcon Infinity platform, and employing different power modulations and amplitudes.

Results: The sensor could consistently identify ultrasound signals emanating from the phaco machine, and provide alerts for set thresholds relevant to continuous phaco time, and total cumulative phaco time.

Conclusions:The presented sensor and alerting system can possibly increase safety of phacoemulsification, and decrease postoperative corneal edema.

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ASP9

Designing a Novel Tool for Corneal Foreign Body Removal

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Purpose: To describe the development process of a designated corneal foreign body removal tool, tailored to the corneal anatomy, injury mechanism and human ergonomics.

Methods: Following guidance from two ophthalmologists experienced in corneal foreign body removal, prototypes of different shapes and sizes were produced by Industrial design students at the Holon InsJtute of Technology employing Photochemical machining process (PCM).

Results: The produced tools were examined by the ophthalmologists using a model of a Styrofoam sheet aTached to a slit lamp and a shortlist of tools were chosen for further refinement and development.

Conclusions: CooperaJon between clinicians and designers resulted in a rapid and efficient development of a tool aimed at solving an unmet clinical need. PCM process is a promising technique for fast prototyping of ophthalmic tools.

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ASP10

Annular Dark Shadow as a Potential Familial Marker for Keratoconus: A Preliminary Investigation

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Purpose: To investigate the presence of Annular Dark Shadow (ADS) among first-degree relatives of keratoconus patients and explore its potential as a familial risk factor.

Methods: Keratoconus (KC) patients and their first-degree relatives underwent comprehensive ocular examinations, including best-corrected visual acuity (BCVA, measured in Snellen), corneal tomography (using the Sirius system), slit-lamp biomicroscopy, and retinoscopy. The ADS was evaluated using an iPhone 14Plus camera in conjunction with a Welch Allyn handheld ophthalmoscope. KC severity was graded according to the Belin ABCD classification method.

Results: To date, one family has participated in the study. The family consists of a 17-year-old proband, a 38-year-old mother, and four siblings: ages 20, 16, 2, and 8. The proband was diagnosed with bilateral KC, with BCVA of 20/30 in the right eye (RE) and 20/20 in the left eye (LE). The thinnest corneal thickness (TCT) measured 516 µm (RE) and 534 µm (LE). Additional findings included posterior ectasia and a scissoring reflex in both eyes. KC severity was graded as A0 B1 C0 D1 (RE) and A0 B0 C0 D0 (LE). The mother also exhibited bilateral KC, with a BCVA of 20/40 (RE) and 20/25 (LE), TCT of 375 µm (RE) and 438 µm (LE), and Munson's sign in the RE. Both eyes showed posterior ectasia and a scissoring reflex. KC severity was graded as A4 B4 C3 D2 (RE) and A2 B3 C2 D1 (LE). The siblings showed no clinical signs of KC and maintained good BCVA. However, the ADS was observed bilaterally in the proband, the mother, and in three of the four siblings, who did not exhibit KC.

Conclusions: Annular Dark Shadow may serve as a familial marker for keratoconus. Additional research is needed to assess its role in early detection and inheritance patterns.

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ASP11

Descemet membrane endothelial keratoplasty compared to ultrathin Descemet stripping automated endothelial keratoplasty: a meta-analysis

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Purpose: To compare the clinical outcome of Descemet membrane endothelial keratoplasty (DMEK) and ultrathin Descemet stripping automated endothelial keratoplasty (UTDSAEK) in patients with corneal endothelial dysfunction due to Fuchs' endothelial dystrophy or pseudophakic bullous keratopathy.

Methods: A systematic review and meta-analysis were conducted based on a literature search using the Embase, PubMed, Cochrane CENTRAL, Clinicaltrials.gov, and WHO ICTRP databases. Eligible studies were randomized controlled trials (RCTs) and cohort studies that compared the clinical results of DMEK and UT-DSAEK (graft<130µm) in the target population, with a minimum follow-up period of 12 months, published until February 20, 2022. Risk of bias was evaluated using the Revised Cochrane risk-of-bias tool (RoB-2) for RCTs and the Risk of Bias in Non-Randomized Studies-of Interventions (ROBINS-I) system for cohort studies. The study protocol was registered in PROSPERO (CRD42022340805).

Results: The search yielded 144 records of which 8 studies (3 RCTs, 2 fellow-eye studies, and 3 cohort studies) were included, encompassing 376 eyes, 187 and 189 in the DMEK and UT-DSAEK groups, respectively. The 12-months logarithm of the minimum angle of resolution best corrected visual acuity (logMAR BCVA) was better in the DMEK group (mean difference -0.06 [95% confidence interval (CI) -0.10, 0.02]), but with higher odds of rebubbling (odds ratio 2.76 [95% CI 1.46, 5.22]). Heterogeneity was significant ($\chi 2=11.65$, P=0.04; I2=57%). Findings were consistent when excluding retrospective studies, including only studies with low risk of bias or RCTs only. Sensitivity analysis limited to studies with DSAEK grafts<70µm showed comparable visual results of the two procedures (mean difference -0.03 [95% CI -0.12, 0.03]). Risk of publication bias was significant for 12-months logMAR BCVA (Egger test P=0.023) but not for rebubbling, for which data from all included studies were available (P=0.234).

Conclusions: DMEK leads to an improved 12-month visual acuity compared to UT-DSAEK. The use of thinner DSAEK grafts (<70µm) could potentially achieve visual outcomes comparable to DMEK. The higher risk of rebubbling with DMEK necessitates an appropriate selection of patients. Further studies to investigate the implications of rebubbling on long-term graft survival as well as the incidence of rare complications such as graft rejection, graft failure or glaucoma are warranted

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ASP12

Effect of Pupil Size and Corneal Spherical Aberrations on Premium Lenses' Optical Performance

Benjamin Stern

Purpose: To analyze the effects of pupil size and corneal spherical aberrations on premium intraocular lenses (IOLs).

Methods: The study involved in vitro wavefront acquisition of multiple IOLs, including Eyhance (Johnson & Johnson), Isopure (BVI), Luxsmart (Bausch & Lomb), RayOne EMV (Rayner), Vivity IQ (Alcon), ATLara (Zeiss), RayOne trifocal (Rayner), PanOptix (Alcon), Finevision (BVI), and ATLisa Tri (Zeiss). This data was acquired using the NIMO TEMPO system (Lambda-X, Nivelles, Belgium). Through-focus Modulation Transfer Function (MTF) curves were computed for 168 synthetic numerical eye models, with apertures ranging from 2 to 5.5 mm (in 0.5 mm increments) and corneal spherical aberrations spanning from -0.49 to 0.91 µm (in 0.07 µm increments).

Results: Each premium lens behaves differently under various optical conditions. Refractive Extended Depth of Focus lenses show a significant dependence on pupil size and corneal spherical aberrations, with a notable myopic shift observed in vitro, particularly in the LuxSmart lens. Diffractive lenses, even those described as pupil-independent, such as the ATLisa Tri, exhibit dependence on pupil size, especially under very small or very large pupil conditions.

Conclusion: The in vitro behavior of EDOF and multifocal lenses depends on corneal spherical aberrations and pupil size, and these factors must be considered when selecting a lens, as the behavior also varies with each IOL design. This consideration is particularly important when planning the implantation of premium IOLs after refractive corneal surgery, where corneal spherical aberrations may be pathological.

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ASP13

The effects of corneal flap side-cut angle on flap stability of femtosecond LASIK surgery

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Purpose: To assess the impact of two side-cut angle profiles on surgical outcomes following femtosecond laser in situ keratomileusis (FS-LASIK).

Methods: This retrospective cohort study included patients who underwent wavefront-optimized femtosecond LASIK surgery between 2023 and 2024, with complete medical records and a minimum follow-up period of one month. Eyes with a 70-degree side-cut angle were matched with those with a 120-degree angle. Monovision surgeries and any intraoperative complications were excluded from the analysis.

Results: A total of 318 pairs of matched eyes were included in the study. The mean age of participants was 26.9 $\pm$ 7.2 years, ranging from 17 to 54 years, with 54% being female. The average follow-up period was 35.5 $\pm$ 29.9 days. Post-surgical flap striae occurred more frequently in eyes with a 120-degree angle (3.1% vs. 0.9%, p=0.05). There were no significant differences in diffuse lamellar keratitis, post-op flap re-lift and irrigate, halos, or glare. Safety and efficacy indices were comparable across groups.

Conclusion: Using a 70-degree side-cut angle may reduced the prevalence of post-surgical striae, with no other differences in complications and similar safety and efficacy indices.

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ASP14

A Novel Multi-Parameter Point-of-Care Tear Film Test for Diagnosis of Dry Eye Syndrome, Severe Meibomian Gland Dysfunction, and Responsiveness to Therapy

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Purpose: Accurate dry eye syndrome (DES) diagnosis is complex and requires many tests. This study aimed to assess the efficacy of a novel, point-of-care, multi-parametric device (TeaRx™, DiagnosTear Ltd., Israel) to distinguish between DES patients and healthy controls, to identify severe meibomian gland dysfunction (MGD) cases within DES patients, and to predict objective responsiveness to cyclosporine A (CsA) therapy at baseline.

Methods: This was an investigator-initiated prospective clinical trial. The TeaRx™ technology is based on a minimally invasive collection of tear fluid using a novel microfluidic device and semi-quantitative assessment of five tear proteins (Lactoferrin, Albumin, Lysozyme, Mucin, and IgA) by immunochromatography (IC). In this study, 593 participants were graded according to the TFOS-DEWS II criteria: 495 DES patients and 98 healthy controls. Optimal logistic regression models were selected to correlate the semi-quantitative readouts of the subjects' five proteins, ages, and genders to the DES and MGD severity and responsiveness to CsA therapy. The performance of the selected models was evaluated using ROC analysis. Youden's Index was used to find the optimal combination of sensitivities and specificities.

Results: TeaRx™ differentiated between DES subjects at all severity levels vs. healthy controls at sensitivity, specificity, and accuracy levels of 72%, 63% and 70.1%, respectively, and between severe DES vs. healthy controls at sensitivity, specificity, and accuracy levels of 80.6%, 66.7% and 68%, respectively. In addition, TeaRx™ identified the presence of severe MGD vs. non-MGD, within the tested cohort of eligible DES patients, at sensitivity, specificity, and accuracy levels of 80.6%, 61.3% and 76%, respectively. Finally, TeaRx™ could predict CsA responsiveness at baseline at sensitivity, specificity, and accuracy levels of 94%, 63% and 77%, respectively. Notably, the NPV was 92.3%, indicating the promising potential of TeaRx responders before CsA therapy initiation.

Conclusions: The results of this study suggest that the TeaRx™ point-of-care, multi-parametric technology has the potential as a single diagnostic device for assessing the presence and severity of DES, differentiating between MGD and non-MGD DES cases, and predicting the response to CsA therapy.

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Teprotumumab Exacerbates Damage in a Mouse Model of Optic Neuropathy

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Purpose: To evaluate the potential neuroprotective effects of intravenously administered Teprotumumab (Tepezza, TPZ) in a murine optic nerve crush (ONC) model.

Methods: Forty wild-type C57BL6 mice underwent ONC to the right eye, intravenous-retro orbital TPZ injection, or both. The mice were divided into four groups: ONC only (n=10), ONC with TPZ treatment (ONC+TPZ, n=13), TPZ without ONC (TPZ only, n=12), and untreated controls (n=5). Retinal and optic nerve histology and immunohistochemistry studies were performed on five mice per group. Molecular analyses were conducted on five, eight, and seven mice in the ONC-only, ONC+TPZ, and TPZ-only groups. Ischemic-, inflammation-, apoptosis- and stress- related genes were analayzed. The contralateral eyes served as internal controls (n=10 with TPZ; n=7 without TPZ). Retinal ganglion cell (RGC) loss and retinal thickness were quantified. Immunohistochemical staining for MMP3, Iba1, GFAP, and NeuN was performed and analyzed.

Results: Two of 13 eyes in the ONC+TPZ group developed phthisis. The mean RGC loss in the ONC+TPZ group was 37.4 ± 10%, compared to 23± 5% in the ONC-only group. Notably, the TPZ-only group exhibited a 7% RGC loss. Severe retinal and optic nerve inflammation was observed in the ONC+TPZ group compared to other groups. Intense MMP3 staining was localized in the superficial retinal nerve fiber layer. Molecular analyses of ONC+TPZ revealed significantly upregulated inflammation marker *Tgfb1* (3.5-fold) and thrombotic marker *Pai-1* (57-fold).

Conclusions: Tepezza did not demonstrate neuroprotective effects in the ONC model. Instead, it induced the expression of inflammation, ischemia, and thrombosis markers. When combined with ONC, it exacerbated retinal and optic nerve damage, leading to severe retinal destruction and phthisis.

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NGP2

The incidence of subsequent high intracranial pressure in patients undergoing early, open, and wide strip craniectomy for sagittal synostosis

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Background: The incidence of secondary bone closure following strip craniectomy for sagittal synostosis (SS) has not been systematically described. Secondary closure leading to high intracranial pressure (ICP) may cause silent papilledema, optic atrophy, and blindness.

Purpose: To investigate the long-term follow-up of children who underwent early, open, and wide strip craniectomy for sagittal synostosis. Analyze the incidence of secondary closure that led to increased intracranial pressure and the subsequent need for surgical or medical intervention.

Methods: A single-center, retrospective, observational study of children who underwent early, open, and wide strip craniectomy for sagittal synostosis with a follow-up of 2 to 25 years (Av=9.1y, SD±6.2y).

Results: The study cohort included 286 children who underwent strip craniectomy for SS at the age of 2-4 months. Three of 286 developed papilledema with documented increased intracranial pressure (formal ICP monitoring for 3 days). Two of them required secondary cranial vault expansion at 1.8 and 1.9 years. The third patient was diagnosed with papilledema and borderline high values of ICP at the age of 2.8 years. He was treated with acetazolamide, resulting in persistent normalization of his fundoscopic exam, even after the acetazolamide treatment was discontinued.

Conclusion: This study verifies that the incidence of secondary closure is very low following early, open, and wide strip craniectomy for SS. However, careful clinical and ophthalmological follow-up is advised during the first few years following surgery.

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Alterations in pupil light reflex kineticks in patients with Optic Neuritis

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Purpose: The aim of this study is to evaluate the kinetics of rod-, cone-, and melanopsin-mediated pupil light responses (PLR) to small focal chromatic light stimuli presented at central and peripheral retinal locations in patients with optic neuritis (ON).

Methods: The PLR kinetics of ON patients (3 males and 7 females, mean age ± standard deviation: 32.3 ± 8.82 years) were compared to the PLR of 20 age- and gender-similar healthy volunteers. Chromatic pupilloperimetry was used to measure the PLR for small (0.43°) red and blue light stimuli (peak wavelengths: 485 nm and 625 nm, respectively) presented at 54 locations within the 24-2 visual field (VF). All participants underwent Optical Coherence Tomography imaging, standard Humphrey SITA Standard perimetry, and best-corrected visual acuity assessment.

Results: The percentage of pupil contraction (PPC) for blue and red light stimuli was lower by more than 2 standard errors (SEs) from the mean of controls in the majority of VF test targets (mean ± SE: 60% ± 12 % and 55% ± 10 %, respectively) in ON eyes, even in patients with normal visual acuity. In addition, a significant reduction was observed in the maximal contraction velocity (MCV) for blue and red light stimuli in 53.1% and 55% of VF test targets, respectively. No significant differences were observed in the latencies of MCV and pupil contraction.

Conclusions: These findings highlight substantial functional impairment of coneand rod-mediated PLR in ON eyes, which may present a novel surrogate functional biomarker for the detection of ON.

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Oculomotor dysfunctions among Israeli Defense Force soldiers admitted to an inpatient rehabilitation unit for polytrauma: the impact of co-occurring traumatic brain injury

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Purpose: This prospective observational study of Israeli Defense Force (IDF) soldiers admitted to an inpatient rehabilitation unit for (mostly blast) polytrauma examined the prevalence and phenotype of oculomotor dysfunction and the impact of co-occurring traumatic brain injury (TBI).

Methods: Soldiers were diagnosed with TBI if their injury resulted in immediate traumatically-induced loss of consciousness, peri-traumatic amnesia, alteration of consciousness, or evidence of acute trauma on head CT. Injury mechanism was coded as blast versus non-blast. Soldiers underwent a comprehensive oculomotor evaluation and completed the Brain Injury Vision Symptoms Survey (BIVSS). Convergence insufficiency (CI) and convergence deficit (CD) were defined according to accepted clinical criteria. Baseline features, BIVSS total score, CI, and CD frequency were compared between soldiers with TBI versus without TBI using t-tests and chi-square tests.

Results: Among N=31 male soldiers (mean age:25±7y, range:19-43y), N=20 had TBI (4 non-blast, 16 blast, 17 mild, 2 moderate, 1 severe), N=4 had high-level blast injury without clinical/imaging evidence of TBI, and only N=7 had neither TBI nor high-level blast injury. BIVSS total score was significantly higher among soldiers with TBI vs. without TBI (36.6 vs. 23.9, p=0.0497). There was no significant difference between prevalence of CI (42% vs. 55%, p=0.45) or CD (39% vs. 38%, p=1.00) among soldiers with versus without TBI.

Discussion and Conclusions: While CI and CD were surprisingly common among all injured soldiers in this rehabilitation unit, those with TBI reported more vision symptoms. The high prevalence of CD among soldiers without TBI may be due to TBI-exposure mis-classification (e.g., if soldiers with high-level blast injury without TBI under-reported TBI symptoms) or due to other war-injury related factors, such as cumulative sub-concussive brain injuries from low-level blast or current psycho-active medication use. Further research is needed in larger cohorts to determine the phenotype of ocular abnormalities associated with war-related polytrauma in order to inform targeted rehabilitation to optimize quality of life.

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NGP5

Predicting Structural Reliability in Ophthalmology Using Sequence-Based Analysis of Humphrey Visual Field Test Results in glaucoma patients

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Purpose: Currently, several reliability indices for high visual function (HVF) are available; however, some of them fail to adequately align with the specific needs of clinicians.
The objective of this research is to develop a novel and supplementary reliability index for HVF through the application of artificial intelligence models.

Methods: The study included patients who have attended the glaucoma clinic at Sheba Medical Center As a preprocessing step, structure-function patterns of each eye separately are analyzed using two parameters: 1. Thickness percentile distribution of the optical coherence tomography (OCT) retinal nerve fiber layer (RNFL), 2. Pattern of points missed during the HVF test.

We define a specific area in the structure-function as reliable if the points in the field align with the anatomical integrity of that region, and vice versa. For instance, a region is considered unreliable if it contains points falling below the normal threshold distribution (below the 5th percentile) in an area with otherwise normal anatomy.

A machine learning/deep learning model is utilized to model HVF test points consisting of spatial coordinates and binary detection labels as a sequence.

After training on data from hundreds of patients, the model will predict region reliability using only HVF input.

Results: The study population included patients (N=554) between the ages of 19 to 100 (mean=63.9 std=18.03) with a distribution of 50% men and 50% women.

Preliminary analyses show a good match in the predictive ability of the model when compared to structure function. Tentative findings indicate the potential for accurate prediction of regional reliability, with areas showing distinct functional loss aligning closely with structural anomalies.

Conclusions: The integration of sequence-based machine learning models into clinical workflows could significantly enhance the diagnostic utility of HVF testing. By enabling precise predictions of structural reliability based on functional test results, this approach has the potential to improve early detection and monitoring of glaucoma patients . This study underscores the importance of leveraging advanced computational tools to bridge the gap between functional and structural assessments, thereby advancing personalized care and optimizing outcomes in ophthalmology.

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NGP6

Using Major Vessel Position Measurements to Reduce OCT RNFL False Positives

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Abbreviations: OCT: optical coherence tomography; MVP: major vessel position; RNFL: retinal nerve fiber layer; cpRNFL: circumpapillary RNFL;
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Carlos G. De Moraes: Carl Zeiss Meditec, Inc. (C); Novartis (C); Heidelberg Engineering (R); Topcon (F); Galimedix (C); Perfuse Therapeutics (C); Ora Clinical, Inc. (E) Jeffrey M. Liebmann: Novartis (R), Alcon (C), Allergan (C), Thea (C), Carl Zeiss Meditech, (C); Ari Leshno: Santen (C);

Keywords: circumpapillary retinal nerve fiber layer thickness; major retinal vessels; optical coherence tomography

Purpose: To determine if retinal major vessel position (MVP) information can be used to adjust the circumpapillary retinal nerve fiber layer (cpRNFL) thickness in regions with false positives (FP) to better capture the major RNFL bundles and thus potentially increase specificity.

Methods: Optic coherence tomography (OCT) scans collected from 239 healthy individuals (239 eyes) were analyzed.1 MVP was determined using Heidelberg Eye Explorer (HEYEX, Heidelberg Engineering, GmBH, Germany) (Fig 1). We focused on scans that had a superior temporal (TS) or inferior temporal (TI) FP sector (i.e., a cpRNFL thickness below the 5th percentile) based on the commercial software measurements. See Fig. 2 (lower left) for 2 FPs at the <1st percentile and 1 FP at the <5th percentile. These sectors were compared to modified MVP-based sectors: the ST and IT MVP-adjusted cpRNFL sectoral thickness was calculated based on the mean cpRNFL thickness at the circle scan area 45° around the superior and inferior MVP, respectively (Fig 2). The remaining area between the ST and IT sectors was used to calculate the thickness of the temporal (T) sector.

Results: There were 34 FP temporal sectors (17 TS, 4 TI, and 13 T) in 24 scans. In all cases, the FP sector was thicker with the MVP-corrected measurement (Fig 2). The mean increase in thickness compared to the commercial measurements was 12.9±1.4um (mean ±SE) ($P<0.001$), 34.3±4.1µm ($P<0.001$), and 30.9±8.2µm ($P=0.032$) in the T, TS, and TI sectors respectively. In addition, the superior and inferior MVP in the eyes with FP was more nasal compared to the remaining 215 eyes in our cohort of healthy individuals (mean difference 6.9±2.0° and 8.9±2.3° respectively; both $P<0.001$).

Discussion: The MVP-adjusted method is a promising surrogate for identifying the location of the main RNFL bundles. It may help capture the thicker area of the cpRNFL in eyes with FP artifacts due to the shift of the RNFL bundle. This method provides improved estimations of the thickness of the major RNFL bundles, and thus, it should reduce the rate of FP and increase the specificity of these measurements.

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NGP7

The association between migraine and glaucoma: A retrospective cohort study

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Purpose: To explore the association between migraine and glaucoma, focusing on prevalence, onset, and glaucoma disease subtypes among migraine patients compared to non-migraine controls.

Methods: This retrospective cohort study analyzed electronic medical records from Clalit Health Services, covering southern Israel between 2000 and 2022. Adults diagnosed with migraine were compared to matched controls without migraine to evaluate glaucoma prevalence, age at diagnosis, and disease subtypes. The study also assessed key outcomes, including age at first ophthalmology visit, intraocular pressure measurements, and glaucoma severity. Differences between the groups were analyzed, and survival analysis was used to explore the timing of glaucoma diagnosis.

Results: Among 30,733 migraine patients and 53,025 controls, glaucoma prevalence was 3.3% vs. 2.5%, respectively (RR = 1.31, 95% CI: 1.15–1.48, $p<0.001$). Migraine patients presented earlier for ophthalmologic care, with first visits at 38.6 years, compared to 49.7 years in non-migraine patients ($p<0.001$), and first intraocular pressure measurements at 41.7 versus 54.0 years, respectively($p<0.001$). They had higher rates of normal-tension glaucoma (22.9% vs. 21.3%, $p=0.036$) and secondary glaucoma (15.7% vs. 11.7%, $p<0.001$) but comparable surgical intervention rates. Fewer glaucoma medications were required in migraine patients, suggesting milder disease progression. Kaplan-Meier survival analysis showed earlier glaucoma onset among migraine patients (log-rank test, $p<0.001$), possibly due to more frequent monitoring.

Conclusions: Migraine is associated with a higher risk of glaucoma and earlier engagement with ophthalmologic care. Shared vascular and neurodegenerative mechanisms may underlie this relationship, warranting further prospective studies to clarify causative pathways and refine management strategies.

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NGP8

Higher Risk and Earlier Onset Glaucoma in Cushing's Syndrome

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Purpose: Glaucoma incidence in patients with endogenous Cushing's syndrome (CS) has never been established. We aim to assess the risk for glaucoma among CS patients compared to controls and determine the age of disease onset.

Methods: A nationwide retrospective matched-cohort study of patients with endogenous CS diagnosed between 2000-2023. Patients with CS were matched in a 1:5 ratio, with a control group individually matched for age, sex, socioeconomic status, and body mass index. Main outcomes were the incidence of glaucoma and disease onset.

Results: A total of 609 patients [396 women (65%); mean age 48.1±17 years] were included in the CS group and 3018 controls. Follow-up duration was 14.6 years (IQR 9.8–20.2) for the study group. The etiology of hypercortisolism was divided into pituitary (259, 42.6%), adrenal (206, 33.8%), and unconfirmed etiology (144, 23.6%) patients. At baseline, 44 (7.2%) CS patients had a diagnosis of glaucoma, compared with 151 (5%) controls. The overall risk for glaucoma was 74% higher in patients with CS compared with matched controls (hazard ratio = 1.74, p=0.002). Patients with CS who developed glaucoma were younger (mean age of 62±14.7 years) than controls (mean ±SD age, 62±14.7 years), (p=0.02). The overall risk for glaucoma in CS was high for both patients in remission and patients with persistent hypercortisolism (p=0.048). Patients with active hypercortisolism experienced an earlier glaucoma onset (82.1±88.0 months).

Conclusions: Endogenous CS is associated with increased risk for glaucoma regardless of remission status and develops at a younger age compared with the general population.

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NGP9

Evaluating compliance in glaucoma treatment: big data analysis of prescription patterns and influencing factors

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Purpose To evaluate compliance with anti-glaucoma eye drop medications in a large health service cohort, focusing on prescription patterns and influencing factors.

Methods An initial cohort of all Maccabi Health Services patients with glaucoma diagnoses aged 18 years and older was assessed, resulting in 109,425 patients. Patients with less than 365 days between enrollment and the glaucoma diagnosis date or a diagnosis date after the follow-up end date were excluded. The final dataset included 79,752 patients with a minimum follow-up of 365 days after the diagnosis date.

Compliance with anti-glaucoma eye drop medications was assessed by comparing prescription fulfillment rates within predefined time gaps (1–3 months) and calculating cumulative percentages of fulfilled prescriptions. A linear regression was performed to evaluate the compliance rate while controlling for confounders.

Additionally, a Cox regression analysis was performed to assess the time to compliance failure, defined as an instance where a patient did not fill their anti-glaucoma eye drop prescription. The cumulative impact of compliance failure events

was assessed by counting the number of consecutive failures (1, 2, or 3 events) to comply with anti-glaucoma eye drop therapy.

Results Of the 79,752 glaucoma-included patients, 40,200 (50.4%) purchased at least one prescription during the follow-up period and were further analyzed. Most patients had validated more than 80% of their total given prescriptions. Patients ≥60 years and patients with comorbidities like cardiovascular or neurologic conditions exhibited increased compliance. Frequent IOP monitoring correlated with higher compliance, with patients undergoing two or more measurements per year achieving +10% higher prescription validation rates. Alterations in prescribed medications were also linked to improved compliance rates. Cox regression revealed higher hazard ratios for compliance failure among patients with reduced clinical monitoring or fewer followups. Survival analysis highlighted a progressive increase in noncompliance over time, with stricter prescription validation gaps resulting in higher failure incidences.

Conclusions Glaucoma patients exhibit high compliance with therapy, influenced by clinical and demographic factors. Frequent monitoring and personalized interventions, such as treatment adjustments and targeted follow-ups, may enhance compliance and improve long-term outcomes for glaucoma patients.

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NGP11

An Innovative Approach to Objective Measurement of Apathy Across the Cognitive Spectrum

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Objectives: Apathy, which predicts cognitive decline and is associated with Alzheimer's Disease, is typically measured subjectively but may benefit from objective methods.

Aims: Create objective tools to measure emotional and cognitive apathy.

Methods: We studied 82 middle-aged individuals with a family history of Alzheimer's. We used objective measures of gaze and autonomic nervous system (ANS) responses to emotional stimuli in a VR environment, and assessed cognitive effort through tasks. Subjective measures included the Apathy Motivation Index (AMI) and the Apathy Evaluation Scale (AES).

Results: Participants averaged 63.2 years old, with 52% women. AMI scores were below cutoffs for moderate and severe apathy. Higher self-reported apathy, especially low Social Motivation (SM), correlated with less variation in galvanic skin response and lower task engagement. Informant-reported apathy was linked to longer gaze fixation on aversive stimuli.

Conclusions: Objective measures of ANS and gaze reactions in VR, combined with cognitive effort tasks, may better capture subtle apathy than traditional questionnaires.

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OOP1

The Effect of Posterior Approach Ptosis Surgery vs. Anterior Approach Ptosis Surgery on Signs of Dry Eye Syndrome

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Purpose: To examine the effect of combined blepharoplasty and M· ller muscle-conjunctival resection (MMCR) compared to combined blepharoplasty and levator aponeurosis advancement (LAA) surgery on dry eye syndrome (DES).

Methods: This is a prospective, comparative case series. Two groups of patients participated in this study: the MMCR group included adult patients with dermatochalasis and ptosis that showed significant improvement after phenylephrine 10% instillation, and the LAA group consisted of adult patients with dermatochalasis and ptosis with good levator function without significant improvement after phenylephrine 10% instillation. The following parameters were compared for all patients before the procedure (baseline) and on postoperative day 90: MRD1, Schirmer test 2, tear break-up time (TBUT), fluorescein staining, and lissamine-green staining (LG).

Results: The patients in both groups (MMCR, LAA) had significant improvement in MRD1 postoperatively (Delata MRD1- 2.65, 1.82, paired t test, $P < 0.01$ and $P < 0.01$, respectively). There were significant decrease in the postoperative TBUT, Schirmer test, and increase in fluorescein staining following MMCR surgery compared with the preoperative values (paired t test, $P < 0.01$, $P = 0.01$, and $P < 0.01$, respectively), while the LAA patients had significant differences in their decrease in TBUT and increase in fluorescein staining, and LG results compared to their preoperative results (paired t test, $P < 0.01$, $P < 0.01$, and $P < 0.01$). The postoperative vs. preoperative change in the Schirmer test results was significantly higher in the MMCR group compared to the LAA group (ANOVA, $P < 0.01$).

Conclusions: Both MMCR and LAA surgical approaches cause an increase in signs of DES. This increase is attributed to both aqueous tear deficiency and evaporative dry eye (EDE) has shown in different tests, following MMCR surgery, and due to EDE alone after LAA surgery. Physicians need to be aware of the risk of DES and discuss it as a potential complication with patients prior to ptosis surgery. LAA may be considered a preferable option compared to MMCR in cases of severe ptosis and DES.

BACK TO PROGRAM

Congenital blepharoptosis: Comparison of two surgical approach results- final study results

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Purpose: Congenital blepharoptosis presents within the first year of life either in isolation or as a part of many different ocular or systemic disorders. Surgical repair is challenging, and recurrence necessitating more than one operation is not uncommon.

Methods: Retrospective clinical analysis comprised 92 children (age range 0;17) with eyelid ptosis, 28 underwent frontalis sling operation while 64 underwent levator resection. All patietns underwent surgical corrections at the Department of ophthalmology of HaEmek Medical Center, between 2006 and 2023, were reviewed. We evaluated Gender predilection, Ethnic origin, type of primary defect, degree of ptosis and recurrence rate according to the chosen surgical method.

Results: The median age of patients in the frontalis sling group was younger compared to those in the resection group (3 vs 6 years, respectively; P=0.073). The mean follow-up time (in months) for patients in the frontalis sling and levator resection groups was 24.44±28.32 and 17.98±23.79, respectively (P=0.164).There were no significant differences in the success or failure outcomes of the operations between the two groups. Amonge patietnts with MRD1 pre-operation is zero or plus, then the MRD1 post-operation is better in the levator resection group compared to the frontalis sling group ($MRD1$!"#$: 1.85 ±1.7 vs 0.89 ±1.04; $MRD1$%&'(: 2.79 ±1.18 vs 1.93 ±1.13) . Conversely, amonge patietns with MRD1 pre-operation is minus, then the frontalis sling group performs better than the levator resection group ($MRD1$)*+'(: 1.93 ±1.17 vs 1.61 ±1.19).

Conclusion: Ptosis rated as MR1 below 0 it is recommended to use the frontalis sling approach. for ptosis rated as MRD1 0 or above is recommended to use the levator resection approach.The above classification could be a substitute for the levator muscle function test which is difficult to perform and and its accuracy is questionable in the children's population.

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OOP3

Association between Acquired Punctal Stenosis and Ocular Surface Disease

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Purpose: To investigate the intricate relationship between punctal stenosis (PS) and ocular surface disease (OSD), with a focus on understanding the role of chronic inflammation in the development and progression of PS. The study also evaluates the eIectiveness of various treatment modalities in resolving symptoms and anatomical obstruction.

Methods: A retrospective cohort study was conducted at Sheba Medical Center, including 213 patients diagnosed with PS from 2012 to 2023. Data collected included demographic information, presenting symptoms, associated conditions, diagnostic details, treatment modalities, and outcomes. Ocular surface disease was identified based on clinical criteria, and tests such as tear breakup time (TBUT) and fluorescein staining were used to assess tear film stability and epithelial damage. Statistical analyses, including Fisher's exact test and Pearson chi-square, were performed using SPSS to evaluate associations between PS, OSD, and treatment outcomes.

Results: Among the 213 patients (mean age 59.1 years, 68% female), PS was predominantly bilateral (75.1%). Initial treatments included punctal dilation (51.2%), punctoplasty with Mini-Monoka stents (50.2%), and fluorometholone drops (23%). Complete symptom resolution was achieved in 34.3%, partial in 24.9%, and no improvement in 30.5%. Punctoplasty with Mini-Monoka stents and subsequent fluorometholone treatment were significantly associated with symptom resolution ($P<0.001$). OSD was identified in 35.2% of the cohort, with conjunctival irritation being the most common symptom. However, OSD symptoms did not significantly correlate with symptom resolution or anatomical outcomes, except for conjunctival irritation post-treatment, which was linked to poorer outcomes ($P=0.03$).

Conclusions: This study underscores the complex bidirectional relationship between PS and OSD, with chronic inflammation playing a pivotal role. The findings highlight the need for a comprehensive, individualized approach in managing PS, addressing both anatomical and inflammatory factors. Punctoplasty with Mini-Monoka stents emerged as an eIective treatment strategy, emphasizing the importance of tailored interventions for optimal patient outcomes. Further research is warranted to elucidate the underlying mechanisms and develop targeted therapies for PS and associated ocular surface conditions.

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OOP4

High-Risk Histopathological Features Following Primary Enucleation in Bilateral Retinoblastoma

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Purpose: To evaluate the presence and impact of high-risk histological features (HRHF) on outcomes in children with bilateral retinoblastoma undergoing upfront unilateral enucleation. While the prognostic significance of certain histopathological features (HRHP) is well-established in unilateral retinoblastoma, their relevance in bilateral cases remains understudied.

Methods: This study involved children diagnosed with bilateral retinoblastoma who underwent upfront enucleation between 2011 and 2020. Those presenting with extraocular involvement were excluded. Data were obtained from 21 centers across 12 countries, including demographic, clinical, and histopathological information. HRHF were defined as the presence of massive choroidal invasion and/or retrolaminar optic nerve invasion. The primary outcomes assessed were metastasis and mortality.

Results: A total of 211 children with bilateral retinoblastoma underwent upfront unilateral enucleation. The average age at diagnosis was 18.6 ± 17.8 months, with 105 (49.8%) females. The mean time from presentation to enucleation was 1.5 ± 5.8 months, and the average follow-up duration was 41.1 ± 33.8 months. Among these children, 89 (42.2%) exhibited at least one HRHF, with 63 (29.9%) having massive choroidal invasion and 52 (24.6%) showing retrolaminar optic nerve invasion. Among children with HRHF, 8/79 (10.1%) who received adjuvant treatment developed metastases compared to

1/10 (10.0%) without adjuvant treatment ($p = 1.000$), and 10/79 (12.7%) vs. 3/10 (30.0%) died ($p = 0.159$).

Among children without HRHF, 3/69 (4.3%) who received adjuvant treatment developed metastases compared to 3/53 (5.7%) without adjuvant treatment ($p = 1.000$), and 3/69 (4.3%) vs. 4/53 (7.5%) died ($p = 0.466$).

Conclusion: In children with bilateral retinoblastoma undergoing upfront unilateral enucleation, HRHF were present in 42.2% of cases. Irrespective of the status of the contralateral eye, adjuvant treatment was associated with a non-statistically significant trend toward lower mortality rates among children with HRHF (12.7% vs. 30.0%, $p = 0.159$). Among children without HRHF, outcomes were similar regardless of adjuvant treatment. The role of HRHF in bilateral retinoblastoma requires further investigation.

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OOP5

Sebaceous Carcinoma of the Eyelid Metastasis Showing Small Cell Carcinoma-Like Features: a Case Report

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Purpose: To report a rare case of sebaceous cell carcinoma (SC) of the eyelid with lymph node metastasis exhibiting small-cell carcinoma-like features, a phenomenon not previously described.

Methods: A 71-year-old male presented with a right upper eyelid lesion, initially diagnosed as low-grade SC. Surgical excision with clear margins and reconstruction was performed. Recurrence led to further excision and eventual detection of a cervical lymph node metastasis with high-grade carcinoma with neuroendocrine features.

Results: Immunohistochemical analysis confirmed metastasis resembling small-cell carcinoma. PET-CT and MRI excluded primary lung malignancy. The patient received carboplatin and etoposide chemotherapy.

Conclusion: SC can mimic benign lesions and exhibit aggressive metastatic behavior despite early detection and surgical excision, underscoring the need for vigilant follow-up and multimodal management.

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OOP7

Association Between Blinking and Ocular Surface Disturbances: A Prospective Comparative Analysis

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Purpose: To explore possible association between blinking pattern and dry eye.

Methods: A single center, cross sectional study. Two groups of patients participated in this study: patients diagnosed with dry eye syndrome vs. patients without dry eye diagnosis. The voluntary blink was recorded using a smart-phone high-speed camera, and the videos were blindly analyzed by a senior oculoplastic surgeon (GBS) for brow lift, blepharospasm, imbrication, lagophthalmos, margin entropion, retraction, lid separation delay, lash ptosis, dermatochalasis, and an increase in tear lake. Patients were assessed for dry eye using the ocular surface disease index score (OSDI), tear break-up time (TBUT), Schirmer's test, fluorescein and lissamine green stains. For each patient only the right eye was included to avoid inter eye correlation.

Results: 54 patients were included, with 27 in each group. The mean age was 65.3 years (range 26-87), and 31 (57%) were females. The mean visual acuity was 20/26. Dry eye patients were significantly younger (61 vs. 70 years, P=0.03). Additionally, they had a shorter tear breakup time (7 vs. 9 seconds), a lower Schirmer score (9 vs. 14mm), and increased fluorescein staining (P<=0.05 for all). Lissamine green staining was similar in both groups. The female gender was more prevalent in the dry eye group (78% vs. 37%, P=0.002, chi-square). Blepharitis and MGD were both associated with the diagnosis of dry eye. Initially, none of the blinking characteristics were more prevalent in the dry eye group. However, we noticed that 10 patients in the control group had OSDI scores similar to those of dry eye patients. Therefore, the data were reanalyzed according to OSDI score. Patients with moderate to severe dry eye (OSDI >= 23) experienced more eyelid margin rotation during blinking (P=0.037, chi-square).

Conclusion: Patients with moderate to severe dry eye, as indicated by their OSDI score, showed more eyelid margin rotation during blinking. This, along with the increased prevalence of blepharitis and MGD, may suggest potential surgical treatment options to address the ocular surface disturbances in dry eye patients.

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OOP8

Ophthalmologic Abnormalities in Cleft Lip and Palate

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Purpose: The failure of fusion of facial processes that causes cleft lip and palate (CLP) may also result in ocular abnormalities, given their proximity and simultaneous embryonic development. The purpose of this study was to examine ophthalmologic findings of patients with CLP.

Methods: We performed a retrospective review of patients diagnosed with CLP who underwent ophthalmologic examination from 2009 to 2020 at the Children's Hospital of Philadelphia. Demographic information, ophthalmologic findings, genetic data, and cleft characteristics were collected. Primary outcomes were the type and incidence of ophthalmic disorders and their associations with CLP anatomical and syndromic/genetic risk factors.

Results: Among 687 included patients, the most common ocular disorders were refractive errors (41.6%), strabismus (30.9%), and nasolacrimal duct obstruction (10.5%). The incidence of nasolacrimal duct obstruction was highest in bilateral cleft lip (22.7%), followed by unilateral cleft lip (10.2%) and no cleft lip (8.6%). Subjects with an associated syndrome were more likely

to have strabismus, refractive error, vitreoretinal pathologies, nerve pathology, lagophthalmos, and chorioretinal coloboma. Additionally, patients with Pierre Robin sequence were more likely to have refractive error and vitreoretinal pathologies.

Conclusions: This study demonstrates an association between cleft severity and nasolacrimal duct obstruction. While our methodology precludes assignation of causality, this is possibly due to the disruption of fusion of facial processes that occurs in cleft lip and/or palate, which may also impact the development of the orbit and ocular adnexa during embryogenesis. Heightened awareness of ocular pathology may advance multidisciplinary care for patients with CLP.

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OOP9

Twenty years of Chalazion ,Big Data Analysis from the CLALIT HMO

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Background: Chalazion is a frequent eyelid pathology. Often, the initial approach for treating chalazion is conservative. In chronic or resistant cases, invasive intervention may be warranted using surgical incision and drainage or intralesional corticosteroid injection.

Purpose: This study aims to identify big-data epidemiological trends of chalazia, to evaluate the clinical outcomes and resolution rates treated conservatively, or surgically.

Methods: An Electronic Medical Record (EMR) retrospective cohort study was conducted using the Clalit Health Maintenance Organization's database, encompassing demographic information, medical history, registered treatment, medical procedures, and outcomes.

Results: Our analysis identified 611,993 chalazion cases diagnosed in 412,365 patients between January 2003 and December 2022. Altogether 56,840 chalazion procedures were performed, indicating 9.3% of all cases requiring invasive intervention. Invasive intervention was more likely to be required in older age groups ($P<0.0001$), with 1.8% (1,821 out of 102,150) of cases under 18 requiring invasive intervention compared to 8.1% (21,393 out of 263,524) in the 18–45-year-old age group and 13.7% in the group of patients older than 45 (33,626 out of 246,319).

A high positive correlation was found between the incidence of chalazion and mean monthly temperature ($r=0.71$, $p<0.001$). A temperature of 21 degrees was found to be a cutoff for monthly average temperature for a higher prevalence of chalazia (specificity=0.91, sensitivity=0.79, AUC=0.90). As for the efficacy of conservative management, the rate of patients requiring an invasive intervention after using topical medications was 6% (9% for a combination ointment of neomycin/polymyxin B/dexamethasone, 5% for Chloramphenicol, 6% for Tobramycin and 4% for Azithromycin), and 7% for those treated conservatively with no medically active products other than lubricating drops.

Conclusions: The study emphasizes the effectiveness of conservative treatment in managing chalazion. The influence of age and seasonal variations on chalazion's prevalence and management outcomes highlights environmental and demographic factors in its etiology. These insights may help ophthalmologists optimize chalazion treatment strategies and highlight the need for further research into the factors affecting treatment outcomes.

BACK TO PROGRAM

R1

Diet Habits in Israeli Age-Related Macular Degeneration Patients

Tzippora Greenberg

Purpose : Age-related macular degeneration (AMD) is a leading cause of vision loss, influenced by genetic and environmental factors such as diet. While dietary influences on the risk for developing AMD have been studied, limited data exists on Israeli AMD patients. This study aims to investigate the relationship between AMD and dietary patterns in Israel .

Methods : We collected dietary data from 103 AMD patients using the Israeli Ministry of Health's Food Frequency Questionnaire (FFQ), which assesses the frequency of consumption of over 100 food groups. Nutrient intake for 26 key nutrients was assessed using the NutRatio software and categorized as normal, high, or low based on age- and gender-specific Dietary Reference Intake (DRI) recommendations, specifically the Estimated Average Requirement (EAR). Comparisons were made against the Mabat Zahav survey (2014–2015), a national study including 1,705 individuals aged ≥65. Statistical differences were evaluated using Fisher's exact test. Adherence to the Mediterranean diet was assessed using the Israeli Mediterranean Diet Adherence Score (I-MEDAS), a scoring system ranging from 0 to 17. I-MEDAS scores were compared to the Hadera District Study (HDS), which assessed adherence among 1,092 Israelis aged 25–74 .

Results : After excluding four participants with incomplete responses (<75% completion), data from 99 patients were analyzed. Israeli AMD patients showed low intake of key nutrients, including vitamin A (low in 28 out of 99 patients), vitamin D (89 patients), and zinc (50 patients). Comparisons with the Mabat Zahav dataset indicated that compared to the general population, AMD patients had higher vitamin A intake ($p < 0.00001$), higher zinc intake ($p= 0.0006$), with no significant difference for vitamin D ($p = 0.3184$). The median I-MEDAS score for AMD patients was 9, comparable to the national median of 8 reported in the HDS study described above. This score represents an average adherence to Mediterranean diet.

Conclusions :
AMD patients demonstrated low age-adjusted nutrient intake according to DRI recommendations, yet higher intake of certain nutrients, such as vitamin A, compared to the general Israeli population described in the Mabat Zahav survey. Adherence to the Mediterranean diet was similar to the Israeli population, as reported in the HDS. Future work will include cataract patients as controls to further explore dietary patterns and AMD risk, and consider the potential benefits of dietary modifications in Israeli AMD patients .

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R2

Delivery of sub Retinal Soft Mono Layer Retinal Pigment Epithelium Implant

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Purpose: Clinical studies suggest that RPE transplant may delay geographic atrophy progression in AMD patients. Our purpose is to examine a novel device for a novel soft monolayer RPE sheet implantation to the subretinal space in a domestic pig in an in vivo study

Methods: A novel RPE implant comprised of natural biocompatible scaffold with a printed monolayer of polygonal RPE cells was developed. Implants demonstrate high viability, density, morphology, identity to RPE markers such as PMEL 17 and potency by measuring PEDF secretion. For safe delivery of the RPE implant into the subretinal space a novel delivery device has been developed A patented safe folding of the RPE implant into the device allows to transplant a 2 x 4 mm RPE implant through a standard 20 G trocar. In order to insert the RPE implant into the subretinal space a 25 G pars plana vitrectomy performed followed by a retinal bleb formation using a 41 G canula A 25 G trocar replaced by a 20 G trocar, the device is inserted into the subretinal space and the 2 x 4 mm RPE implant is released, followed by flattening the retina. Animals were followed for 3 months, during which OCT imaging and clinical examination took place.

Results: A total of six eyes of six female domestic pigs were included in this prospective study. Four study eyes underwent subretinal RPE transplant (two with systemic and topical immunosuppression and two with short systemic and full topical immunosuppression) and two control eyes which underwent the procedure without RPE transplant. At the end of the follow up period, all eyes were without inflammation signs, retinas were attached with normal neuroretinal layers and without evidence of proliferative vitro retinopathy, intraretinal nor subretinal fluid nor photoreceptor atrophy on OCT. Histopathological examination demonstrated the presence of human RPE cell monolayer, with no immune cell activity

Conclusion: A subretinal transplant of a novel printed RPE sheet implant with the aid of a novel 20 G delivery device may be a safe method for RPE transplantation

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R3

Artificial retinal implant composed of 3D scaffold integrated with photoreceptors and retinal pigment epithelium cells

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Purpose Retinal degeneration, including conditions such as Age-related Macular Degeneration (AMD) and Retinitis Pigmentosa (RP), leads to irreversible vision loss due to the damage or loss of retinal pigment epithelium (RPE) cells, which in turn causes photoreceptor (PR) cell degeneration. Existing treatments, including gene therapy and pharmacotherapy, can slow the progression of these diseases but are limited in their ability to fully restore vision. Cell replacement is a promising therapy, some degree of vision restoration following the sub-retinal transplantation of photoreceptors or their supporting cells - retinal pigment epithelium (RPE), has been demonstrated, but restoring only one layer, whether PR or RPE, is insufficient to fully recover vision. This research aims to go beyond conventional cell replacement by developing an artificial retina that mimics the natural retinal environment.

Methods We developed a combined RPE-PR retinal implant. RPE cells provide essential support and maintenance for PR cells, promoting their survival and functionality. Cells were seeded onto a scaffold in two layers, mimicking their natural arrangement in the retina, and embedded in a collagen matrix that mimics the extracellular matrix (ECM). The first layer consisted of RPE cells, either human cell line ARPE-19 or RPE cells isolated from mice. The second layer consisted of photoreceptor precursors (PRP) isolated from GFP-Nrl transgenic mice, enabling easy tracking through green fluorescence. The scaffolds were fabricated from either poly(glycerol sebacate) (PGS), a degradable material, or IP-S, a non-degradable material printed using the two-photon Nanoscribe device.

Results We observed that the seeded cells adhered to the scaffolds, entered the microwell structures, and formed a layered structure. The collagen hydrogel provided a biocompatible environment, promoting cell survival and maturation. Overall, we achieved a bilayered retinal implant. The device was implanted into the sub-retinal space of a blind rat model.

Conclusions These preliminary results demonstrate the feasibility of developing a functional retinal implant combining RPE and PR cells. The scaffold design provides a supportive environment for cell integration and survival, laying the groundwork for future advancements in biological implants for vision restoration in patients with retinal degeneration.

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R4

Small heat shock superfamily of proteins as a retinal defense mechanism against pathogenic amyloid beta

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Purpose: Amyloid beta (Aβ), a neurotoxic peptide group found in drusen, has been implicated in the complex pathogenesis of age-related macular degeneration (AMD). We previously demonstrated that adipose tissue-derived mesenchymal stem cell exosomes (AT-MSC-Exosomes), renowned for their anti-inflammatory and immunomodulatory properties, provide robust protection against Aβ-mediated retinotoxicity *in vivo* and *in vitro.* This study explored the molecular mechanisms underlying the exosome-mediated preservation of retinal function observed *in vivo*.

Methods: Wild-type rats (n=3) received intravitreal injections of AT-MSC-derived exosomes (10µl) in the experimental eye, while the control eye received vehicle alone, two days before bilateral Aβ administration. Electroretinography was conducted to confirm the protective effects. Six days post-Aβ injection, rats were sacrificed, eyes were enucleated, and neurosensory retinas were extracted. Mass spectrometry was performed using a Q Executive HFX mass spectrometer, with data analyzed through MaxQuant software. Annotation enrichment analysis was generated via the STRING database. Proteomic findings were validated using immunofluorescence of matching retinal sections. Fluorescent labelling of the exosomes confirmed their retinal uptake.

Results: In the proteomic analysis, a total of 3940 proteins were successfully identified and quantified, with 32 defined as upregulated and 21 downregulated in eyes treated with unopposed Aβ compared to their fellow eyes treated with AT-MSC-exosomes prior to Aβ exposure. Protein interaction analysis revealed that the most enriched pathway was "Lens development in camera-type eye" GOBP0002088), with strength 1.84 and P-Value 1.20E- 14. Of the 12 proteins annotated with this term, eleven dysregulated proteins belonged to the α-, β-, and γ- crystallin family. Immunostaining targeting the B-subunit confirmed the modulation of α-crystallin (αB-crystallin) expression in retinal astrocytes by the AT-MSCexosomes.

Conclusion: The increased expression of crystallins, known as the heat-shock response, indicated the activation of this intrinsic retinal defense mechanism against amyloid fibrils. In contrast, retinas treated with AT-MSC-exosomes did not exhibit this protective response, suggesting the exosomes' potential to mitigate amyloid-induced stress. The specific localization of αB-crystallin in retinal astrocytes reveals their activated state and potential migratory response to the amyloid insult. These findings underscore the complex interplay between amyloid pathology and retinal neurodegeneration and highlight the modulation of the heat-shock response as a potential target for amyloid-mediated retinal degeneration.

BACK TO PROGRAM

R5

Single cell study of hypothermic effect of retinal survival during ischemia

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Purpose: Retinal ischemia is associated with a rapid decline in function eventually leading to irreversible retinal damage. Here, we studied the effect of ischemia and hypothermia on retinal function while dissecting the effect on the various components of the retinal circuitry.

Methods: Using an isolated retina of a wild-type rat we investigated the effect of hypothermia on ischemia damage (15-240min at 21 or 37°C). Ischemia was induced at the isolated retina level, where the supply of oxygenated medium was switched on and off; oxygen content was found to be 13.5 mg/L and 8.7mg/L respectively. Next, several electrophysiological response features induced by 1sec flashes were investigated, namely: the number of active RGCs, the RGCs firing rate, response latency, and the amplitude of the various components of the micro electroretinogram.

Results: Our experiments revealed that the percentage of cells whose response was restored following an ischemia of 15min at 37C period was ~40% decreasing to ~20% for 60min and to almost 0% for 120min. Importantly, hypothermia to 21°C resulted in improved survival with an observed resuscitation of 20% of the cells following 120min ischemia Furthermore, it is worth noting that a relative preservation of the firing rate for cells who survived ischemia (even up to 2hrs), was evident. A similar protective effect on ERG signals was observed where a temperature decrease resulted in preserved ERG amplitudes to only 50% of their baseline values even following a prolonged ischemia of 120mins. Moreover, a high correlation between the firing rate and ERG amplitude was found ($R2>0.8$, $P<0.0001$).

Conclusion: Our observations suggest that the lower temperature may provide a neuroprotective effect, allowing the cells to preserve their functionality and recover more efficiently after the ischemic insult. These results form the basis for our hypothesis, that cooling tissue lower than 21°C will yield an even more prominent neuroprotective effect on retina tissue in cases of prolonged ischemia.

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R6

Photoreceptor to Retinal Pigment Epithelium Atrophy Ratio and Longitudinal Atrophy Growth in Age-Related Macular Degeneration

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Purpose: To evaluate how the baseline ratio of the photoreceptor (PR) layer atrophy, to the retinal pigment epithelium (RPE) layer atrophy relates to the progression of atrophy in these layers over time in eyes with geographic atrophy (GA) secondary to agerelated macular degeneration (AMD).

Methods: Macular Optical Coherence Tomography (OCT; Spectralis, Heidelberg Engineering) scans from 146 patients with AMD (287 eyes) were analyzed using automated segmentation and annotation performed with the RetinAI OCT Segmentation Discovery tool (Ikerian AG). Atrophy measurements were obtained for each eye at baseline and for all available follow-up visits (mean ☐} SD number of visits: 50 ☐} 71; mean ☐} SD interval between visits: 59 ☐} 90 days). All included eyes had measurable atrophy areas at baseline. The relationship between the baseline PR/RPE atrophy area ratio and the longitudinal progression rates of PR and RPE atrophy was assessed using Spearman's correlation test. Atrophy expansion rates were calculated as the change in atrophy area (mm2/year), averaged across all visits for each eye.

Results: The mean age ☐} SD of participants was 79.39 years ☐} 9.06, with 64 males and 82 females. Fifty-seven participants (106 eyes) had macular neovascularization. The mean atrophy area at baseline of the combined Ellipsoid Zone, Outer PR Segment, and Interdigitation Zone layers was 4.09 mm2 ☐} 6.51, while the mean atrophy area at baseline of the RPE layer was 2.60 mm2 ☐} 5.04. The baseline PR/RPE atrophy ratio had a mean of 3.73 ☐} 10.91. A positive correlation was observed between the baseline PR/RPE atrophy ratio and the longitudinal atrophy progression in both the PR layer (Spearman's rho = 0.168, P = 0.004) and the RPE layer (Spearman's rho = 0.229, P = 8.7×10^{-5}).

Conclusions: This study highlights an association between the PR/RPE atrophy ratio at baseline and the longitudinal progression of atrophy in these layers respectively. These findings suggest that structural biomarkers derived from OCT at baseline can potentially provide valuable insights into GA progression, aiding in improved risk stratification and disease management strategies.

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P1

The Objective Scatter Index (OSI) and Cataract Assessment in the Pediatric Population

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Purpose: Pediatric cataract should be evaluated and addressed promptly because of the risk of amblyopia. However, young children are often unable to cooperate with visual function testing, and even the slit lamp examination is sometimes challenging. The Objective Scatter Index (OSI) was developed to objectively assess the optical quality of the eye, using the double-pass technique. Visual acuity, contrast sensetivity and visual function index (VF-14) are correlated with OSI, and OSI appears to be the most effective parameter for decision making in cataract surgery in adults. The purpose of this study was to evaluate the real life applicability of the OSI for the management of pediatric cataract.

Methods: We collected all OSI measurments with the HDA Analyzer and failed attempts to measure OSI in patients 0-16 years of age from 2021-2024, along with additional information from the ERM, including age, age at surgery, type of cataract and visual acuity. We used the Pearson correlation to assess the correlation between OSI and visual acuity.

Results: Sixty two children (F:M 38:24) aged 1 month to 13 years of age (median 7 years) were examined by the HDA Analyzer. Of those, 15 younger patients (median 15 months of age) had unsuccessful examinations. Eighteen children had follow-up examination, 8 before surgery and 11 following surgery. Bilateral examinations were successfully performed in 34 children, and the total number of examinations was 176. All children underwent a complete ocular exam, and had an anterior segment pathology. The most common pathology was cataract. Twenty patients had posterior sub capsular catarcts (PSC), 14 had nuclear cataracts and 5 had traumatic cataracts. LogMAR visual acuity and OSI were found to be moderately positively correlated (p <0.00001) for all examination that had a full record. All eyes (10) who had full records before and after surgery had both significantly improved visual acuity (average improvement 0.4· 0.26 LogMAR) and significantly improved OSI (average improvement 5.04· 2.4).

Conclusions:OSI is an objective measure for the optical disturbance caused by cataract and can be used in the decision to operate as well as a method to follow unoperated cataracts in children.

BACK TO PROGRAM

P2

Clinical findings, multimodal imaging and electrophysiology of pediatric patients with unilateral perifoveal annular lesion

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Purpose: Unilateral perifoveal lesions, such as torpedo maculopathy, have been characterized thoroughly so clinicians can differentiate benign and stationary lesions from sight threatening and progressive perifoveal findings. Herein we characterize a newly defined perifoveal annular lesion in 6 pediatric patients.

Methods: This retrospective case series was conducted at Schneider Children's Medical Center. Data gathered from 2013 to 2024, from patients with identified annular, unilateral macular lesions and documented office retinal examinations who completed retinal imaging. These consecutive patients subsequently underwent follow-up. Detailed imaging and ocular electrophysiologic data information were analyzed for the patients.

Results: Six patients were diagnosed incidentally with an asymptomatic, flat, hypopigmented, annular lesion, with well-defined margins that was typically located temporal to the macula. Visual acuity was 6/6 in all patients. The lesion's size was ~1.5 disc diameter, it was easily noticed as hyper-reflectant lesion in infra-red (IR) imaging and hyperautofluorescent in fundus autofluoresence imaging. Optical coherence tomography (OCT) cross section through the lesion showed only minimal retinal pigment epithelium (RPE) irregularity in some patients. Full field electroretinography (ERG) and multifocal ERG were normal.

Conclusions: In this case series study of newly defined imaging-based macular lesion, all patients had excellent visual acuity in both eyes. No progression was noted in size of lesion or OCT images during follow up. These findings support a stationary benign course, at least in childhood and teenage ages; thus, we recommend follow up with periodic retinal imaging, however there is no need for the use of sedation if such an assessment.

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Prospective Open Label Randomized Controlled Clinical Study Evaluating the Efficacy of Perceptual Learning among Patients with Congenital Nystagmus

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Conflict of Interest: The authors declare that they have no conflicts of interest.

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Background: There are limited treatment options to improve vision in patients with congenital nystagmus. We examined the use of repeated visual stimulation with Gabor Patches to achieve that goal.

Methods: In a prospective randomized (3:1) controlled open label study, patients aged 9-55 years with congenital nystagmus and best corrected visual acuity (BCVA) between 20/40–20/200 were included. The treatment group underwent visual stimulation for four months, controls were followed without treatment. BCVA, contrast sensitivity, and stereoacuity were assessed.

Results: 26 patients were treated and 10 served as control. Mean age was 22.47±12 years. 13/26 (50%) of treatment subjects achieved driving license BCVA (20/40) vs 1/10 (10%) of controls. Distance treated BCVA improved by 0.11±0.06 logMAR (one Snellen line) compared with 0.013±0.06 logMAR in controls (p=0.001). Near BCVA improved by 0.20±0.18 logMAR (2 Snellen lines) compared with 0.06±0.06 logMAR in controls (p=0.020). Mean stereoacuity and contrast sensitivity improved by 801±730’ and 292±391% in the study group as opposed to 246±376’ and 152±67% in controls respectively (p=0.031; p=0.157).

Conclusions: Visual perceptual learning using Gabor Patches resulted in a significant improvement in near and distance visual acuity, which allowed 50% of patients to achieve a driving license BCVA. A corresponding improvement in stereopsis and contrast sensitivity was noted. Further studies will identify which patients will benefit most from this treatment.

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Surgical Outcomes of Patients with Mild to Moderate Exodeviation with and without Combined Superior Oblique Palsy

Edward Barayev, Dahlia Palevski, Miriam Ehrenberg, Gad Dotan, Ronit Friling, Uri Elbaz, Amir Sternfeld

Introduction: Superior oblique palsy (SOP) is the most common vertical strabismus. Primarily characterized by vertical misalignment, most cases of SOP also include horizontal strabismus, mostly exotropia (XT).[1] While the exodeviation of SOP can sometimes be comparable to that of intermittent exotropia (IXT), surgical outcomes vary widely due to different etiologies.[2] This study aimed to compare the surgical outcomes of exodeviation in pediatric patients with combined SOP and exodeviation to those with IXT without a vertical component.

Methods: A retrospective analysis covered patients undergoing strabismus surgery from January 2010 to September 2022. The SOP+XT group, comprising patients with both SOP and XT, was matched with the IXT control group. Surgical success was defined by residual horizontal strabismus ≤10PD or residual vertical deviation ≤4PD, and lack of additional surgery for residual or consecutive strabismus.

Results: Among 45 eligible patients, 17 were in the SOP+XT group and 28 in the IXT group. At follow-up, SOP+XT patients exhibited significantly lower horizontal measurements at distance (1.5±2.3PD vs. 5.8±5.8PD, p=0.01) and near (1.3±2.1PD vs. 6.8±6.7PD, p=0.001). Additional surgery rates were lower in the SOP+XT group (5.9% vs. 21.4%). No SOP+XT patient had residual exotropia exceeding 10PD, whereas 21.4% in the IXT group did. The success rate was higher in the SOP+XT group (94.1% vs. 57.1%, p=0.008).

Conclusion: SOP+XT patients demonstrated superior surgical outcomes for exodeviation compared to those with isolated IXT, emphasizing the distinction between these groups and the potential impact on surgical expectations. These findings highlight the need for extended follow-up in IXT cases .

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Evaluation of the G-ROP Model for Retinopathy of Prematurity in the Israeli Preterm Population: A Multicenter Prospective Study

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Purpose: To evaluate the predictive performance of the G-ROP screening model for identifying infants at risk of developing retinopathy of prematurity (ROP) in a multicenter cohort of Israeli preterm infants.

Methods: This prospective multicenter study included 116 preterm infants from three hospitals: Ichilov (n=20), Carmel (n=42), and Shamir (n=54). Of these, 93 infants (80.2%) had complete clinical data. The G-ROP model incorporates six criteria—including GA <28 weeks, birth weight ≤1050 g, three weight gain thresholds and the presence of hydrocephalus—was applied to predict ROP. Receiver operating characteristic (ROC) analysis was performed to assess the model's predictive performance.

Results: Among 93 infants, 21 (22.6%) developed ROP. The G-ROP model achieved an area under the curve (AUC) of 0.629 (p=0.073, 95% CI: 0.507–0.751). The model identified 95.2% of ROP cases, though one infant who developed ROP did not meet any of the G-ROP screening criteria. Alternative analyses incorporating adjusted GA thresholds (≤29 weeks) and birth weight showed improved predictive performance, with an AUC of 0.681 (p=0.012).

Conclusions: The G-ROP model demonstrated moderate predictive performance in this Israeli cohort. While it identified most infants at risk for ROP, one infant who developed type I ROP fell outside its screening criteria. The findings highlight the importance of validating and potentially refining screening tools to ensure their accuracy in diverse populations.

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G1

A homozygous frameshift mutation in KHDC4 causes syndromic Leber congenital amaurosis in Arab Christian patients

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Purpose: yndromic diseases constitute about 30% of the inherited retinal diseases (IRDs). In the current research, we aim to study the clinical and genetic aspects of two siblings with Leber congenital amaurosis (LCA) combined with additional extra-ocular symptoms and investigate the novel gene identified using an in-vitro and in-vivo zebrafish knockout model.

Methods: SNP array and whole-exome sequencing were performed on two sisters of Arab Christian family (MOL0111). Variant segregation analysis was performed using Sanger sequencing. Two KHDC4 knockout zebrafish models (null mutations in exons 3 and 12) were established using CRISPR/Cas9. Sanger sequencing and gel acrylamide electrophoresis were used for genotyping. Cloning, site-directed mutagenesis, confocal microscopy, and minigene alternative splicing assay were used to study the pathogenicity of the identified variant. Optokinetic response (OKR) system was designed for visual acuity testing.

Results: Two sisters of Arab Christian origin suffering from typical LCA, mental retardation, and facial dysmorphism were recruited for the study. Electroretinography (ERG) was performed on both sisters in early childhood, demonstrating extinct photopic and scotopic responses. SNP array analysis revealed a homozygous region on chromosome 1 (chr1:114533436-167441820) in both sisters. Exome sequencing was conducted on both sisters and their father, but no pathogenic variants were identified in known IRD-associated genes. Further analysis revealed a homozygous deletion (c.1535_1538del, p.Lys512Argfs*8) in a novel gene KHDC4 (KIAA0907). Immunohistochemistry on human retinal sections showed the expression of KHDC4 in the outer nuclear layer and inner segment of the photoreceptor (Figure 1). Overexpression of the KHDC4:(p.Lys512Argfs8) mutant showed abnormal localization of the protein in the nucleus. Further minigene alternative splice assays confirmed the loss of KHDC4 function due to the (p.Lys512Argfs*8) variant. Evaluation of the retinal function and structure of the knockout zebrafish are underway, using a special optokinetic response (OKR) system as well as a functional analysis of the novel protein.

Conclusions : This is the first study linking a KHDC4 mutation as a causative gene for syndromic LCA in humans validated by zebrafish model.

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G2

Optimization of gRNA for Enhanced RNA Editing of Mutations Causing Inherited Retinal Diseases

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Purpose: Adenosine to inosine (A-to-I) RNA editing is a post-transcriptional process by which adenosines are selectively converted to inosines in double-stranded RNA (dsRNA) substrates by the adenosine deaminase acting on RNA (ADAR) enzymes. The two major ADAR genes, ADAR1 and ADAR2, are ubiquitously expressed, and could be harnessed for site-directed RNA editing as a novel genetic therapeutic approach. To allow ADAR recruitment, a guide RNA (gRNA) that is complementary to the target sequence, around the mutation, needs / must be to be designed aiming to induce the formation of dsRNA. The purpose of this study is to identify the most effective and safe gRNAs for RNA editing of mutations that cause inherited retinal diseases (IRDs).

Methods: We used a cellular reporter system involved the PZ-donor plasmid. Three different plasmids were designed: the first contained the target sequence only, the second contained the gRNA only, and the third in which we clone the gene fragment upstream to a loop structure that includes a barcode and the gRNA in cis with the target sequence. The plasmids were transfected into ADAR1/2-overexpressing HeLa cells. Editing levels were measured through Sanger and next-generation sequencing (NGS).

Results: Co-transfection of two plasmids: the first containing the target sequence and the second containing the gRNA resulted in up to 40% editing of the target. The stem-loop structure demonstrated higher editing levels (up to 80%) on the *GUCY2D* c.2513G>A autosomal dominant mutation. Using this system, we also tested a library of 235 different gRNAs attached to barcodes in a single experiment. We observed that certain modifications enhanced editing levels compared to the conventional gRNA (up to 60% improvement). Off-target analysis of NGS results revealed 17 off-target sites in the *GUCY2D* sequence, with a maximum editing level of 50% compared to the target base editing level. In general, higher on-target editing levels were correlated with higher off-target editing levels, suggesting that mismatches in gRNAs are necessary to reduce off-target effects before in vivo experimentation.

Conclusion: RNA editing using the endogenous ADAR enzymes could provide a promising genetic therapeutic approach for treating IRDs. Future research will focus on analyzing the results from the gRNA library experiments to determine if specific mismatches can increase on-target editing levels without increasing, or even while decreasing, off-target effects. The RStudio code developed for this study enables simultaneous analysis of multiple experiments, serving as a valuable tool for evaluating the success of RNA editing.

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G3

Effect of Systemic Immune Status on Disease Progression in the *Fam161a* Knock-out Mouse Model of Retinitis Pigmentosa

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Purpose: Inherited retinal diseases (IRDs) are primarily driven by genetic mutations, but additional factors such as the immune system may also affect disease progression. We investigated the impact of systemic immune status on the course of disease in a novel immunodeficient NSG-*Fam161a* KO mouse model of retinitis pigmentosa (RP).

Methods: Visual and retinal function as well as retinal structure were evaluated in *Fam161a* KO and NSG-*Fam161a* KO mice at 4, 6, 12, 18 and 24 weeks of age. Visual acuity (VA) was assessed using optomotor response tests and retinal function via fullfield electroretinography (ffERG) (VA and ffERG; n=6-9/group per time point). Retinal structure was serially examined by *in-vivo* fundus autofluorescence (FAF) and optical coherence tomography (OCT) imaging (n=4/group). Outer nuclear layer (ONL) thickness was measured using Image Scope software (n=7-9/group). All results are presented as mean±SEM and statistical significance was determined using a two-tailed Student's t-test.

Results: NSG-*Fam161a* KO mice exhibited accelerated retinal degeneration compared to *Fam161a* KO mice. VA was significantly lower in NSG-*Fam161a* KO mice from 6 weeks onward (0.34±0.01 versus 0.38±0.004 cpd, $p<0.001$), with a larger difference by 24 weeks (0.02±0.02 versus 0.20±0.01 cpd, $p<0.001$). Scotopic ffERG b-wave amplitudes at 4 weeks were already significantly reduced in the immunodeficient KO mice as compared with their immunocompetent KO counterparts (307.1±30.8 µV versus 434.8±45.6 µV, $p<0.05$). Photopic responses were also reduced, with 1Hz amplitudes at 4 weeks being 37.7±3.9 µV in NSG-*Fam161a* KO versus 60.8±5.5 µV in *Fam161a* KO mice ($p<0.01$). FAF imaging showed larger and more numerous hypo- and hyperautofluorescent spots in NSG-*Fam161a* KO mice at 18 and 24 weeks, with significant ONL thinning as early as 4 weeks on OCT. Histology revealed earlier ONL thinning, indicating faster photoreceptor loss. For instance, at 6 weeks ONL thickness in the nasal periphery was 19.8±1.1µm in NSG-*Fam161a* KO mice versus 34.2±0.7µm in *Fam161a* KO mice ($p<0.001$).

Conclusions: The findings suggest that an intact immune system may play a protective role in modulating the progression of inherited retinal degeneration. New insights into the complex interplay between genetic factors and immune status in RP pathogenesis may potentially open new avenues for therapeutic interventions in IRDs.

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G4

PRPF31 heterozygous mutations: effects on cell dynamics and mitochondrial function in iPSC-derived RPE models

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Purpose: Heterozygous mutations in the gene encoding the RNA splicing factor *pre-mRNA processing factor 31* (*PRPF31*) are a leading cause of autosomal dominant retinitis pigmentosa (RP). Whole transcriptome analysis revealed that *PRPF31* mutations are associated with the mis-splicing of numerous genes, including mitochondrial and ciliogenesis-related genes. This study aimed to investigate the association between *PRPF31* mutations, mitochondrial function, ciliogenesis, and paracrine secretion in PRPF31-RP patient-derived retinal pigment epithelium (RPE) models.

Methods: Mitochondrial function was assessed in fully differentiated PRPF31-RP iPSC-RPE models using the Agilent Seahorse XFe96-Pro Analyzer, which measures the oxygen consumption rate (OCR). Ciliogenesis was evaluated through immunofluorescence staining for the cilia marker ARLB13, and cilia length and number were automatically quantified. Paracrine secretion profiles of VEGF and PEDF were tested using R&D Systems ELISA kits, analyzing the basal and upper media of the cultured RPE cells, respectively.

Results: Protocols for testing mitochondrial function, ciliogenesis, and paracrine secretion in fully differentiated RPE models were established. The basal and maximal OCR were lower in the RPE models of two PRPF31-RP patients compared to the healthy control. Treating the PRPF31-RP patient-derived RPE cells with drugs that elevated the expression of the PRPF31 WT allele increased basal and maximal OCR by two-fold. Aberrant (higher) VEGF secretion was observed on the basal side of PRPF31-RP patient-derived RPE cells compared to healthy controls. Furthermore, cilia length was shorter in PRPF31-RP patients compared to healthy controls, indicating a role for PRPF31 in ciliogenesis and cell proliferation.

Conclusions: This study highlights the multifaceted role of PRPF31 in mitochondrial function, ciliogenesis, and paracrine secretion in RPE cells, and establishes in vitro outcome measures for drug discovery. These advancements may contribute to precision medicine for PRPF31-RP and other RPE-related disorders.

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G5

Suppressor-tRNA mediated translational readthrough of premature termination codon mutations causing Inherited Retinal Dystrophies

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Purpose: Approximately 11% of the human rare disease-causing mutations are nonsense mutations that introduce a premature termination codon (PTC) leading to production of either truncated protein or causing the mRNA degradation through nonsense-mediated mRNA decay pathway. Around 18% of the Inherited Retinal Dystrophies (IRDs) causing mutations are nonsense. In recent years, translational read through drugs such as PTC124 and suppressor tRNA have emerged as a potential therapeutic option to treat PTCs. Sup-tRNA is derived from a natural tRNA with the anti-codon altered to base-pair with one of three stop codons and amino-acylated to participate in translation elongation at the targeted PTC, which allows the synthesis of a full-length functional protein. In this current study, we tested the sup-tRNA mediated translational read-through on three nonsense mutations: FAM161:p.(Arg523Ter); KIZ:p.(Arg76Ter), and TRPM1:p.(Lys294Ter).

Methods: A pmCheey-EGFP dual reporter plasmid was used to test the read through efficacy of different sup-tRNAs. Read through efficacy was measured using fluorescent microscopy, FACS and western blotting.

Results: Our preliminary results shows that a modified sup-tRNAArg is able to suppress the FAM161:p.(Arg523Ter); KIZ:p.(Arg76Ter), mutations more efficiently compared to natural sup-tRNAArg. Similarly, sup-tRNALys is able to suppress the TRPM1:p.(Lys294Ter) mutation effectively and produce full length protein with wildtype amino acid.

Conclusion: In summary, our preliminary data in cellular models validate and highlight the potential of sup-tRNA mediated readthrough to serve as a therapeutic option for patients with hereditary retinal dystrophies caused by nonsense mutations.

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G6

Cell-Free DNA Methylation in Aqueous Humor

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Purpose: Cell-free DNA (cfDNA) methylation analysis is an emerging field that examines DNA fragments released into bodily fluids, such as aqueous humor (AH), from various tissues. Methylation, an epigenetic modification involving the addition of a methyl group to cytosine, is essential for genes regulation and provides tissuespecific signatures. By analyzing cfDNA methylation patterns, researchers can identify tissue origins, assess cell death rates, and gain insights into disease mechanisms, including those affecting the retina. We aim to evaluate the feasibility of using cfDNA originated from AH, as a biomarker for retinal and anterior segment diseases.

Methods: We collected 15 AH samples from healthy patients undergoing cataract surgery and pooled them into a single sample to obtain a sufficient amount of cfDNA. cfDNA was extracted and treated with bisulfite, which converts unmethylated cytosines to uracils while leaving methylated cytosines unchanged. Bisulfite-treated cfDNA was PCR amplified using panel of established methylation biomarkers primers. The panel included markers for Universal Endothelium, Whole Brain, Astrocytes, Oligodendrocytes, Neurons, and various immune cell types (B cells, CD8+ T cells, Monocytes, Neutrophils, NK cells, T cells, Tregs). The PCR products were subsequently sequenced on an Illumina MiSeq platform. Sequenced reads were separated by barcode, aligned to the target sequences, and analyzed using custom scripts implemented in R.

Results: The analysis revealed the presence of cfDNA in the AH sample, with a concentration of 4.019 ng/ml. This sample contained cfDNA from various sources, with the following relative abundances: Universal Endothelium (4.91%), Whole Brain (0.20%), Astrocytes (1.96%), B cells (5.32%), CD8+ T cells (8.28%), Monocytes (15.73%), Neutrophils (10.02%), T cells (18.97%), and Tregs (3.68%). No cfDNA was detected from Oligodendrocytes, Neurons, or NK cells. Conclusion: This study demonstrates the potential of cfDNA methylation analysis as a novel tool for understanding retinal diseases. The identification of tissue-specific cfDNA origins provides valuable insights into cell turnover in the healthy eye. Future research should focus on validating retina-specific methylation markers and assessing the correlation of such markers with intraocular disease processes.

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OO1

Thyroid blood tests and TED management of tobacco consumers and cannabis consumers

Jonathan Kfir

Background: Previous studies have noted a connection between tobacco smoking and Thyroid Eye Disease (TED), but research on how smoking influences blood test results, management, and long-term outlook in TED is lacking. Moreover, the relationship between TED and cannabis consumption remains unexplored. Thus, this study aims to investigate the association between various TED characteristics and both tobacco and cannabis smoking.

Method: A retrospective review of TED clinic patients' records from 2016 to 2020 at a tertiary center included ophthalmic exams, CAS, lab results, and treatment details. Comparison was made between tobacco users and non-users.

Results: Among the 132 TED patients, 33 (25%) were tobacco users, and 32 age- and sex-matched non-smokers were included for comparison. Tobacco consumers had higher CAS (3.22 vs. 1.73, $p=0.05$) and more optic neuropathy (9% vs. 3%, $p=0.043$). They also showed elevated TSH (2.24 vs. 1.18, $p=0.04$) and TSI (1679% vs. 835%, $p=0.04$) levels. They received steroid treatment more often (27.2% vs. 15.62%, $p=0.04$) and underwent more surgeries ($p<0.01$) than non-smokers. Of the entire cohort, five patients were cannabis consumers; notably, 60% of them received medical treatment and 60% required surgical intervention for TED.

Conclusions: Tobacco use correlates with worse visual function, heightened optic neuropathy risk, elevated thyroid blood markers, and increased likelihood of interventions in Thyroid Eye Disease (TED). Cannabis users require more surgical interventions. Halting tobacco and possibly

cannabis use is vital for TED patients. Larger studies are needed to explore cannabis's impact on TED.

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OO2

Lacrimal gland volume measurements in normal and thyroid orbitopathy patients using Magnetic Resonance Imaging- ongoing study

Nur Khatib MD, Joel Gutovitz, Feda Fanadka MD

Purpose: Previous studies using computed tomography imaging have demonstrated that the lacrimal gland volume is larger among patients with thyroid orbitopathy. The aim of this study to formulate reference values for evaluation of lacrimal gland volumes using Magnetic Resonance Imaging in normal and thyroid orbitopathy patients.

Methods: a retrospective case series of 54 lacrimal glands magnetic resonance imaging (MRI) of 27 normal patients and 54 lacrimal glands MRI's of 27 thyroid orbitopathy patients from July 2015 to November 2023. This research was performed according to the institutional declaration of Helsinki. Normal patients were recruited from a subset of patients hospitalized in the Ophthalmology department with optic neuritis, optic neuropathy, or other neurological cause of visual disturbance unrelated to the lacrimal gland. Patients with thyroid orbitopathy were diagnosed in the Oculoplastic Clinic at Emek Medical Center. All patients underwent a Magentic Resonance Imaging of the brain and orbit. All patients with thyroid orbitopathy underwent endocrinological evaluation, ocular evaluation and orbital MRI examination. Lacrimal glands were evaluated on T2-weighted images using a simple method of volume measurement with Siemens' Synovis imaging software.

Results: The mean volumes for normal and thyroid orbitopathy patients were 0.62 ± 0.11 cm3 and 0.9 ± 0.13 cm3, respectively. Mean lacrimal gland volumes in normal female vs. male patients were 0.66 ± 0.10 vs. 0.58 ± 0.11, whereas in the thyroid group female vs. male patients had volumes of 0.8 ± 0.09 cm3 vs. 0.7 ± 0.15 cm3. Female predominance in the normal group was 46% (6/13) vs. 55% (15/27) in the thyroid orbitopathy group.

Conclusion: Mean lacrimal gland volumes are larger in patients with thyroid orbitopathy compared to normal patients, and MRI considered to be the gold standard for this quantification.

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OO3

Corneal Pathologies in Patients with Thyroid Eye Disease: Prevalence, Clinical Characteristics and treatment

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Purpose: The purpose of this study is to investigate the prevalence, clinical characteristics, and prognosis of corneal conditions in patients with thyroid eye disease (TED), as these conditions can significantly impact the ocular surface.

Methods: This retrospective cohort study included patients diagnosed with TED and treated at the multidisciplinary TED clinic of Sheba Medical Center, Tel HaShomer. For each eye, data on the presence of corneal pathology and clinical characteristics were recorded at both the initial and final evaluations. Information on surgical interventions, corneal clinic visits, and additional treatments was also analyzed.

Results: 121 TED patients included in the study. Among them, corneal pathologies were observed in 64 patients (52%). Most of the cases were bilateral (54 patients, 84.4%). At presentation, 53 patients (82.81%) had punctate epithelial erosions (PEE), 18 patients (28.12%) had a tear break-up time (TBUT) of less than 10 seconds, 5 patients (7.81%) were diagnosed with severe dryness or exposure keratopathy, and 2 patients (3.12%) presented with corneal opacity. Only 6 patients (4.95%) required visits to the corneal clinic, while 12 patients (18.5%) underwent surgical interventions for dry eye: 4 patients received unilateral tarsorrhaphy, 7 patients underwent bilateral tarsorrhaphy, and 1 patient had ectropion surgery. Additionally, 6 patients received other treatments for dry eye, including 5 who had plug insertions and 1 who received intense pulsed light (IPL) therapy. No cases of perforation due to dry eye were reported.

Conclusion: In conclusion, this study highlights the significant prevalence of corneal pathologies in patients with TED with over half of the participants affected. The findings indicate that bilateral involvement is common. While the majority of patients did not require extensive intervention, a subset underwent surgical treatments, underscoring the need for careful monitoring and management of ocular surface conditions in this population. Overall, these results emphasize the importance of a comprehensive approach to the evaluation and treatment of corneal conditions associated with TED to improve patient outcomes. Further research is essential to better understand the underlying mechanisms and optimize clinical guidelines for corneal assessment in TED patients.

BACK TO PROGRAM

OO4

The differences in clinical characteristics and outcomes of ptosis surgery: a report of 260 cases

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Purpose: To examine the preoperative, intraoperative and postoperative characteristics of various ptosis repair surgeries at a major referral center.

Methods: We retrospectively reviewed patients > 18 years of age who underwent ptosis repair surgery between 02/2009 and 12/2021 at a single tertiary center. Congenital cases were excluded. Sub-analysis by ptosis type, surgical technique, and anterior vs. posterior approach surgery was performed. Main outcome measures included residual ptosis defined as Margin-to-Reflex Distance 1 < 2.5 mm at last follow-up, as well as clinically significant residual ptosis requiring re-do surgery.

Results: A total of 260 patients were included, with mean follow up of 259 ± 30 days (28 - 3771 days). Main indication for ptosis surgery was aponeurotic (222 patients). 164 (63.1%) patients underwent Müller's Muscle-Conjunctival Resection, 51 (19.6%) Fasanella-Servant, 35 underwent External Levator Advancement (13.5%), and 10 (3.8%) Frontalis-Sling suspension. Post-op residual ptosis and need for correction was seen in 66 eyes (25.4%) and 48 eyes (18.5%), respectively; however, differences were not significant between groups when analyzing by ptosis type ($p \geq 0.116$), surgery type ($p \geq 0.444$) and anatomical approach ($p = 0.835$).

Conclusions: No significant differences in residual ptosis, as well as referral for re-do surgery were shown between groups when analyzed by ptosis type, surgical choice, as well as anterior vs. posterior approach surgery. Ptosis corrective surgery can be completed using a variety of techniques with good success given that the correct surgical candidate and surgery are chosen.

BACK TO PROGRAM

OO5

Outcomes after multidisciplinary treatment for pediatric and adult orbital rhabdomyosarcoma

Nur Khatib

Purpose: To describe the clinical presentation, imaging characteristics, prognostic factors, histopathology, and treatment outcomes of pediatric and adult orbital rhabdomyosarcomas(RMS). To compare the disease natural history and comparison of treatment approach between adult and pediatric rhabdomyosarcoma.

Methods: We conducted an institutional retrospective study with data from 39 patients with primary orbital pediatric RMS and three cases of adults primary orbital RMS treated between 1995 and 2016 at the Amsterdam University Medical Centers / Emma Children Hospital. We evaluated demographic characteristics, symptoms and signs, imaging characteristics, risk factors and treatment outcomes.

Results: The median follow-up period was 9.4 years (range, 3 to 25 years). The majority of orbital tumors were located in the superior medial quadrant of the orbit. In terms of prognostic factors that affect survival rate of adult RMS are similar to children including age, parameningeal involvement, TNM staging, Intergroup RMS Study Group (IRSG) stage, and histological subtype. The staging of RMS in our cases were in accordance with the staging system for children, which was based on the IRSG and TNM staging system. Of the 39 children, 10 underwent chemotherapy and excision without additional radiotherapy. The 29 patients with additional local treatment received Ablative surgery, MOld technique with after loading brachytherapy and surgical REconstruction (AMORE) (N = 21), proton (N = 4) or external beam radiation treatment (EBRT; N = 4). We found 14 cases with recurrences, 9 of which underwent exenteration and two of them died. Among adults the treatment principles were according to children treatment protocol at our center; patients were required to begin therapy including chemotherapy, radiation and /or surgery once the diagnosis is confirmed. Delayed surgery was recommended, after chemotherapy (ideally after 3-4 courses) if tumor was resectable. Radiotherapy (with a conventional fractionation, and doses - 50 to 60 Gy) was suggested in all cases. The suggested doses of chemotherapy were: ifosfamide 3 g/m2 x 2 days, vincristine 1.5 mg/m2 (max 2 mg) x 1 day and actinomycin-D 1.5 mg/m2 (max 2 mg) x 1 day. Chemotherapy was delivered in 9 to10 courses (administered every 3 weeks). Among children group the 10-year overall survival was 95% and the EFS 63% with functional decimal visual acuity (0.5 or better). Among adults two cases had long term complete remission with no recurrence episodes the 3rd case Although chemotherapy or palliative radiotherapy were offered, the patient refused treatment and died a month after the diagnosis because of metastasis.

Conclusions: Even though the absence of controlled, prospective trials, which is due to extreme rarity of the disease among adults our treatment approach for adults was according to pediatric protocols. Our pediatric orbital RMS series with long term follow up showed 10-year survival rate of 95% by achieving local tumor control and eye preservation in 77% of our study population. From our children RMS experience, orbital RMS are usually incompletely resected (group III) in the majority of cases, therefore it is necessary to treat with postoperative chemotherapy and radiotherapy. We consequently believe that adult RMS patients should always be considered at higher risk even in localized disease and the adult age per se should be seen as an important prognostic factor.

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OO6

Impact of High-Risk Histopathological Features on Outcomes in Unilateral Retinoblastoma: Massive Choroidal Invasion, Retrolaminar Optic Nerve Invasion, Both or None

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Purpose: To evaluate the impact of massive choroidal invasion (MCI) and retrolaminar optic nerve invasion (RLONI), individually and in combination, on the outcomes of children with unilateral retinoblastoma undergoing upfront enucleation. While each feature significantly predicts morbidity and mortality, their combined effect remains underexplored.

Methods: A retrospective analysis was conducted on data from children diagnosed with unilateral retinoblastoma who underwent upfront enucleation between 2011 and 2020. Cases with extraocular involvement at diagnosis were excluded. Data were collected from 21 centers across 12 countries, including demographic, clinical, and histopathological details. High-risk histopathology features (HRHF) were defined as MCI and/or RLONI. The primary outcomes assessed were metastasis and mortality rates.

Results: 1,122 children were evaluated (mean age 31.5±21.1 mo.; 46.3% female). The interval between presentation and enucleation averaged 1.0±3.1 mo., with 42.8±32.7 mo. follow-up. HRHF data were missing for 58 (5.2%) children. Among 1,064 children, 136 (12.8%) had MCI, 151 (14.2%) had RLONI, 100 (9.4%) had both, and 677 (63.6%) had neither. Overall, there was a 4.8% risk for metastases and an 8.1% risk for death. Children with HRHP had higher rates of metastases (8.5 vs 1.2%, $p<0.001$) and death (12.4 vs 1.9%, $p<0.001$). 505 (47.5%) children received adjuvant systemic chemotherapy (IVC). IVC vs. no IVC reduced metastases in MCI (1.6% vs. 33.3%, $p=0.002$) and both (18.5% vs. 62.5%, $p=0.012$), but not in no HRHP (0.0% vs. 1.5%, $p>0.2$) or RLONI (3.4% vs. 16.7%, $p>0.2$). Similarly, IVC vs. no IVC significantly reduced the mortality rate for children with MCI (5.5% vs. 33.3%, $p=0.019$) and both (23.9% vs. 62.5%, $p=0.032$), but not for no HRHP (1.4% vs. 2.1%, $p=1.00$) or RLONI (6.9% vs. 16.7%, $p=0.370$).

Conclusion: In unilateral retinoblastoma, the combination of massive choroidal invasion and retrolaminar optic nerve invasion significantly increases the risk of metastasis and mortality compared with either feature alone. Adjuvant IVC reduces the metastatic and mortality rates only when MCI is present alone or in combination with RLONI.

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AS1

PRIMA-1MET inhibits the development of limbal stem cell deficiency in *Trp63*-mutated ectodermal dysplasia mouse model

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Purpose: Previously, we reported that the small molecular weight compound, PRIMA-1MET, reinstates the activity of mutated p63 protein in ectodermal dysplasia (ED)-derived patient cells that successfully differentiated into skin and corneal epithelial cells in vitro. This latter study paved the way for clinical trial in which 3 ED patients with skin erosions were treated with the compound and the results are promising. The aim of this study was to examine the effect of PRIMA-1MET in genetically induced limbal stem cell deficiency (LSCD) mouse model. Additionally, we aimed to gain insight on the mechanism by which PRIMA-1MET acts, its target genes, its effects on stem cell activity, and the genetic signature of mutant limbal stem cells (LSCs) after treatment.

Methods: We employed an advance transgenic allele that allows an inducible mutagenesis, that stimulates the switch from a transcription of a wild type to a L514F p63-mutated transcript in Pax6+ cells. The compound was intraperitoneally injected to the animals twice a week for up to 4-months. To test the therapeutic effect of the compound, we imaged the eyes and evaluated the transparency and vascularization status of the cornea, we performed immunostaining of LSC and corneal markers, and we performed single-cell RNA sequencing (scRNA-seq) to identify changes in signaling pathways. Quantitative lineage tracing was carried out to evaluate the effects of PRIMA-1MET on mutated LSC dynamics, proliferative capacity, and clonal growth patterns over time.

Results: PRIMA-1MET significantly attenuated the development of neovascularization and opacification of the mutants in aging or following injury. Immunofluorescence staining revealed that treatment with PRIMA-1MET partly improved marker expression of mutated corneas. Lineage tracing analysis showed that PRIMA-1MET partially restored the renewal patterns of the cornea, providing direct evidence that PRIMA-1MET improves the functionality of mutated LSCs. Analysis of scRNA-seq demonstrated that PRIMA-1MET partly restores the characteristic genetic signature of mutated LSCs.

Conclusions: This study demonstrates that PRIMA-1MET effectively prevents the onset of the LSCD phenotype in mutated corneas under homeostatic conditions and following injury. It inhibits neovascularization and preserves corneal transparency. These findings highlight the potential of PRIMA-1MET for rapid translation into clinical applications for patients with LSCD.

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AS2

Point mutation in p63 perturbs limbal stem cell boundary formation and renewal dynamics in vivo

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Purpose: Very little is known about the impact of disease-causing mutations on limbal stem cells (LSC) functionality. The transcription factor p63 is essential for LSC proliferation in vitro. Nevertheless, the impact of p63 mutations on limbus development and LSC function in vivo remains unclear. This knowledge gap is largely due to difficulty of tracing LSCs in vivo, and limits our understanding of LSC deficiency (LSCD) pathogenesis and the development of therapies. To address this, we performed live monitoring of p63-mutated LSCs during pathogenesis in the embryonic and adult murine cornea.

Methods: We generated a tamoxifen inducible switch from wild-type to expression of a mutated L514F *Trp63* allele. LSC clonal dynamics were uncovered by live quantitative lineage tracing and computational simulations. Abnormalities in limbus and cornea were analyzed by microscopy, histology and immunofluorescent stainings. The abnormal molecular pathways were exposed by RNA-sequencing. Clinical diagnosis and genetic analysis were performed for LSCD patients to identify disease-causing mutations.

Results:

Quantitative live lineage tracing reveals that induction of p63 mutant expression in adult mice does not cause LSC loss, but rather significantly accelerates corneal replenishment rate by active LSCs. The mutation also affects the centripetal pattern of cell movement during tissue renewal. Computerized modeling of corneal renewal suggests that p63 mutation increases the frequency of LSC symmetric divisions. Furthermore, corneal injury stimulated pathological wound healing, accompanied by corneal neovascularization and opacification, indicating that p63 mutation in adult stage destabilizes the boundary maintenance by LSCs. Interestingly, activation of the mutation during early eye development affects corneal lineage commitment and results in progressive LSCD that aggravates with age, characterized by abnormal expression of boundary genes, and pro-angiogenic factors. Finally, we report that patients carrying the same L514F mutation

display neovascularization and loss of palisades of Vogt in LSC niche, which are hallmarks of LSCD.

Conclusions: These findings highlight the critical role of p63 in limbus development and in maintaining LSC boundary function. Targeting p63 pathways could be a potential therapeutic strategy for treating LSCD. Finally. the new mouse model is a useful tool to study LSCD and for drug testing.

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AS3

Mitochondria Transplantation Promotes Corneal Epithelial Wound Healing

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Purpose: The integrity of the corneal epithelium is essential in maintaining normal corneal function. Conditions disrupting the corneal epithelial layer range from chemical burns to dry eye disease and may result in impairment of both corneal transparency and sensation. Identifying factors that regulate corneal wound healing is key for the development of new treatment strategies. Here, we investigated a direct role of mitochondria in corneal wound healing via mitochondria transplantation.

Methods: Human corneal epithelial cells (hCECs) were isolated from human corneas and incubated with mitochondria which were isolated from human ARPE-19 cells. We determined the effect of mitochondria transplantation on wound healing and proliferation of hCECs. In vivo, we used a mouse model of corneal chemical injury. Mitochondria were isolated from mouse livers and topically applied to the ocular surface following injury. We evaluated the time of wound repair, corneal re-epithelization, and stromal abnormalities.

Results: Mitochondria transplantation induced the proliferation and wound healing of primary hCECs. Further, mitochondria transplantation promoted wound healing in vivo. Specifically, mice receiving mitochondria recovered twice as fast as control mice following corneal injury, presenting both enhanced and improved repair. Corneas treated with mitochondria demonstrated the re-epithelization of the wound area to a multi-layer appearance, compared to thinning and complete loss of the epithelium in control mice. Mitochondria transplantation also prevented the thickening and disorganization of the corneal stromal lamella, restoring normal corneal dehydration.

Conclusions: Mitochondria promote corneal re-epithelization and wound healing. Augmentation of mitochondria levels via mitochondria transplantation may serve as an effective treatment for inducing the rapid repair of corneal epithelial defects.

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AS4

Proteomic and epitranscriptomic signatures as biomarkers for corneal limbal stem cell deficiency

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Purpose: Limbal stem cell deficiency (LSCD) is an ocular surface disease resulting in pain and blindness. Treatment for LSCD is limited due to late diagnosis relying mainly on late clinical signs. Furthermore, the choice of self or donor limbal cell transplantation is altered by the extent of LSC injury, which clinicians are unable to currently measure. Our goal is to utilize tears as a non-invasive diagnostic tool for early detection of LSCD.

Methods: We quantify protein and RNA levels, as well as the chemical modifications present on RNA transcripts, in tears from healthy and diseased individuals by employing mass spectrometry (MS) and Illumina-based sequencing. Further profiling of the abundance of these molecules in secretomes of cellular models of corneal epithelium during differentiation is used for validation of the clinical results and mechanistic studies. This bench-to-bedside approach facilitates identification of secreted protein and RNA molecules as potential biomarkers, and promotes investigation of mechanistic aspects of LSCD in a tractable cellular model.

Results: MS analysis of tears of healthy and afflicted individuals identified differentially expressed proteins, which are enriched in genes related to differentiation of epithelial cells and RNA processing. Regarding corneal epithelial differentiation, Alpha-Enolase (Eno1), which was previously shown to correlate to LSC function by in vitro immunostaining, was significantly decreased in patients' tears compared to controls (p value=0.002). This finding emphasizes the strength of our methodology in identifying disease-related markers that can potentially improve diagnosis. Additionally, identifying enrichment of RNA processing genes suggests that alteration in the expression of such genes may play a part in the etiology of LSCD. For example, we detected the presence of both · and m6A, which are known to be involved in stem cell and eye development, and suggested their role in the regulation of protein expression in tears.

Conclusions: Our combined analysis of proteomic and epitranscriptomic signatures from clinical and in vitro samples established the ability to detect LSC biomarkers by a novel non-invasive tool via tears. Moreover, our pioneering approach identifies for the first time the presence of RNA modifications in human tears, as well as proposes novel biomarkers for early diagnosis and treatment of LSCD.

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AS5

Bleomycin subconjunctival injection for corneal neovascularization in a rat model

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Purpose: To explore the effectiveness of bleomycin subconjunctival perilimbal injections to treat newly formed corneal neovascularization (NV) in a rat model. Methods: A preliminary study was conducted to establish a sectorial vascularization odel. Rats were chosen for their corneal size, which facilitates NV and monitoring. 10-0 Vicryl or Nylon suture was placed ~1 mm from the limbus in the mid-stromal depth to induce sectorial neovascularization and rats were photographed with a slit-lamp biomicroscope to determine the patterns and rates of NV. Further two studies were conducted; after inducing corneal NV, the rats were divided into two groups. The study group received 0.5 mg/mL Bleomycin subconjunctival injections near the NV areas, while the control group was injected with 0.09% NaCl. Corneas were photographed using a slit-lamp biomicroscope to monitor the regression of corneal vessels in the two groups. Oflox was administered prophylactically to prevent corneal infiltrates. Regression of the NV was determined by analyzing the area occupied by vessels in the cornea using ImageJ software.

Results: The pilot study included 10 rats divided into three groups based on the number of sutures placed. Optimal NV was achieved with two nylon sutures, with peak vessel growth observed between days 7–10. The main experiments included 24 and 30 rats, respectively. In the first experiment, 7 rats received Bleomycin injections on day 7, 4 on day 10, and 7 received saline. Patterns of NV observed in the pilot study were reproducible. Rats in the Bleomycin group showed a nonsignificant decrease in the percentage of vessel area, most notable on day 17. In the second experiment, all rats received topical antibiotics throughout the study to minimize corneal infiltrates, which had caused variability in the first experiment. Each group included 11 rats, injected with either Bleomycin or saline on day 7. By day 17, rats in the Bleomycin group showed significantly reduced NV (9% vs. 15%, $p<0.05$). After euthanasia, the corneas were excised, flattened, and stained with H&E, qualitatively confirming the reduced vascularization in Bleomycin-treated corneas.

Conclusions: Bleomycin was shown to be possibly effective in treating corneal NV in a rat model.

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AS6

Trace Element Analysis in Feline Corneal Sequestrum

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Objective: Black cornea is a complication resulting from long-term use of epinephrine. In cats, a similar clinical presentation is known as feline corneal sequestration (FCS). This study aimed to investigate the trace element composition of FCS, identify similarities to black corneal pigmentation in humans, and improve the understanding of their pathophysiology and clinical implications.

Methods: 11 cats diagnosed with FCS and treated using lamellar keratectomy were included, alongside a control group of four cats euthanized due to systemic, non-ocular conditions. Corneal samples from both groups were collected and preserved at −80°C. Trace element analysis was performed using the Particle-Induced X-ray Emission (PIXE) method with a 1.7 MV Pelletron accelerator. Data were analysed using Mann-Whitney tests for trace element differences.

Results: The study included two females and nine males (mean ±SD age: 4.5 ± 4.1 years; median: 3 years). Lesion sizes ranged from 1 to 8 mm in diameter, with depths of 20%–70%; two cases were bilateral, while seven were unilateral. Three lesions were avascular. The control group consisted of one female and three males (mean age: 7.0 ± 4.1 years; median: 5.5 years). Trace element analysis revealed the highest mean ± SEM peak area levels for chloride (697525 ± 23637 vs 642674 ± 80316) and sulfur (408228 ± 6764 vs 337937 ± 10924), for the FCS vs control groups, respectively; followed by phosphorus, potassium, sodium, calcium, magnesium, zinc, iron and bromide. Bromide (156 ± 15 vs 0; p=0.004) and iron (966 ± 101 vs 0; p=0.047) were found in FCS samples but not in controls.

Conclusion: Elevated levels of bromide and iron in FCS suggest a potential role for these elements in the pathophysiology of this condition. While the characteristic dark discoloration observed in FCS may appear similar to black corneal pigmentation in humans the underlying mechanisms differ.

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AS7

Prospective Randomized Controlled Clinical Study Evaluating the Efficacy of Perceptual Learning in Improving Vision among Patients with Keratoconus

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Purpose: To evaluate the efficacy of Visual Perceptual Therapy among patients with keratoconus.

Methods: This is a prospective randomized controlled open label study performed at Shamir Medical center during 2023-2024. The study comprises 35 patients in the treatment group and 10 patients in the control group. Included were patients between the ages of 14-55 years with stable keratoconus in the past 12 month and stable best corrected visual acuity (BCVA). The treatment group underwent Perceptual Learning Therapy for four months. The control group were followed without treatment. BCVA and contrast sensitivity were assessed.

Results: In our preliminary results, 7 patients were included in the treatment arm. Mean patient age was 35.28±8.7. In the treatment group corrected distance visual acuity (CDVA) improved by 0.24±0.08 logMAR (2.4 ETDRS line) and visual acuity for near improved by 0.06±0.07 logMAR (0.6 ETDRS lines). In addition, contrast sensitivity improved by 11116.82±187.2% in the treatment group.

Conclusions: In this prospective randomized controlled open label study, visual perceptual learning resulted in significant improvement in distance visual acuity as well as a certain improvement in near visual acuity, with a corresponding trend for improvement in contrast sensitivity among patients with keratoconus.

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AS8

Copper can be detected in tears of undiagnosed patients with Wilson disease

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Purpose: Wilson disease (WD) is a rare autosomal recessive disorder characterized by the accumulation of copper in the body. It is caused by mutations in the ATP7B gene, resulting in defective copper metabolism. Ocular manifestations of Wilson disease are common and can be seen as Kayser-Fleischer rings, corneal deposits, and cataracts. The importance of early diagnosis and treatment cannot be overstated, as Wilson's disease if left untreated, can lead to severe neurological and hepatic dysfunction.

Methods: This study investigated the copper and other trace elements concentration in tears of suspected WD patients using particle-induced X-ray emission (PIXE). Five participants (3 females, 2 males) aged 36-65 years (mean age, 49.8 ± 5.52 years) were recruited for the study. Tears were collected from both eyes of each participant using Schirmer tear strips. Analysis was performed using PIXE, and the resulting values concerning chlorine (Cl) were normalized. Each individual was carefully examined, documenting suspected copper deposits in the anterior segment.

Results: One patient had bilateral Kayser-Fleischer rings. Subsequent genetic testing confirmed the diagnosis of WD. Furthermore, calcium (mean relative concentration 9.75x10-3±4.27x10-3) and copper (mean relative concentration 9.58x10-4±2.59x10-4) were detected only in the tears of the WD patient, in addition to an unusually high concentration of sodium, phosphorus, sulfur, and potassium as compared to negative samples ($p=0.17$, $p=0.02$, $p=0.04$, $p=0.14$ respectively). Repeated exams following treatment did not detect copper in tears.

Conclusion: Using a novel approach for elemental analysis, it is possible to detect copper in tears of patients with WD. Copper was detected only in samples of a WD and not in healthy subjects. Early diagnosis is important, as it can prevent clinical manifestations. PIXE can assist in biomedical diagnosis being highly sensitive for non invasive tears analysis.

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AS9

Detection of Subclinical Corneal Edema in Patients With Fuchs Endothelial Dystrophy Using Galilei Corneal Tomography

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Keywords: Fuchs Endothelial Corneal Dystrophy, Cornea, Corneal Endothelium, Galilei Tomography, Specular Microscope.

Purpose: To evaluate the efficacy of the Galilei device in detecting and distinguishing subclinical corneal edema in patients with Fuchs Endothelial Dystrophy (FED).

Methods: We divided the patients into four groups based on their FED Characteristics. FED patients with clinical edema, subclinical edema (transparent corneas with CCT>550µm), no edema (transparent corneas with CCT<550µm), and a group of patients with healthy corneas. To identify FED patients, we reviewed endothelial images from the specular microscope that exhibited potential FED characteristics. Only those with Galilei tomography report (Galilei V6.4.2 ©SIS Ltd, surgical instrument systems, Switzerland) and medical records describing the presence of FED were selected. Patients who had keratoconus, glaucoma, traumas and gone through previous corneal surgeries were excluded. We evaluated pachymetry and posterior depression maps and recorded the presence of three main parameters for each patient – irregular isopachs, displacement of thinnest point and focal posterior corneal surface depression.

Results: 55 eyes of 30 FED patients and 30 eyes of 18 healthy patients were included in this study. All three parameters were observed in the eyes of the different groups as follows: 100% in the clinical edema group (n=23), 75% in the subclinical edema group (n=16), 43.75% in the no edema group (n=16), and 3.33% in the healthy corneas group (n=30). Subclinical edema showed a significant difference compared to the healthy cornea group (p=0.0007). While the difference compared to the no edema group was not statistically significant (p=0.149), the sensitivity (75%) and ROC curve analysis (AUC = 0.79) suggest that the Galilei corneal tomography demonstrates good accuracy in subclinical edema identification.

Conclusion: Our results show that Galilei is able to assist in detection of subclinical edema in patients with FED. Based on our findings, Galilei can be used as a tool for assessing subclinical edema in patients with clear corneas who present with FED characteristics.

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AS10

Dual therapy with tacrolimus and sodium hyaluronate enhances tear film stability in evaporative dry eye disease: insights from a spontaneous canine large animal model

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Purpose: To evaluate the efficacy of a dual therapeutic approach combining tacrolimus and hyaluronan-based lubricant for the management of evaporative dry eye disease (EDED) in dogs, compared to hyaluronan monotherapy.

Methods: Fifty-four client-owned dogs with EDED were randomly assigned to three groups (n = 18 each): Group 1 received 0.03% tacrolimus and 0.3% hyaluronan twice daily; Group 2 received 0.3% hyaluronan four times daily; and Group 3 received 0.3% hyaluronan twice daily. Blink rate, ocular scoring, corneal esthesiometery, Schirmer tear test, tear film breakup time (TFBUT), punctate fluorescein staining, lissamine green staining, and owner-reported symptoms were assessed at baseline, 15, and 45 days post-treatment.

Results: Group 1 showed the most significant improvements, with TFBUT increasing by +57% by Day 15 and +93% by Day 45, accompanied by notable reductions in ocular discharge and conjunctival hyperemia. Clinical signs and owner-reported symptoms, including redness, discharge, and pruritus, improved more rapidly and comprehensively in Group 1. While Groups 2 and 3 also improved, changes were less pronounced despite the higher dosing frequency in Group 2. No significant differences were observed in corneal sensitivity or corneal abnormalities such as fibrosis or neovascularization.

Conclusions: The combination of tacrolimus and hyaluronan resulted in greater enhancements in tear film stability and clinical outcomes than hyaluronan alone. This dual therapy effectively addresses both immunologic and lubricative deficiencies associated with EDED, offering a promising strategy for comprehensive management. Future studies should investigate the comparative benefits of different formulations and explore advanced diagnostics for precise differentiation of tear film deficiencies.

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Comparing Surgeons' Muscle Properties While Using Standard Surgical Microscope versus an Ophthalmic Exoscope with an Augmented-Reality Headset

Purpose: To quantitatively analyze surgical ergonomics between a standard operating microscope (SOM) and an Ophthalmic exoscope with an Augmented-Reality headset (Beyeonics)**.**

Methods: Prospective, controlled, comparative study measuring the muscle tension of 9 Ophthalmic surgeons while performing a dry lab cataract surgery using a standard microscope compared with a Beyeonics operating system. Participating surgeons had various operating experience ranging from residents (up to 5 years of surgical experience), young specialists (5-10 year's experience), and highly experienced specialists (20+ years of experience). The surgeons' neck and upper back muscle tension, stiffness, and other muscle qualities were measured using a MyotonPro device placed at the Sternocleidomastoid (SCM) and two positions on the Upper Trapezius muscles (TM1 and TM2) during preoperative, intraoperative, and postoperative time points.

Results: Use of the SOM led to a significant increase in SCM tension during surgery compared to pre-surgery levels (11.5933hz ± 0.9676 vs 10.9744hz ± 0.9650), with a mean difference of 0.6189hz (95% CI 0.2932 to 0.9445, $p<0.05$). In contrast, the use of the Beyeonics system did not result in significant changes in muscle tension at any measurement site during the procedure ($P>0.05$). In addition, Significant differences in Stiffness were observed in the Mid-operative time ($p = 0.039$), with higher values recorded for the SOM microscope than Beyeonics (204.71 ± 38.83 vs. 181.90 ± 27.66 N/m). For the TM1 and TM2, the analysis did not reveal significant differences in muscle qualities between the SOM and Beyeonics microscopes across any of the time points.

Conclusions: This study offers quantitative insights into surgeon ergonomics. It suggests that using the SOM increases muscle tension and stiffness in the SCM muscle compared to using the Beyeonics. This indicates that the Beyeonics system may alleviate intraoperative muscle fatigue compared to the SOM.

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NG1

Extracellular vesicles from stressed non-pigmented ciliary epithelial cells alter gene expression in trabecular meshwork cells

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Purpose: Extracellular vesicles (EVs) secreted by non-pigmented ciliary epithelial (NPCE) cells under oxidative stress may contribute to primary open-angle glaucoma (POAG) pathogenesis by altering gene expression in human trabecular meshwork (HTM) cells. This study investigated the impact of microRNAs (miRNAs) carried by NPCE-derived EVs on HTM cell gene expression under oxidative stress conditions.

Methods: NPCE cells were exposed to oxidative stress, and EVs were isolated from control and stressed cells. HTM cells were treated with these EVs, followed by microarray analysis to identify differentially expressed miRNAs in EVs and mRNAs in HTM cells. Bioinformatics analysis was used to explore miRNA-mRNA interactions, enriched Gene Ontology (GO) terms, and miRNA-mRNA-GO networks.

Results: The study identified 54 differentially expressed miRNAs in stressed NPCE-EVs. In HTM cells treated with stressed NPCE-EVs, 88 genes were upregulated and 58 downregulated. GO analysis of upregulated genes showed enrichment in processes such as extracellular matrix organization, cell proliferation, and adhesion. Downregulated genes were associated with oxidative phosphorylation and ATP biosynthesis. Notably, 59 out of 88 upregulated genes are known targets of downregulated miRNAs. Network analysis identified 39 interactions between downregulated miRNAs and upregulated genes involved in key biological processes relevant to POAG pathogenesis.
Conclusions: This study provides new insights into the potential role of NPCE-derived EVs and their miRNA cargo in POAG, suggesting novel mechanisms for disease progression and potential therapeutic targets for further investigation.

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NG2

Studying Critical Flicker Frequency Threshold (CFF) in glaucoma subjects: anatomical and Functional Correlations

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Purpose: Early detection of optic disc structural and visual field functional changes in people with glaucoma is crucial for monitoring and treatment of the disease before irreversible damage occurs. Here we present a known visual function feature, the critical flicker frequency (CFF), as a possible measure of the early detection of glaucoma.

Methods: To investigate whether changes in CFF can predict glaucoma progression, CFF values in patients with Glaucoma were assessed. Next, the correlation between these values and OCT imaging combined with visual field measurements (the gold standard for diagnosing glaucoma) were evaluated to assess the feasibility of using CFF as a measure for monitoring glaucoma. Towards this end, we developed a system based on an analog output device to independently drive two LEDs through a custom-written MATLAB code to elicit sinusoidal flickering stimuli and for psychophysically measuring the perceived CFF thresholds.

Results: Our results revealed a significant correlation between Ganglion Cell Complex (GCC) measurements, one of the parameters used to determine glaucoma progression extracted from OCT imaging, and CFF ($R2 = 0.51$, $P<0.005$). Moreover, we found a correlation between CFF values and the visual field mean deviation (VF 10-2-MD, $R2 = 0.71$, $P<0.005$). In contrast, no significant correlation was observed between CFF and broader retinal structural-RNFL ($R2<0.5$, $p>0.05$). These results validate our hypothesis that CFF values can serve as a reliable measure for monitoring glaucoma. .

Conclusions: We present evidence that CFF values are highly correlated with gold standard measurements used in the monitoring of glaucoma. Further research is needed to determine whether CFF can serve an early marker of glaucoma induced visual field loss.

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NG3

Preclinical efficacy of EXOPTEN: a novel exosome-based therapy for acute optic nerve pathology

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Purpose: Central Nervous System (CNS) injuries are devastating neurological conditions. The recovery and axonal growth are limited due to the poor innate regenerative capacity of the adult CNS and a hostile recovery environment. ExoPTEN is an exosome-based drug developed for acute Spinal Cord Injuries (SCI) treatment by enhancing neural regeneration and reducing apoptosis. ExoPTEN is composed of mesenchymal stem cell-derived extracellular vesicles (EVs) loaded with siRNA targeting phosphatase and tensin homolog (PTEN**)**, a critical inhibitor in the mTOR signaling pathway. We assessed the efficacy of ExoPTEN for the treatment of optic nerve (ON) lesions.

Methods: First, studies were conducted using two SCI rat models: spinal cord transection and compression. Exosomes loaded with ExoPTEN were administered intranasally and intrathecally after the injury. Efficacy was evaluated using MRI, BBB locomotor tests, von Frey sensory tests, and immunohistochemistry. The successful SCI studies were emulated in a rat ON crush (ONC) model. Retinal ganglion cell (RGC) survival was assessed by staining retinal flat-mounts with Brn3a, a specific marker of RGCs. RGC function was determined using electroretinography by measuring the amplitudes of the positive scotopic threshold response (pSTR).

Results: In both SCI models, ExoPTEN significantly improved motor, sensory, and structural parameters, as confirmed by MRI behavioral tests and histological analyses. Treatment of the ONC model with ExoPTEN resulted in over 2-fold higher pSTR amplitudes compared to treatment with naïve EVs or no treatment. Brn3a staining indicated higher RGC survival in ExoPTEN-treated eyes compared to naïve EVs exosome treatment (p=0.0025).

Conclusions: Strong positive preclinical data demonstrate ExoPTEN's promising therapeutic approach to acute SCI and ON injuries.

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NG4

Acute Optic Neuropathy in Older Adults: Differentiating Between MOGAD Optic Neuritis and Nonarteritic Anterior Ischemic Optic Neuropathy

Hadas Stiebel-Kalish

Purpose: Myelin oligodendrocyte glycoprotein antibody-associated disease optic neuritis (MOGAD-ON) and nonarteritic anterior ischemic optic neuropathy (NAION) can cause acute optic neuropathy in older adults but have different managements. We aimed to determine differentiating factors between MOGAD-ON and NAION and the frequency of serum MOG-IgG false positivity among patients with NAION.

Methods: In this international, multicenter, case-control study at tertiary neuro-ophthalmology centers, patients with MOGAD presenting with unilateral optic neuritis as their first attack at age 45 years or older and age-matched and sex-matched patients with NAION were included. Comorbidities, clinical presentations, acute optic disc findings, optical coherence tomography (OCT) findings, and outcomes were compared between MOGAD-ON and NAION. Multivariate analysis was performed to find statistically significant predictors of MOGAD-ON. A separate review of consecutive NAION patients seen at Mayo Clinic, Rochester, from 2018 to 2022, was conducted to estimate the frequency of false-positive MOG-IgG in this population.

Results: Sixty-four patients with unilateral MOGAD-ON were compared with 64 patients with NAION. Among patients with MOGAD-ON, the median age at onset was 56 (interquartile range [IQR] 50-61) years, 70% were female, and 78% were White. Multivariate analysis showed that eye pain was strongly associated with MOGAD-ON (OR 32.905; 95% CI 2.299-473.181), while crowded optic disc (OR 0.033; 95% CI 0.002-0.492) and altitudinal visual field defect (OR 0.028; 95% CI 0.002-0.521) were strongly associated with NAION. On OCT, peripapillary retinal nerve fiber layer (pRNFL) thickness in unilateral MOGAD-ON was lower than in NAION (median 114 vs 201 µm, $p < 0.001$; median pRNFL thickening 25 vs 102 µm, $p < 0.001$). MOGAD-ON had more severe vision loss at nadir (median logMAR 1.0 vs 0.3, $p < 0.001$), but better recovery (median logMAR 0.1 vs 0.3, $p = 0.002$). In the cohort of consecutive NAION patients, 66/212 (31%) patients with NAION were tested for MOG-IgG and 8% (95% CI 1%-14%) of those had false-positive serum MOG-IgG at low titers.

Conclusion: Acute unilateral optic neuropathy with optic disc edema in older adults can be caused by either MOGAD-ON or NAION. Detailed history, the degree of pRNFL swelling on OCT, and visual outcomes can help differentiate the entities and prevent indiscriminate serum MOG-IgG testing in all patients with acute optic neuropathy.

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NG5

Seasonal Variation of Idiopathic Intracranial Hypertension

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Purpose

Idiopathic Intracranial Hypertension (IIH), also known as pseudotumor cerebri, is a clinical condition characterized by elevated intracranial pressure without a known cause. It is associated with risk factors such as obesity in females of childbearing age. However, the relationship between IIH and seasonal variation, as well as its impact on disease severity, remains unclear. In pediatrics, a suggested connection exists between IIH development and autumn-winter seasons which are associated with viral and bacterial infections. Our purpose is to establish a plausible correlation between IIH and a seasonal variation.

Methods: A retrospective review of medical records was conducted for all patients diagnosed with IIH at the Neuro-Ophthalmology Unit between December 2009 and December 2022. The collected data included date of symptoms, lumbar puncture opening pressure, body mass index (BMI), medical history, and visual field parameters (mean deviation). Disease severity was evaluated based on the degree of papilledema.

Results: 128 of the 154 patients (83%) were females, the cohort's mean age was 27.8±9.6 years, their mean BMI was 32.94±5.5. A seasonal distribution analysis revealed a statistically significant increase in the incidence IIH during the summer months (June–August), accounting for 52 out of 154 cases (33.77%, P=0.03). However, no significant association was observed between seasonality and the severity of optic nerve edema.

Conclusions: This study demonstrates a significant correlation between seasonality and the incidence of IIH in adults. In contrast to pediatric populations, where IIH cases were more prevalent during autumn and winter, our findings indicate a notable increase in IIH cases during the summer months. This seasonal trend may be associated with the link between IIH and obesity, as decreased physical activity during the summer months, possibly due to excessive heat, could lead to weight gain and worsen the condition.

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NG6

Evaluation of the ocular neuroprotective effects of 3K3A-activated protein C using a mouse model of optic nerve crush

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Purpose: There is an unmet need for neuroprotective treatments for optic nerve pathologies. Our previous studies were the first to establish 3K3A-activated protein C (APC) cytoprotective activities in the retina. Combined with the proven neuroprotective actions in degenerative systemic neurologic diseases, our findings highlight the therapeutic potential of 3K3A-APC for the treatment of multifactorial ocular neurodegenerative pathologies. The present study aims to elaborate on 3K3A-APC beneficial activities in the retina and optic nerve and focus on its ability to inhibit neurodegenerative key pathways. We have focused on the neuroprotective effects of 3K3A-APC on RGC survival, and destructive inflammatory processes by using the optic nerve crush (ONC) injury mouse model.

Methods: The study cohort included 30 C57BL/6 mice, divided into ONC+3K3A-APC treatment (n=10), ONC only (n=12), and a control group (n=8). 3K3A-APC (1µg/µl) or saline was injected intravitreally 1 hour and 7 days after ONC induction. Immunofluorescence of retinal cryosections and flat mounts was used to evaluate RGC survival (anti-RBPMS, abcam) and microglia activation (anti-Iba1, Fujifilm Wako). Apoptotic cell counts were determined using In Situ TdT-Mediated dUTP Nick End-Labeling (TUNEL) Immunostaining on days 3 and 14.

Results: Retinal flat mounts and cryosection images taken 14 days post-ONC demonstrated a significant loss of RGCs (10 ± 5 cells/100µm) in the ONC-only group. Treatment with 3K3A-APC significantly preserved RGC survival, with 33 ± 17 cells/100µm ($p<0.01$), a level that was not statistically different from the control group (57 ± 10 cells/100µm).
Following ONC, microglial cells translocated to retinal layers and exhibited an activated morphology. Treatment with 3K3A-APC led to a marked reduction in microglia-positive staining and the return of microglial cells to a ramified morphology, indicative of a non-activated state.

Conclusions: This study demonstrates that 3K3A-APC has significant neuroprotective effects on RGCs following optic nervinjury. Treatment with 3K3A-APC mitigated the loss of RGCs and reduced microglial activation, suggesting a dual mechanism involving neuroprotection and anti-inflammatory effects. These findings underscore the potential therapeutic role of 3K3A-APC for optic nerve pathologies. Further studies are warranted to explore its long-term effects and potential for clinical translation in treating ocular neurodegenerative diseases.

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AI1

Predictive Model for APOE4 Carriers Using Retinal Imaging and machine learning

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Purpose: Alzheimer's disease (AD) is a leading cause of morbidity worldwide, yet early detection remains a significant challenge. APOE4, a major genetic risk factor for AD, presents an opportunity for predictive diagnostics among cognitively normal adults at high risk for AD due to parental history of the disease, participants of the Israel Registry for Alzheimer's Prevention (IRAP) study. IRAP participants undergo a thorough assessment of cognitive function, brain volumetric imaging via MRI, and genetic testing for Apo E genotype. This study aimed to predict APOE4 carrier status using a multimodal approach combining unstructured raw retinal imaging data and structured MRI, cognitive function, and automatic retinal thickness measures.

Methods: Data from 186 participants, 33% of whom were APOE4 carriers aged 40-69, were analyzed. Inputs included raw retinal OCT imaging and infrared fundus images, as well as tabular data that included brain MRI (total intracranial volume, gray matter, and Hippocampal volumes), cognitive function, and retinal layer thickness metrics. Using ensemble technique, we trained machine learning models, including tree-based XGBoost on tabular data and transformer-based Timesformer on images that were combined into one hybrid model prediction.

Results: The Timesformer model and the XGBOOST model reached ROC AUC of 70% - 63%, balanced accuracy of 67% - 62%, with sensitivity of 80% -75%, respectively. While the hybrid ensemble model improved performance and achieved ROC AUC of 69% with a balanced accuracy of 69% and sensitivity of 90%.

Conclusion: This study demonstrates the potential of combining retinal imaging, and machine learning models to predict genetic risk factors of AD, bridging the gap between non-invasive early diagnostics and genetic risk assessment for Alzheimer's disease. By combining imaging and cognitive function and brain imaging measures, we enhance the ability to mark correctly potential patients' risk factors for AD.

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AI2

Near InfraRed Imaging for the Assessment of Geographic Atrophy Using Deep Learning

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Purpose: Geographic-atrophy (GA), an advanced form of age-related-macular-degeneration (AMD). Fundus-Autofluorescence (FAF) is currently the gold-standard imaging for the assessment of GA dimensions and progression. However, blue-FAF modality has several limitations, specifically failure to reliably demonstrate foveal involvement and lacking multiple sequential FAF imaging. Near-Infrared-Reflectance (NIR) is a non-invasive imaging modality. GA on NIR images is defined as sharply demarcated hyperreflective regions ≥250 µm in diameter. Our study aimed to assess the use of an artificial-Intelligence (AI) algorithm to automatically identify GA lesions using NIR.

Methods:
We analyzed patients with GA secondary to AMD at Rabin Medical Center. Inclusion criteria included patients aged 50 years and older with GA confirmed by NIR and OCT imaging. Patients with poor NIR imaging quality or GA secondary to other conditions were excluded. The control group consisted of patients with healthy-appearing retinas. Two datasets were prepared: one for binary classification and another for GA localization. Different deep learning models (ResNet50, EfficientNetB0, Vision Transformer B16, and YOLOv8 variants) were trained and were tested based on accuracy, precision, sensitivity, F1-Score and DICE coefficient.

Results:
A total of 113 GA patients (179 eyes) and 119 control patients (151 eyes) were included. The classification dataset included 330 images (54% of GA patients) and the localization dataset comprised 659 images. Vision Transformer B16 achieved the best classification performance: 98.5% precision, 98.4% sensitivity and 98.5% accuracy. EfficientNetB0 and ResNet50 also performed well, with accuracy above 95%. For GA localization, YOLOV8-Large achieved the highest sensitivity (91%), precision (91%), IoU (84%) and DICE coefficient (88%).

Conclusion
GA in dry-AMD can be identified and quantified reliably using NIR images. An AI model was developed for the purpose of identifying GA on NIR images.
This model can set grounds for NIR-based GA assessment on a routinely available imaging modality to consider treatment with emerging therapies for suitable candidates.

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AI3

Automatic Identification and segmentation of choroidal vessels on Optical Coherence Tomography, Using AI

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Purpose: Pachychoroid is characterized by dilated pachy-vessels seen on optical coherence tomography (OCT). Age-related macular degeneration (AMD) is characterized by the presence of drusen and a variety of choroidal anatomy. Our study aimed to assess the use of an AI model to identify pachy-choroid from AMD and segment choroidal vessels from OCT images.

Methods: 109,348 OCT B-scan images were collected from eyes with AMD and pachychoroid-related diseases. OCT images were analyzed and labeled according to the presence of pachy-vessels or no-pachy-vessels by a retina specialist. Subsequently, pachy-vessels were segmented by a retina specialist. The data was allocated by a ratio of 8:1:1 for training, testing, and validation.
A convolutional-neural-network (CNN) based model was proposed to classify the probability of the presence of pachy-vessels based on a binary image label. Four CNN architectures were compared: ConvNext-large-224, MobileNet, ResNet-50, and the EfficientNet-b0.
Moreover, four types of models were analyzed, three single-slab models: Central, peripheral, and random. A fourth model was based on multiple slab prediction.
The Yolo v8 large model was used to segment the choroidal vessels from B-scan OCT scans. The models' performance was internally validated and evaluated using enhanced depth imaging (EDI).

Results: 68,556 AMD and 40,792 Pachychoroid-related disease OCT B-scan images were included in the analysis.
The median age of the participants in the AMD group was 87.92(interquartile range[IQR],81.9-93.63]) years, and in the pachychoroid-related diseases 61.03[IQR], 45.77-71.52]) years. In the AMD group, men were 43.87%(n=86), and in the Pachychoroid-related group 30.95%(n=52).
The central slab model achieved an AUC of 0.95(sensitivity:81%, Specificity:94%), the peripheral slab model achieved an AUC of 0.92(sensitivity:90%, Specificity:89%), the random slab model achieved an AUC of 0.94(sensitivity:89%,
Specificity:93%), and the multi-slab model achieved an AUC of 0.96(sensitivity:76% Specificity:96%).
The YOLO v8 large achieved high accuracy for choroidal vessels segmentation in non-EDI (IOU) and EDI (IOU)

Conclusions: We examined the performance of an AI-CNN image algorithm model to identify pachychoroid in OCT and choroidal vessel AI segmentation using the YOLO. The central-slab model exhibited similar performance as the multi-slab. This insight may enhance our capability to differentiate the two entities, minimizing misdiagnosis and leading to more efficient and tailored treatment for patients.

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AI4

A Behavioral-Based Machine Learning Predictive Model for Myopia in Children

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Purpose: To develop a predictive model for myopia in children that emphasizes behavioral factors, utilizing a matched cohort study design, and to investigate the impact of each predictive feature on the probability of developing myopia.
Methods: This study used data from the iRead Study, which examined myopia prevalence and progression in children. Participants (ages 5-12 years, 64 myopic: non-myopic, 36 female: 126 male) with best-corrected visual acuity of 6/9 or better underwent cycloplegic autorefraction and wore an Actiwatch for 10–14 days to measure light exposure, activity, and sleep. Parents completed a questionnaire on demographics, near work, education, and screen use. Myopia was defined as spherical equivalent refraction ≤ −0.50 D. The cohort was matched for age, gender, and educational system. Predictive variables included objective measure of physical activity, sleep, and light exposure and subjective measures of near work and demographic factors. Statistical regression models adjusted for age, gender, group, and daylight exposure. Machine learning (ML) models were developed using 19 features selected via SHapley Additive exPlanations (SHAP) values and domain relevance, with performance evaluated using AUC metrics.
Results: Regression analyses identified significant associations between myopia and several factors, including longer school days $p<0.04$) and more time reading and writing ($p<0.01$) and doing near work ($p<0.04$). The Machine Learning Balanced Random Forest (BRF) model achieved an AUC of 0.7, sensitivity of 0.64 and specificity of 0.68 for predicting myopia. SHAP analysis highlighted key predictors. Longer hours in school, writing and reading, near work and age were positive predictors while longer hours outdoors was a negative predictor.
Conclusions: This study demonstrates the feasibility of predicting myopia in children using demographic, environmental, and behavioral factors. The results emphasize the role of modifiable lifestyle behaviors in assessing and mitigating myopia risk, offering a foundation for targeted prevention strategies.

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AI5

Machine Learning Analysis of Factors Influencing Suboptimal Visual Outcomes Post-Cataract Surgery

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Background: Cataract surgery often improves visual acuity, but some patients do not achieve clinically significant enhancements, defined as an increase of at least one row (5 letters or 0.1 in BCVA). This study explores factors associated with suboptimal outcomes post-surgery.

Methods: A retrospective cohort study at Hadassah Medical Center reviewed patients undergoing cataract surgery from January 2018 to February 2022. The study assessed demographic variables, surgical complications, surgeon experience, and surgery timing, comparing patients with and without significant BCVA improvements. Machine Learning (ML) predicted non-significant improvements, with SHAP analysis determining the impact of various variables.

Results: From 691 eyes of 590 patients, 561 had pre-operative BCVA data. The average age was 71.8±10.7 years; 50.6% female. Preoperative BCVA improved from 0.71±0.72 to 0.24±0.33 LogMAR, a mean increase of 57.9%. Still, 22.9% of patients (129/561) showed non-significant improvements. Regression analysis adjusting for pre-operative BCVA, identified key predictors: operated eye side ($p=0.01$), only eye ($p=0.005$), multiple preoperative risk factors ($p=0.006$), and resident experience, especially third-year residents ($p=0.01$), along with the preoperative cataract risk score ($p=0.01$). ML model achieved an AUC of 0.83 and sensitivity of 76%. SHAP analysis showed pre-operative BCVA as the primary predictor, with values worse than 0.4 BCVA indicating a higher likelihood of non-significant improvement. Additional factors included age, residency experience, surgery month, operated eye side, and preoperative cataract risk score.

Conclusions: The study identified pre-operative BCVA, surgeon experience, only eye, and multiple preoperative risk factors as key predictors of post- surgery visual outcomes. Notably, preoperative BCVA worse than 0.4 strongly suggests lesser improvement. The side of the eye operated on and surgery timing also were influential but require further investigation. Findings emphasize the importance of personalized patient assessments and targeted improvements in surgical training.

Keywords: Cataract surgery, BCVA, Visual Outcome, Machine Learning, SHAP analysis, Predictive modeling.

SHAP dependence plot showing the cutoff in preoperative BCVA that impacts visual outcomes. Positive SHAP values increase the likelihood of non-significant BCVA improvements. Age is indicated by a color gradient. The vertical dashed line at BCVA = 0.35 marks the threshold for identifying patients at risk for non-significant improvements.

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