האגודה הישראלית לחקר העין והראיה
Israeli Society for Vision & Eye Research

PROGRAM & ABSTRACTS
42nd Annual Meeting

Einan Hall, Azrieli Center, Modiin
March 3rd, 2022

תכנית ותקצירים
הכינוס השנתי ה-42
אולם עינן, מרכז עזריאלי, מודיעין

3 במרץ, 2022

עריכת התוכנית: דר' סאמר חטיב, דר' שירי סודרי, דר' אביגיל בריוזקין, פרופ' שחר פרנקל

הפקת הכינוס ועיצוב והבאה לדפוס:

דבורה מרקס אוחנה, פרופ' שחר פרנקל

ISRAELI SOCIETY FOR VISION AND EYE RESEARCH The 42nd Annual Meeting, March 3rd, 2022 Program at a glance	
Session	**Time**
Gathering and Coffee	08:30
Opening remarks	08:55
Cornea & Refraction Moderators: Irit Bahar & Michael Mimouni	09:00
Neuro-ophthalmology & Visual Function Moderators: Nitza Goldenberg-Cohen & Eyal Aloni	09:40
Oculoplastics, Oncology & General Moderators: Daniel Briscoe & Oded Sagiv	10:20
Coffee break	11:00
Retina & AMD Moderators: Shiri Soudri & Samer Khateb	11:20
Genetics & Retinal degeneration Moderators: Dror Sharon & Dinah Zur	12:05
Awards & General meeting	12:45
Guest Lecture - Dr. Daphne Haim-Langford Behind the scenes of innovation	13:00
Lunch	13:40
Animal Models & Therapy Moderators: Ron Ofri & Avigail Beryozkin	14:20
Glaucoma & Anterior Segment Moderators: Assaf Kratz & Noa Gefen	14:55
Closing remarks	15:35

יושבי ויושבות הראש של האגודה הישראלית לחקר העין והראייה

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
Prof. Saul Merin	1986-1989	פרופ' שאול מרין ז"ל
Prof. Shabtay Dikstein	1990-1993	פרופ' שבתאי דיקשטיין
Prof. Fabian Abraham	1994-1996	פרופ' פביאן אברהם ז"ל
Prof. Ido Perlman	1997-1999	פרופ' אידו פרלמן
Prof. Jacob Pe'er	2000-2003	פרופ' יעקב פאר
Prof. Ahuva Dovrat	2004-2006	פרופ' אהובה דברת ז"ל
Prof. Mordechai Rosner	2007-2009	פרופ' מרדכי רוזנר
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	פרופ' שחר פרנקל

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

Prof. Shahar Frenkel - Chairman	**פרופ' שחר פרנקל- יו"ר**
Prof. Jaime Levy – Treasurer	**פרופ' חיים לוי - מזכיר-גזבר**
Prof. Michal Kramer	**פרופ' מיכל קרמר**
Prof. Yossi Mandel	**פרופ' יוסי מנדל**
Dr. Samer Khateb	**דר' סאמר חטיב**
Dr. Shiri Soudry	**דר' שירי סודרי**
Dr. Avigail Beryozkin-Muniz	**דר' אביגיל בריוזקין-מוניץ**
Dr. Ido Didi Fabian	**דר' עידו דידי פביאן**

עבודות מצטיינות 2021

מלגות נסיעה ל- ARVO למרצות של העבודות המצטיינות 2021 ניתנות בעזרת מענקים שנתרמו באדיבות **משפחת מרין לזכרו של פרופ' שאול מרין ז"ל ועמותת "לראות".**

Lina Zelinger
Neurobiology Neurodegeneration & Repair Laboratory, NEI, Bethesda, MD, USA
The message in the non-coding RNAs of the mammalian retina

Anna Altshuler
Department of Genetics & Developmental Biology, The Rappaport Faculty of Medicine & Research Institute, Technion, Haifa, Israel
Capturing limbal epithelial stem cell population dynamics, signature & niche

80% ממקרי העיוורון ניתנים למניעה באיתור 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 ,בנוסף, עד היום אנו מעורבים ב- 21 מחקרים רפואיים בתחום הראייה.

בעלי תפקידים בעמותת לראות

נשיא העמותה	יו"ר העמותה	מנכ"ל העמותה
פרופ מרדכי שני	אוהד להב	נדין הולנדר

חברי הועד המנהל:

פרופ אדו פרלמן : יו"ר המועצה המדעית,

פרופ איתי חוברס, פרופ שלמה מלמד, פרופ אריה סולומון, פרופ אירית בכר, פרופ נועם שומרון , פרופ' דב וינברגר, פרופ' ענת לוינשטיין, פרופ' חנא גרזוזי, פרופ' יעקב פאר, פרופ' אהוד אסיה, פרופ' דרור שרון, פרופ' יאיר מורד, פרופ' אבי סלומון, פרופ' חני ורבין, ד"ר רונית לוינגר, ד"ר יפית שטרק, , מר מרק עמוס, ד"ר ניר ארדינסט.

הפרויקטים של עמותת לראות

בדיקות בקהילה

קשישים

עשרות אלפי קשישים בישראל, מקבלים את הידרדרות ראייתם, לעיתים עד לכדי עיוורון, כגזירת גורל. הם לא מודעים לכך שהרפואה השתכללה והתקדמה כך שניתן במקרים רבים להציל ולשפר משמעותית את ראייתם ואת איכות חייהם.

לשם כך, החלטנו בעמותת לראות להביא את המרפאה לסביבתם הקרובה של הקשישים - למועדון, למרכזי יום ומתנסים, שם אנו עורכים ימי בדיקות מרוכזים הפרויקט מתקיים בכל הארץ.

מאז מגפת הקורונה עמותת לראות מקיימת שירות של ביקורי בית של רופא עיניים ו/או אופטומטריסט למרותקים לביתם.

ילדים

קוצר ראייה ועין עצלה הן שתי בעיות העיניים נפוצות בקרב ילדים. בשיתוף עם גני ילדים ורשויות מקומיות אנו עורכים בדיקות עיניים לילדים החל מגיל פעוטות ועד גילאי בית ספר.

הנגשת מידע ויעוץ רפואי

עמותת לראות מחויבת להעלאת מודעות לבריאות העין ומניעת עיוורון.

העמותה מעמידה לרשות הציבור הרחב פורומים מקצועיים אונליין בהובלת רופאים בכירים בנושאים שונים כמו: אובאיטיס, גלאוקומה, סכרת, קטרקט ועוד.

המטה הישראלי למחקר חדשני בתאי גזע

כחלק ממאמץ לאומי עמותת לראות מובילה את הקמתו של המטה הישראלי למחקר בתאי גזע אשר ישמש כגוף המאגד תחתיו חוקרים מכל התחומים ויוביל מחקר חדשני בתאי גזע.

חודש המודעות:

מדי שנה בחודש דצמבר העמותה יוצאת בקמפיין ארצי להעלאת מודעות לבעיות שונות הקשורות בראייה ועיוורון. זהו פרויקט שהתחיל עוד בשנת 2008 ומאז נוחל הצלחה וחשיפה לקהלים ממוקדים (קשישים, משפחות וקרובים של קשישים, קהילה מדעית ורופאים). במסגרת פעילויות חודש המודעות מתקיימות הרצאות, חשיפה במדיה, הפקת מגזין בנושא קידום בריאות העין בשיתוף איגוד רופאי העיניים בהוצאת עיתון 'הארץ' ועוד.

בקרו אותנו באתר: https://www.eyes.org.il/Home, להרשמה לניוזלטר:
https://www.eyes.org.il/%D7%A6%D7%95%D7%A8-%D7%A7%D7%A9%D7%A8

WWW.EYES.ORG.IL
NADINE@EYES.ORG.IL

Guest speaker

Thursday, March 3rd, 2022, at 13:00

The Einan Convention Hall in the Azrieli Mall - Modiin

Dr. Daphne Haim-Langford

Behind the scenes of innovation

Dr. Haim-Langford is the founder and CEO of Tarsier Pharma. She has over 20 years of experience in the biomedical industry as an investor, entrepreneur, and executive. Prior to founding Tarsier Pharma, she served as VP of business development at Xenia venture capital, where she managed the life sciences practice, led investments in the medical technology and biotechnology space, and served on the boards of pharmaceutical, medical device, and biotechnology companies in various stages of product development (from early pre-clinical through clinical development, up to sales & marketing, M&A deals). Few examples include Meditate (Acquired by Olympus for up to $285 million), Orthospace (Acquired by Stryker for up to $220 million), Omnix Medical, and others. At Xenia, she also co-founded and served as the Chairperson of the board at Eximore, an ophthalmic drug delivery company.

Before joining Xenia, Dr. Haim-Langford was VP of Business Development at Medingo (Acquired by Roche for $200M million). She co-founded the Israeli Biomimicry Organization, a non-profit organization aimed to increase awareness of the biomimicry discipline and drive inspiration by nature as a source for biomedical innovations. Dr. Haim Langford holds a Ph.D. in Biophysics from the Technion, the Israeli Institute of Technology.

AC	First name	Family name	title	Session	page #
AC	Rima	Sheety	Objective Comparison of Low vs. High ADD Multifocal Soft Contact Lenses	Cornea	17.
	Eitan	Livny	Tomography Masquerade Syndrome	Cornea	18.
AC	Meydan	Ben Ishai	Outcomes of corneal neurotization using processed nerve allografts: a five patients successful case series	Cornea	19.
	Eyal	Gal	Objective and Subjective Evaluation of Novel Soft MiniScleral Contact Lenses for Keratoconus	Cornea	20.
	Eliane	RozaneS	Outcomes of Repair of Total Graft Detachment following Descemet's Membrane Endothelial Keratoplasty	Cornea	21.
	Zipora	Boim	Ocular parameters and calculated IOL: comparison of new optical biometric devices with a gold standard and a corneal topographer	Cornea	22.
AC	Nadav	Levinger	Visual outcomes of cataract surgery after radial keratotomy	Cornea	23.
AC	Nadav	Levinger	Visual Outcome of IntraLase-assisted LASIK enhancement to correct post PRK residual refractive error	Cornea	24.
	Gad	Serero	Is oblique astigmatism reminiscent of meridional amblyopia?	Cornea	25.
AC	Eman	knaane	Unravelling the influence of LOX and niche biochemical rigidity on limbal stem cell function and corneal integrity	Cornea	26.
AC	Assaf	Gershoni	Syndecan-1 expression in the corneal epithelium of keratoconus patients, and its correlation to disease severity	Cornea	27.
	Yoav	Nahum	Finite element modelling of circular corneal incisions	Cornea	28.
AC	Itay	Nitzan	The definition-dependent nature of myopia prevalence: a nationwide study of 1.5 million adolescents	Refraction	29.
AC	Alon	Peled	Myopia and early onset type 2 diabetes: A nationwide cohort study	Refraction	30.

AC	**Daphna**	**Landau Prat**	**Recovery of vision after optic nerve sheath fenestration in children and adolescents with elevated intracranial pressure**	**Neuro Ophthalmology**	**31.**
AC	**Dmitriy Yehonathan**	**Kurbet**	**Inter-session and inter-examiner reliability of the Mallett Unit associated phoria test**	**Neuro Ophthalmology**	**32.**
AC	**Ronen**	**Spierer**	**Surgical outcomes of medial rectus advancement for consecutive exotropia**	**Neuro Ophthalmology**	**33.**
AC	**Auria**	**Eisen-Enosh**	**Improving Visual Function Following Temporal Perceptual Learning**	**Neuro Ophthalmology**	**34.**
	Hadas	**Stiebel-Kalish**	**Steroid-sparing maintenance immunotherapy for MOG-IgG associated disorder**	**Neuro Ophthalmology**	**35.**
AC	**Kfir**	**Inbal**	**Oculomotor Measures Of Visual Working Memory Load**	**Neuro Ophthalmology**	**36.**
AC	**Laura**	**Benhaim Sitbon**	**Heterophoria alters lateral cortical interactions**	**Neuro Ophthalmology**	**37.**
	Shimrit	**Shani**	**Visual tracking smoothness as a diagnostic marker of traumatic brain injury**	**Neuro Ophthalmology**	**38.**
	Ron	**Meidan**	**The spatial and chromatic attributes of the pupillary response to aversive pattens: towards the development of a screening tool for visual hyper-sensitivity**	**Neuro Ophthalmology**	**39.**
AC	**Itay**	**Shekel**	**Studying Prosthetic and Natural Vision Cortical Interaction in V1 at the Population and Cellular Level.**	**Neuro Ophthalmology**	**40.**
AC	**Noah**	**Rappeport**	**Visual crowding: a bottleneck for visual function acquisition after sight retrieval**	**Neuro Ophthalmology**	**41.**
	Revital	**Zilka**	**The varied severity of motion sickness can be predicted by differences in audio-visual binding**	**Neuro Ophthalmology**	**42.**
AC	**Avital**	**Moshkovitz**	**The central visual field might mediate night vision in normally developed populations and Albino subjects**	**Neuro Ophthalmology**	**43.**
AC	**Yakov**	**Vega**	**Neuroretinal rim thickness in optic disc edema**	**Neuro Ophthalmology**	**44.**
	Guy	**Barnett-Itzhaki**	**Evaluation of distance stereoacuity in children with a novel digital application**	**Visual function**	**45.**

	Ahuva	**Ravid-Saffir**	**Development and validation of a questionnaire for assessing Parents' awareness and perception of vision screening and exams for children: a Delphi study**	**Visual function**	**46.**
	Josh	**Kruger**	**VARIANTS OF THE CLOVERLEAF PATTERN THAT ARE ASSOCIATED WITH INATTENTIVENESS DURING AUTOMATED PERIMETRY**	**Visual function**	**47.**
	Tamara	**Wygnanski-Jaffe**	**Reading Performance Improvement in Amblyopic Children Using Dichoptic Eye-tracking Training and an Eye-tracking Based- 30 Second Reading Test**	**Visual function**	**48.**
AC	**Yossi**	**Eshel**	**Chromatic Pupilloperimetry for Objective Diagnosis and Monitoring of Patients with Pseudotumor Cerebri**	**Visual function**	**49.**
	Avi	**Caspi**	**Utility of eye tracking in a visual cortical prosthesis**	**Visual function**	**50.**
	Ravid	**Doron**	**Objective measures of viewing behavior of myopic and non-myopic adults during near tasks**	**Visual function**	**51.**
AC	**Dima**	**Shbita**	**Rod, cone and melanopsin mediated pupil responses to focal light stimuli in the central and peripheral retina in Fragile X carriers**	**Visual function**	**52.**
AC	**Daphna**	**Landau Prat**	**Outcome of primary monocanalicular stent placement in pediatric Down's syndrome patients with congenital nasolacrimal obstruction**	**Oculoplastics**	**53.**
	shiran	**madgar**	**The role of thyroid stimulating immunoglobulin (TSI) in evaluating Thyroid Eye Disease**	**Oculoplastics**	**54.**
AC	**Noa**	**Kapelushnik**	**Why posterior approach ptosis surgery can fail**	**Oculoplastics**	**55.**
AC	**Lital**	**Smadar**	**The tobacco consumption effect on the clinical findings, treatment and prognosis of TED patients**	**Oculoplastics**	**56.**
AC	**Ofira**	**Zloto**	**Reliability of Ptosis diagnosis on assessment via video consultation**	**Oculoplastics**	**57.**
AC	**Yakov**	**Rabinovich**	**Eyelid cysts over three generations**	**Oculoplastics**	**58.**
AC	**Zvi**	**Gur**	**Outcomes of Mueller's Muscle Conjunctival Resection: Ethnic Considerations**	**Oculoplastics**	**59.**

AC	**Zvi**	**Gur**	**Outcomes of Unilateral Mueller's Muscle Conjunctival Resection: Implication of Hering's Law**	**Oculoplastics**	**60.**
AC	**Lital**	**Smadar**	**The Correlation Between Chronic Usage of Topical Anti-Glaucoma Eye Drops and Lower Eyelid Increased Laxity**	**Oculoplastics**	**61.**
AC	**Zvi**	**Gur**	**Scleral Contact Lens Designed to Reduce Ptosis**	**Oculoplastics**	**62.**
AC	**Malak**	**Sultan**	**Ocular related emergencies at Hadassah Medical Center emergency department: a retrospective study**	**General**	**63.**
	Vicktoria	**Vishnevskia Dai**	**Uveal melanoma Patients reported outcomes (PROMS)**	**Oncology**	**64.**
	Maya	**Eiger-Moscovich**	**BAP1 immunohistochemistry in post-brachytherapy uveal melanoma**	**Oncology**	**65.**
AC	**Ofira**	**Zloto**	**SECOND-LINE THERAPY IN YOUNG PATIENTS WITH RELAPSED OR REFRACTORY ORBITAL RHABDOMYOSARCOMA**	**Oncology**	**66.**
AC	**Ofira**	**Zloto**	**Periocular Presentation of Solitary Plasmacytomas and Multiple Myeloma**	**Oncology**	**67.**
AC	**Noa**	**Jackson Amichay**	**PRIMA (PRegnancy In uveal Melanoma Analysis) Study - A European OOG MultiCenter Study**	**Oncology**	**68.**
AC	**Noa**	**Jackson Amichay**	**Elevated intraocular pressure following intravitreal methotrexate for vitreo-retinal lymphoma**	**Oncology**	**69.**
AC	**Abeer**	**Hammod**	**Responses to treatment of retinoblastoma in the IAC and IVitC era**	**Oncology**	**70.**
	Joel	**Hanhart**	**Optical coherence tomography structural and angiographic assessment of retinal and choroidal crystals in Infantile Nephropathic Cystinosis**	**Retina**	**71.**
	Dan	**Schwartz**	**Is Myopic Macular Degeneration a Choroidopathy?**	**Retina**	**72.**
AC	**Nadav**	**Levinger**	**Comparison of The Retinal and optic nerve head vascular networks using OCT-A between hypoxic and normal subjects**	**Retina**	**73.**

	Efrat	**Simon**	**Investigating the survival and function of retinal ganglion cells in an organotypic culture: An in-vitro model for studying synaptogenesis**	**Retina**	**74.**
AC	**Dolev**	**Dollberg**	**Long-term follow up on patients treated with laser for retinopathy of prematurity**	**Retina**	**75.**
	Gilad	**Rabina**	**The Association of Choroidal Thickness with Rhegmatogenous Retinal Detachment Surgery Outcomes**	**Retina**	**76.**
	Ron	**Abutbul**	**Screening for retinal pathologies via anomaly detection and localization in OCT scans**	**Retina**	**77.**
AC	**Dana**	**Barequet**	**Foveal-Splitting Rhegmatogenous Retinal Detachment – a New Entity?**	**Retina**	**78.**
	Jonathan	**Levine**	**Abnormal Renal Profiles and Diabetic Eye Disease in Latino and African American Cohorts**	**Retina**	**79.**
	Ygal	**Rotenstreich**	**Rapid distribution of bevacizumab throughout the posterior segment in rabbit eyes following suprachoroidal delivery using a novel injection system.**	**Retina**	**80.**
	Zehavit	**Goldberg**	**Intrinsic Expression of Coagulation Factors and Protease Activated Receptor 1 (PAR1) in Photoreceptors and Inner Retinal Layers**	**Retina**	**81.**
	Joel	**Hanhart**	**Pseudophakia as a Surprising Protective Factor in Neovascular Age-Related Macular Degeneration**	**AMD**	**82.**
	Or	**Shmueli**	**Geographic atrophy area measurement: comparison between fundus autofluorescence and OCT**	**AMD**	**83.**
AC	**Brice**	**Vofo**	**Clinical outcome of a modified treat-and-extend protocol in the treatment of neovascular age-related macular degeneration.**	**AMD**	**84.**
	Gilad	**Rabina**	**COVID-19 Pandemic Lockdowns Impact on Visual Acuity of Neovascular AMD Patients: A Large cohort**	**AMD**	**85.**
AC	**Efrat**	**Naaman**	**The retinal toxicity of the pro-inflammatory and amyloidogenic S100A9 proteins**	**AMD**	**86.**
AC	**Amanda**	**Qarawani**	**PEDF-derived peptide inhibits Amyloid-β internalization and ameliorates retinal toxicity**	**AMD**	**87.**

AC	**Baty**	**Rinsky**	**Development of Blood Biomarkers for anti-VEGF Treatment Response in Neovascular Age Related Macular Degeneration**	**AMD**	**88.**
	Leslie	**Rebibo**	**Intravitreal dexamethasone palmitate nanocapsules as a potential novel treatment for choroidal neovascularization**	**AMD**	**89.**
	Devora	**Potash miller**	**Evaluation of HOBAM-11 as a Potential Novel Anti-angiogenic Therapy for Neovascular Age Related Macular Degeneration**	**AMD**	**90.**
AC	**Michelle**	**Grunin**	**Spatial modeling of variants in complement genes associated with age-related macular degeneration**	**AMD**	**91.**
	Tamar	**Ben-Yosef**	**Autosomal dominant retinitis pigmentosa with reduced penetrance due to an intronic mutation in PRPF31**	**Genetics**	**92.**
AC	**Yogapriya**	**Sundaresan**	**Dual mutational mechanism of the KIZ c.226C>T mutation as the cause of autosomal recessive retinitis pigmentosa**	**Genetics**	**93.**
AC	**Nina**	**Schneider**	**RNA Editing of Israeli Founder Nonsense Mutations causing IRDs using Site-Directed Adenosine Deaminase Acting on RNA**	**Genetics**	**94.**
AC	**Shai**	**Ovadia**	**The gene networks regulating retinal pigmented epithelium differentiation are controlled by SWI/SNF complexes**	**Genetics**	**95.**
	Dror	**Sharon**	**Identification of autosomal recessive novel genes and retinal phenotypes in members of the solute carrier (SLC) superfamily**	**Genetics**	**96.**
	Ayellet	**Segre**	**Integrating gene regulation and single cell expression with genetic associations identifies genes and cell types contributing to primary open angle glaucoma**	**Genetics**	**97.**
AC	**Ofek**	**Freund**	**Novel mutation in COL9A1 causes autosomal recessive high myopia in Bedouin family**	**Genetics**	**98.**
AC	**Tamar**	**Hayman**	**structural variant analysis of a large set of whole exome sequencing data from Israeli and Palestinian patients with inherited retinal diseases**	**Genetics**	**99.**
AC	**Manar**	**Salameh**	**abca4 c.859-25A>G,a frequent palestinian founder mutation affecting the intron 7 branchpoint,is associated with early-onset stargardt disease**	**Genetics**	**100**
	Libe	**Gradstein**	**Hermansky-Pudlak syndrome in a Bedouin family is caused by a novel splice-site mutation in HPS5**	**Genetics**	**101**

	Idan	**Hecht**	**Micro-chromosomal deletions and NR5A2 gene involvement with autosomal dominant nystagmus.**	**Genetics**	**102**
AC	**Avigail**	**Beryozkin**	**FAM161A is expressed in rods and all cone types in the mouse and human retina**	**Retinal degenerations**	**103**
	Ifat	**Sher**	**Synthetic formulations of 9-cis beta carotene for treatment of retinitis pigmentosa**	**Retinal degenerations**	**104**
	Issac	**Levy**	**The effect of insulin degrading enzyme inhibitor drops on corneal wound healing (rat model)**	**Animal models**	**105**
AC	**Dahlia**	**Palevski**	**Anti-inflammatory and retinal blood barrier stabilization activities of 3K3A-Activated Protein C in a murine model of acute ocular inflammation**	**Animal models**	**106**
AC	**Gil**	**Ben-David**	**Cannabinoid 2 (CB2) receptor upregulation in experimental autoimmune uveitis (EAU)**	**Animal models**	**107**
AC	**Nitay**	**Zuk-Bar**	**Study on the BAF (SWI/SNF complex) subunit BAF155 activities in the development and maintenance of pigmented eye lineages in mammals.**	**Animal models**	**108**
AC	**Inbal**	**Benhar**	**Single cell profiling of non-neuronal retinal cells after optic nerve axotomy reveals tissue dynamics in CNS injury**	**Animal models**	**109**
	Dikla	**Arad**	**The effect of hemodialysis on intraocular pressure in dogs**	**Animal models**	**110**
AC	**Basel**	**Obied**	**Cobalt trace elements injected to mice may cause retinal toxicity**	**Animal models**	**111**
	Alon	**Zahavi**	**Multimodal analysis of gadolinium in mouse tissues**	**Animal models**	**112**
AC	**Lionel**	**Sebbag**	**Precorneal retention time of ocular lubricants: A fluorophtometric study in a large animal model (dogs)**	**Therapy**	**113**
AC	**Daphna**	**Landau Prat**	**Silicone sling frontalis suspension for congenital ptosis: outcome of 174 consecutive cases**	**Therapy**	**114**
AC	**Daphna**	**Landau Prat**	**Patient-specific orbital implants vs. pre-formed implants for internal orbital reconstruction**	**Therapy**	**115**
AC	**Daphna**	**Landau Prat**	**Management of congenital nasolacrimal duct obstruction in down syndrome**	**Therapy**	**116**

AC	**Daniel**	**Raz**	**Oxidative stress facilitates exogenous mitochondria internalization and survival in retinal ganglion precursor cells**	**Therapy**	**117**
AC	**Ofira**	**Zloto**	**Medical Cannabis Oil for Benign Essential Blepharospasm: A Prospective, Randomized Controlled Pilot Study**	**Therapy**	**118**
AC	**Asaf**	**Shemer**	**Decreased effectiveness of 0.01% atropine treatment for myopia control during prolonged COVID-19 lockdowns**	**Therapy**	**119**
AC	**Anfisa**	**Ayalon**	**Behavior of Intravitreally Injected Drugs Simulated by Two Models of the Silicone Oil Filled Eye**	**Therapy**	**120**
AC	**Anfisa**	**Ayalon**	**Wetting of the Amphiphilic Retinal Surface and its Implications for the use of Silicone Oil as a Tamponading Agent in Retinal Surgery**	**Therapy**	**121**
AC	**Karny**	**Shouchane-Blum**	**The association between pupil diameter and apparent chord mu length value**	**Therapy**	**122**
	Moria	**Oz**	**The neuroprotective effect of Phlomis viscosa Poiret and Ficus benjamina in the treatment of optic nerve crush**	**Therapy**	**123**
	Elie	**Beit-Yannai**	**SMAD7 miRNA delivery by NPCE exosomes Attenuate Wnt Signaling in Trabecular Meshwork Cells In Vitro**	**Glaucoma**	**124**
	Assaf	**Kratz**	**Assessment of the iCare Home 2, a New IOP Self-Measurement Tonometer**	**Glaucoma**	**125**
	Oren	**Pe'er**	**Association between obesity and intraocular pressure in dogs**	**Glaucoma**	**126**
AC	**Reut**	**Ifrah**	**validation of the cobra high definition meibographer in symptomatic and asymptomatic patients**	**Anterior Segment**	**127**
	Ruby	**Shalom-Feuerstein**	**Identification of murine limbal epithelial stem cell population dynamics, signature and niche**	**Anterior Segment**	**128**
	Rita	**Zlatkin**	**Pupillary dilation and axial length in patients with high myopia**	**Anterior Segment**	**129**
AC	**Shira**	**Hadad-Porat**	**Identification of the role of immune cells in controlling limbal epithelial stem cells**	**Anterior Segment**	**130**
AC	**Mohammed**	**Darawshe**	**Gadolinium detection in tears of humans and mice**	**Anterior Segment**	**131**

	Tal	**Zobok**	**Do mineral dietary supplements affect the levels of trace elements in tears of athletes?**	**Anterior Segment**	**132**
AC	**SHALINI**	**DIMRI**	**Uncovering mechanisms of corneal healing following catastrophic limbal stem cell loss**	**Anterior Segment**	**133**
AC	**Waseem**	**Nasser**	**Pathophysiology and rescue of P63-related limbal stem cell deficiency**	**Anterior Segment**	**134**
AC	**Yulia**	**Sheinfeld**	**Changes in tears or sweat elements levels before and after physical activity in athletes may predict dehydration**	**Anterior Segment**	**135**

23 AC

Objective Comparison of Low vs. High ADD Multifocal Soft Contact Lenses

Rima Sheety, Wasim Sheety, Eyal Gal, Liat Gantz
Department of Optometry and Vision Science, Hadassah Academic College

Purpose

This prospective, case series examined the objective and subjective visual quality of low vs. high addition Dispo Air Multi daily multifocal contact lenses (Cooper Vision, Israel) in a cross-over design.

Methods

Healthy participants were fit with both low and high addition multifocal contact lenses, each worn for a week. The first lens was randomly determined. For each type of lens worn, the physiological fit was evaluated with a slit lamp, and the distance and near Snellen visual acuity (VA), higher order aberrations (L80+ Wavefront aberrometer, Visionix Luneau, Chartres, France), the Pelli-Robson and FACT (Vision Science Research Group, USA) contrast sensitivity (CS) was measured, and a subjective questionnaire was filled out. Results were compared using a Wilcoxon Signed Rank test.

Results

Eight participants (6 females, 2 males, mean age: 50.38 ± 5.95, range: 40 to 56) were included in the case series. Their best spherical refraction in the right and left eyes was -2.10±2.48 and -2.30±2.34 DS, respectively. The mean distance and near VA with low and high addition was 0.8 and 0.74 and 0.7 and 0.83 Snellen Decimal, respectively. Both lenses significantly improved VA from baseline but were not significantly different from each other. Low addition lenses improved distance FACT CS significantly more than the high addition lenses by 24-30% for 3, 6, 12, and 18 cycles/deg. However, higher order aberrations and Peli Robson CS was not significantly different between the lenses. There was no subjective preference for any lens, and the majority of participants reported no differences between the two lenses.

Conclusion

The performance of low and high addition multifocal contact lenses was similar for all quantitative and qualitative measures, except for the FACT CS which was improved with the low addition lenses. As such, this is the recommended lens for optimal visual quality.

29

Tomography Masquerade Syndrome

Eitan Livny(1,2), Alexander Chorny(1,3), Yoav Nahum(1,2), Ruti Sela(1,2), Ori Mahler(4,5), Asaf Gershoni(1,2), Irit Bahar(1,2)

(1)Department of Ophthalmology, Rabin Medical Center, Petah-Tikva, Israel (2)Sackler faculty of medicine, Tel-Aviv University, Tel-Aviv, Israel (3)Department of Ophthalmology, Soroka Medical Center, Beer-Sheva, Israel (4)Deaprtment of Ophthalmology, Shamir Medical Center, Be'er Ya'acov, Israel (5)Enaim Medical Center, Tel-Aviv, Israel

Purpose: To describe a series of patients that were previously diagnosed with corneal ectasia based on their tomography and topography data. Upon further examinations and Anamnesis review, the diagnosis was changed and corneal ectasia was ruled out.

Methods: Descriptive case series.

Results: The following cases will be discussed: 1) A patient with severe strabismus in which the tomography scans were done repeatedly when the eye was not aligned perpendicular to the scanning tomographer. This resulted in a false impression of Keratoconic corneal configuration. 2) A patient that had a huge Salzmann nodule, which looked as an ectasia on topography. The corneal surface normalized following surgical removal of the nodule. 3) A patient with unexplained vision deterioration that had a pathologic posterior corneal elevation on tomography. She was diagnosed with keratoconus, only later to realize that the measured diameter chosen for BFS on the Pentacam tomographer was wrong. After correction to an appropriate BFS diameter, Keratoconus was ruled-out. 4) A patient with complaints of sub-optimal vision in her right eye following LASIK in both eyes, was diagnosed with post-LASIK ectasia OD. The Topography showed central steepening of the right cornea and a normal post-op flattening in her left cornea. After careful anamnesis, it was found that her preoperative refraction in the right eye was hyperopic and left eye myopic, thus the right eye Lasik hyperopic treatment was confused for an ectasia.5) A patient that was diagnosed with post-PRK ectasia (based on his topographic parameters) was found to have a significant stromal haze in this eye during examination, explaining the pseudoectatic topography. Posterior elevation and other tomographic parameters were not in accordance with ectasia.

Conclusions: Ectasia-mimicking topographies/tomographies are rare. This case series describes causes for pseudoectasia that were not previously reported. The comprehensive ophthalmologist should be aware of such cases, which may substantially alter the treatment and prognosis of these patients.

33,AC

Outcomes of corneal neurotization using processed nerve allografts: a five patients successful case series

Meydan Ben Ishai, Inbal Avisar
Rabin Medical Center

Purpose: To report and present a case series of five patients who underwent corneal neurotization surgery with very good outcomes.

Methods: Five eyes of five female patients with neurotrophic keratopathy underwent corneal neurotization surgery at our establishment between 2018 and 2021. All cases were indirect sural nerve neurotization. Collected data included stage and etiology of NK as well as comorbidities, prior treatment history, neurotization technique, donor nerve site, preoperative and postoperative examination findings (i.e., ocular surface quality, corneal clarity, corneal sensation by Cochet-Bonnet esthesiometry, and visual acuity [VA]), and follow-up duration. Differences between preoperative and postoperative values were analyzed.

Results: All five procedures were carried out with no intra-operative complications. Mean visual acuity before surgery was 0.94 (±0.79) and following the procedure it improved to 0.84 (±0.86) (P=0.86). Mean Cochet-Bonnet esthesiometer score was 0.7 (±0.5) before surgery, this significantly improved to 3.0 (±1.67) after surgery (P=0.02). All five patient were satisfied with the result and gained good corneal sensation and major improvement of the keratopathy. All patients with a persistent epithelial defect preoperatively showed complete corneal healing by their last follow-up visit. Median follow-up duration was 25.8 months (±11.8).

Conclusion: Corneal neurotization is a novel surgical treatment for neurotrophic keratopathy. It is a relatively simple procedure with very good outcomes. Our experience suggests that corneal neurotization using nerve transfers and sural nerve grafts for patients with deteriorating neurotrophic keratitis is a safe procedure in adults. It successfully restored corneal sensation in all patients in our study and improved visual acuity for most.

35

Objective and Subjective Evaluation of Novel Soft MiniScleral Contact Lenses for Keratoconus

Eyal Gal 1, Joan Gispets2, Meira Zyroff1, Efrat Netanya1 Liat Gantz1
1- Department of Optometry and Vision Science, Hadassah Academic College, 2- University Vision Centre, Universitat Politicnica de Catalunya, Terrassa, Barcelona, Spain

Purpose: This prospective case series examined the objective and subjective visual quality of a new soft mini scleral contact lens for keratoconus (miniScK, Cooper Vision, Israel).

Methods: Participants with keratoconus between the ages of 40-60 were fit with a miniScK which was worn for two weeks. The physiological fit was assessed with a slit lamp and the Efron grading scale. Low and high contrast distance and near Snellen visual acuity (VA), higher order aberrations (HOA) and tomography (VX130 wavefront aberrometer), and Pelli-Robson contrast sensitivity (CS) were measured with the habitual vs. miniScK corrections. Participants reported daily hours of wear, and graded their visual quality and comfort using a Likert scale. Results were compared using Mann-Whitney U tests.

Results: Twenty one eyes of 11 keratoconic patients (8 female, mean age: 38 ± 13, range: 18-65) were included. Their mean best spherical and cylindrical refractions were -1.88 ± 3.10 and 3.36 ± 2.67, DS respectively. Participants reported a mean daily wear time of 6.44 ± 3.24 hours (ranging between 3-14 hours, with one patient wearing only one hour daily). Mean visual quality and comfort scores were 3.9 ± 0.9 and 2.9 ± 0.9, respectively. Itchy eyes, dry eyes and secretions were reported in 12, 2, and 2 eyes, respectively. Mean conjunctival and limbal redness, corneal oedema and staining and MGD scores were all < 1.2. Low contrast VA was not significantly improved (0.37 to 0.39, p=0.35), while high contrast VA was significantly improved (0.55 to 0.83 Snellen decimal, p<0.0001) with the lenses compared to habitual correction. The lenses significantly improved the total root mean square (4.7± 1.6 to 2.0 ± 0.7, p < 0.001) but not total HOA (1.3 ±0.6 to 0.8± 0.5, p= 0.08) or CS (1.2 ± 0.5 to 1.5 ± 0.2, p=0.23).

Conclusions: The lenses provided acceptable visual acuity with a mean wear duration of six hours and good subjective visual quality. However, lens comfort should be improved, with the majority experiencing itchy eyes and an overall comfort score of 2.9/5.

37

Outcomes of Repair of Total Graft Detachment following Descemet's Membrane Endothelial Keratoplasty

Eliane Rozanes, Avital Adler, Peter Ciechanowski, Yoav Nachum, Shmuel Graffi, Uri Elbaz, Irit Bahar, Eitan Livny
Department of Ophthalmology, Rabin Medical Center

Purpose: To present the outcomes of attempts to salvage total graft detachment following Descemet's membrane endothelial keratoplasty (DMEK).

Methods: A search of the electronic medical records of two tertiary medical centers for all patients who underwent DMEK yielded six cases of postoperative total graft detachment (2.54%). Graft salvage was attempted in all cases using repeated intracameral graft staining, unfolding, and reattachment to the stroma under 20% hexafluoride gas.

Results: In all cases, a free-floating totally detached graft was identified in the anterior chamber shortly after surgery. Salvage surgery resulted in a central, well-oriented, and fully attached graft. In three cases, the primary graft failed, and in two, the corneas cleared at first but failed after 2 months and 1 year respectively. In one case, the cornea remained clear during 1 year of follow-up but had a very low endothelial cell density.

Conclusion: Reattachment of fully detached DMEK graft is technically possible, but graft manipulation during the primary and secondary operations is likely to damage the endothelial cells, resulting in primary or early graft failure. If graft salvage is attempted, the probability of primary or early graft failure should be discussed with the patient, and expectations should be tempered accordingly.

44

Ocular parameters and calculated IOL: comparison of new optical biometric devices with a gold standard and a corneal topographer

Zipora Boim (1), Rivkah Lender(1), Devora Mirsky(1), Riki Greenberger(1), Lee Ben-Yaakov(1), Chaya Kashtan(1), Ibrahim Naffar(1), Shira Shine(1), Itay Chowers(1), Hadas Ben-Eli(1,2)
(1) Department of Ophthalmology Hadassah-Hebrew University Medical Center, Jerusalem, Israel (2) Department of Optometry and Vision Science, Hadassah Academic College, Jerusalem, Israel

Purpose: To compare ocular parameters measured by the Anterion (Heidelberg Engineering) and Eyestar 900 (Haag Streit Diagnostics) to those measured by the IOLMaster 700 (Carl Zeiss-Meditec). Final intraocular lens (IOL) calculation based on the measurements of each device was also compared, and corneal measurements were compared to those of the Pentacam (Oculus) topographer.

Methods: Participants were cataract surgery candidates aged 40 and above. Compared values were axial length (AL), anterior chamber depth (ACD), steep and flat K, cylinder and axis. IOL was calculated for each biometry device using the mean values of every parameter and the Barrett and Kane formulas. Statistical analysis was performed using paired sample t-test, Friedman test, Pearson's coefficient and Cohen's d effect size. Interchangeability of the biometry devices was analyzed using Bland and Altman.

Results: A total of 196 eyes (98 participants) were included in this study (47.9% female, mean age 68.8±9.7y, range 42-88y). Group 1 consisted of 157 eyes measured with the Eyestar and IOLMaster, with 48 eyes measured by Pentacam. Group 2 consisted of 38 eyes measured with the Anterion and IOLMaster, with 22 eyes measured by Pentacam. When comparing the IOLMaster to the Eyestar, no significant difference was found in mean AL or ACD (P=0.79, Cohen’s d 0.009; P=0.09; Cohen’s d 0.03, respectively). A significant difference was found in steep K measurements between the IOLMaster (44.52±1.92D), Eyestar (44.49±1.95D) and Pentacam (44.88±1.76D) (P=0.01). When comparing the IOLMaster to the Anterion, mean AL was 23.68±1.27mm vs. 23.57±1.27mm, respectively (P=0.006; Cohen’s d 0.08). Mean ACD was 3.27±0.73mm vs. 3.38±0.78mm (P=0.04; Cohen’s d 0.14). No significant difference was found in any corneal parameter between these devices and the Pentacam. Significant correlations were found in all four devices in all parameters other than flat and steep K axes. Bland and Altman analysis demonstrated agreement in all parameters of all biometry devices other than ACD between the IOLMaster and Eyestar. Using the Barrett and Kane calculators, spherical equivalent (SE) of the suggested IOL tended to be 0.50D lower with the IOLMaster.

Conclusions: The IOLMaster, Eyestar and Anterion show excellent agreement and interchangeability, with corneal measurements correlating well to the Pentacam. However, it is important to note that devices differed in the suggested IOL, which could impact the residual refraction. This observation requires further study in order to achieve maximal refractive results.

55 AC

Visual outcomes of cataract surgery after radial keratotomy

Nadav Levinger(1,2), Nir Erdinest(1,2), Naomi London(3), Eliya Levinger(1,4), Irit Barequet(1,5), Dana Barequet(1,4), Ori Mahler(1,6), Shalhevet Goldfeather Ben Zaken(1,7), Joseph Douieb(1), Shmuel Levinger(1)
1)Enaim Medical Center Jerusalem & Tel Aviv, Israel (2)Hadassah Medical Center, Jerusalem, Israel (3)Private Practice, Jerusalem, Israel (4)Tel Aviv Sourasky Medical Center, Tel Aviv, Israel (5)Goldschleger Eye Institute, Sheba Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Hashomer, Israel (6)Shamir medical center department of ophthalmology (7)Department of Ophthalmology, Kaplan Medical center, Rehovot Israel

Purpose: To evaluate the visual outcomes following cataract surgery in patients that had previously radial keratotomy (RK).

Methods: A high volume clinic retrospectively reviewed all cataract surgeries performed in eyes that had RK previously between 2016 and 2021. Twenty-seven eyes of 22 patients were identified. The mean age was 57.96±7.81, and 63% were males. The average time from the RK procedure to the cataract surgery was 35-40 years. The IOL power was calculated using a combination of SRK/T formula, manifest refraction, and Sirius tomography. The IOLs used were Alcon monofocal and fineVision trifocal.

The preoperative and postoperative best-corrected visual acuity (BCVA) and the postoperative uncorrected distance visual acuity (UDVA) and near (UNVA) were retrieved from the follow-up visits.

Results: The average postsurgical UCVA at distance was 0.42±0.22, and at near was Jaeger 7±4.61. None of these patients suffered from ectasia, and the average thinnest point pachymetry was 559±14.58 µm. The efficacy index at 16 months (postoperative UCVA/preoperative BCVA) was 0.62. The safety index at 16 months (postoperative /preoperative BCVA) was 1.05. Three eyes were treated with MFIOL. The UCVA was 0.5 and J2 in this group of eyes. No intraoperative complications were noted, but there was a change in the refraction for several months until stability was achieved.

Conclusion: Cataract surgery performed on patients with previous RK surgery was shown here to be a safe procedure providing positive results without significant complications. Some patients may get good VA with MFIOL.

56 AC

Visual Outcome of IntraLase-assisted LASIK enhancement to correct post PRK residual refractive error

Shmuel Levinger (1), Nir Erdinest(1,5), Eliya Levinger(1,2), Irit Barequet(1,3), Dana barequet(1,2), Shalhevet Goldfeather Ben Zaken(1,4), Ami Hirsh(1), Israel Kremer(1), Joseph Douieb(1), Nadav Levinger(1,5)
(1)Enaim Medical Center Jerusalem & Tel Aviv, Israel (2)Tel Aviv Sourasky Medical Center, Tel Aviv, Israel (3)Goldschleger Eye Institute, Sheba Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Hashomer, Israel (4)Department of Ophthalmology, Kaplan Medical center, Rehovot Israel (5)Hadassah Medical Center, Jerusalem, Israel

Purpose: To report the visual outcomes of IntraLase-assisted LASIK performed to enhance residual refractive errors in patients who previously underwent photorefractive keratectomy (PRK).

Methods: Observational case series. Preoperative best-corrected visual acuity (BCVA) and uncorrected visual acuity (UCVA) and postoperative UCVA were collected, as well as epithelial optical coherence tomography (OCT) images.

Results: Four eyes of three patients were identified. One patient underwent PRK 16 years prior, the second 6 years prior, and the third more than five years prior.

Preoperative epithelial OCT was available for three of the eyes with a min max epithelial thickness of 62 microns. The flap was performed at a depth of 110 microns. For the fourth patient, an intraoperative epithelial OCT was available, and the flap thickness was 120 micron.

The average preoperative UCVA and BCVA were 0.15±0.04 and 0.87±0.25, respectively. The average postoperative UCVA was 0.65±0.41, and all three patients achieved a BCVA of 1.0. Efficacy and safety at 1 month postoperatively were 0.88 and 1.2, respectively. There was a statistically significant difference between the presurgical UCVA versus the postsurgical UCVA ($P<0.05$).

There were no significant intra or postoperative complications.

Conclusion: IntraLase-assisted LASIK has shown to be a safe and effective treatment for residual refractive error after PRK. The use of anterior segment OCT and epithelial map has paramount importance in surgical planning to assist for safe and predictable outcomes.

76

Is oblique astigmatism reminiscent of meridional amblyopia?

Gad Serero , Maria Lev, Uri Polat
School of Optometry and Vision Science, Faculty of Life Sciences, Bar-Ilan University, Ramat Gan

Introduction: Adapting to oblique astigmatism correction has always been a challenge for practitioners and patients who frequently complain of permanent discomfort.

Lateral interaction is the ability of a neuron to affect its neighboring neurons by inhibiting or exciting their activity. It was suggested that lateral interactions are shaped and developed during childhood and impaired when the visual input is distorted in the blurred meridian (meridional amblyopia). We hypothesized that lateral interactions in adult visual cortex with oblique astigmatism are reminiscent of the abnormal lateral interactions of meridional amblyopia. Oblique astigmatism induces blurry images in orthogonal meridians in each eye, resulting in two conflicting images, which may affect the development of binocular vision.

Methods: Fully corrected subjects (n=21), divided into oblique astigmatic (OA,n=8) and normal controls (n=13), were tested for contrast detection and lateral interaction in different orientations and eyes (monocular, binocular).

Results: The monocular lateral interactions were normal in the clear meridian and abnormal in the blurred meridian in the oblique astigmatic group, reminiscent of the lateral interaction of meridional amblyopia.

Conclusion: Our results show that patients with oblique astigmatism with normal and fully corrected vision may have abnormal lateral interactions similar to meridional amblyopic patients. Thus, we suggest that the anisotropy in meridional lateral interaction observed in our study could represent a “cortical trace” induced by an atypical visual experience in oblique astigmatism during the sensitive period, which is retained in adulthood.

94 AC

Unravelling the influence of LOX and niche biochemical rigidity on limbal stem cell function and corneal integrity

Ruby Shalom-Feuerstein, Eman Knaane
Department of Genetics and Developmental Biology, Technion, Haifa.

Purpose: Extracellular matrix (ECM) remodeling and biomechanical changes are seen in various ocular diseases and may affect stem cells. However, very little is known about how the limbus ECM rigidity influences the cornea and control limbal stem cells (LSC) fate. Lysyl oxidase (LOX) enzyme family proteins catalyze covalent crosslinking of collagen and elastin, thereby increases the stromal tissue stiffness. Interestingly, variation in LOX expression have been associated with corneal pathologies including keratoconus. However, the contribution of LOX to the disease etiology and its impact on LSC function is poorly understood. Therefore, the purpose of this study is to characterize the expression of LOX family genes and unravel the influence of LOX and the modulation of the niche on LSC function and tissue integrity.

Methods: In silico analysis of published single cell RNA sequencing databases was performed to characterize the expression of LOX, as well as four LOX-like family members (LOXL1-4) in murine and human cornea cell populations. In addition, the expression of LOX family genes was examined in cultivated human limbal epithelial, corneal epithelial and mesenchymal cell populations, was examined by quantitative real-time polymerase chain reaction to confirm the in silico analysis. Immunofluersecnt staining was performed to identify cell populations in vitro. To explore the influence of LOX and matrix rigidity in vivo, the transparency and marker expression of the corneal of transgenic animals that ubiquitously over express LOX gene (LoxOE) was examined.

Results: The LOX enzyme family members were found to be specifically detected in clusters of corneal fibroblast and not in limbal/corneal epithelial lineage. Notably, LOX and LOXL1 were the predominantly expressed isoforms in the cornea whereas other LOX family genes were barely expressed or were undetectable. LoxOE corneas displayed severe opacification that was coupled with typical signs of conjunctival cell invasion into the cornea which are typical hallmarks of LSC deficiency.

Conclusion: This study collectively suggests that LOX genes and matrix stiffening and remodeling may plays a critical role in LSC function. A better understanding of how the ECM regulates corneal structure and integrity and how ECM remodeling affects diseases including keratoconus will contribute to the development of new therapeutics.

10 AC

Syndecan-1 expression in the corneal epithelium of keratoconus patients, and its correlation to disease severity

Assaf Gershoni(1,2); Eitan Livny(1,2); Dahlia Palevski(1,2); Yael Nisgav (3); Tami Livnat(3); Assaf Achiron(2,4); Doron Yablekovich(2,5); Irit Bahar(1,2); Uri Elbaz(1,2)
1Department of Ophthalmology, Rabin Medical Center, Petah-Tikva, Israel 2Sackler Medical School, Tel Aviv University, Tel Aviv, Israel 3Eye Research Laboratory, Felsenstein Medical Research Center, Rabin Medical Center, Petach Tikva, Israel 4Department of Ophthalmology, Souraski Medical Center, Tel Aviv, Israel 5Department of Gastroenterology, Sheba Medical Center, Tel Hashomer, Israel.

Purpose: To demonstrate the presence of Syndecan-1 (sdc1) in the corneal epithelium of patients with keratoconus, estimate its expression levels and examine whether a correlation exits to disease severity.

Methods: This study examined the corneal epithelium of 44 keratoconus eyes (44 patients) undergoing epi-off crosslinking (CXL) procedure. Epithelial samples were analyzed for sdc1 presence and levels through immunohistochemistry and enzyme-linked immunosorbent assay (ELISA), respectively. Prior to CXL, each patient underwent corneal tomography imaging (Pentacam), from which we retrieved the Kmax value, an accepted measure for disease severity. To examine correlation between Kmax and sdc1 levels in the corneal epithelium, we utilized Pearson's and Spearman's correlation coefficients.

Results: In immunohistochemistry, sdc1 is shown to be located in the basal layer of the epithelium and not in the outer layers. The mean Kmax value was 55.5±6.9, and mean sdc1 levels were 338.6±260. No correlation was found between scd1 levels and disease severity, represented by Kmax, by pearsons' ($r=0.13$, $p=0.36$) and Spearman's ($r=0.02$, $p=0.89$) correlation coefficients. Differentiation of sdc1 levels in patients with a more severe disease from those with a milder one, showed no statistical difference between patients with Kmax under 50 (n=13), and over 60 (n=15), and between patients with Kmax under 45 (n=3) and over 65 (n=4), ($p=0.235$ and 0.69, respectively)

Conclusions: Syndecan 1 resides in the basal layer of the epithelium of keratoconus patients. No correlation was found between sdc1 levels in the epithelium and disease severity, and therefore sdc1 cannot serve as a marker for disease severity or progression.

113

Finite element modelling of circular corneal incisions

Yoav Nahum[1], Stav Madhian[2], Alexander Bondarenko[2], Amit Ron[2], Yair Goldberg[2], Gil Marom [3], Moshe Brand[2]","[1] Ophthalmology Department, Rabin Medical Center, Petach Tikva [2] Department of mechanical engineering and mechatronics, Ariel University, Ariel [3] School of mechanical engineering, Tel Aviv University, Tel Aviv

Purpose: To perform and validate Finite element method (FEM) of corneal circular relaxing incisions of a spherical cornea, a cornea with regular astigmatism and a cornea with keratoconus.

Methods: Solidworks CAD software and previous published bio-mechanical models were used to create a theoretical 3D model of the human cornea. Data obtained from a Pentacam corneal topography of a healthy patient, and from another patient with keratoconus were used to create a similar patient-based model. Abaqus FEM software was used to analyze the changes caused by circular relaxing incisions preformed at different depths and diameters, radially and perpendicularly to the corneal surface. A Python-based code was used to calculate the radii of curvature at the central 3mm and 6mm of the cornea, for the purpose of evaluating the changes in refractive power caused by the incisions.

Results: The theoretical model demonstrated that a circular incision caused flattening of the central cornea, that increased when the incisions were deeper and closer to the cornea. Maximal flattening effect of 2.7 diopters was demonstrated with a 450µ deep incision of 6mm diameter. Flattening of 2.16 diopters occurred when a similar incision was applied onto a keratoconic eye model. In both models, incisions done radially to the corneal surface caused more flattening than incisions that were done perpendicularly to the corneal surface. A similar incision applied onto a cornea with regular astigmatism of 7.89D caused flattening of both flat and steep meridians, with decrease of astigmatism by 1.1D at 3mm diameter, and of 1.6D at 6mm diameter, which was significantly smaller decrease than that demonstrated by our group in previous studies of paired arcuate incisions.

Conclusion: Our FEM model demonstrated that circular incisions caused flattening effect on regular and ectatic corneas. Recently published clinical outcomes of this treatment modality could assist in the validation of this model.

5 AC

The definition-dependent nature of myopia prevalence: a nationwide study of 1.5 million adolescents

Itay Nitzan (1), Inbal Akavian (1), Adi Einan-Lifshitz (2,3), Asaf Shemer (2,3), Arnon Afek (2,4), Alon Peled (2,3)
(1) Israel Defense Forces Medical Corps, Ramat Gan (2) Sackler Faculty of Medicine, Tel Aviv University (3) Department of Ophthalmology, Assaf-Harofeh Medical Center, Zerifin (4) Central Management, Chaim Sheba Medical Center at Tel Hashomer, Ramat Gan

Purpose: The exact definition of myopia varies considerably within the literature. The purpose of this study was to examine the relationship between myopia definitions and resultant prevalence estimates.

Methods: A population-based cross-sectional study of 1,588,508 adolescents assessed for medical fitness for mandatory military service at age 17 years between 1993 through 2015. Nine definitions of myopia and seven definitions of high myopia were examined, based on common use in literature. Prevalence estimates for each definition were calculated and compared to the reference-definition (right eye spherical equivalent (SE) ? -0.50D and ? -6.00D for myopia and high myopia, respectively), to yield a rate ratio (RR) across definitions.

Results: Applying the right eye SE ? -0.50D reference definition yielded a 31.0% myopia prevalence. While some definitions resulted in a similar prevalence, using a right eye SE of ? -0.75D; ? -1.00D or least minus meridian of ? -0.75D definitions yielded 28.8%, 26.3%, and 26.9% myopia prevalence, respectively, which corresponded to a 7.1%, 15.1% and 13.4% reduction in myopia RR, respectively. The prevalence of high myopia demonstrated considerable alternations, with a 1.7-fold increase in prevalence for the narrower threshold of SE ? -5.00D compared to SE ? -6.00D reference definition (4.2% and 2.4%, respectively).

Conclusions: The prevalence of myopia and especially high myopia varies between frequently applied definitions, considering diverse thresholds, eye-lateralization, and spherical vs. astigmatic refractive components. This variability stresses the need for a universal standardization of myopia definitions. This study may provide a crude estimate of a “conversion rate” across definitions, allowing to execute comparison between studies results.

16 AC

Myopia and early onset type 2 diabetes: A nationwide cohort study

Alon Peled(1,2) Itamar Raz(3) Inbar Zucker(1,4) Estela Derazne(1) Jacob Megreli(5,6) Orit Pinhas-Hamiel(1,7) Adi Einan-Lifshitz(1,2) Yair Morad(1,2) Eran Pras(1,2) Miri Lutski (4) Tali Cukierman-Yaffe(4,8) Ofri Mosenzon(3) Dorit Tzur(6,9) Amir Tirosh(1,8) Hertzel Gerstein(10) Arnon Afek(1,11) Gilad Twig(1,6,8,9)

1 Sackler Faculty of Medicine, Tel Aviv University. 2 Ophthalmology department, Assaf-Harofeh , Zerifin 3 Diabetes unit, Hadassah, Jerusalem. 4Ministry of health, Israel CDC. 5 Braun school, Hebrew university, Jerusalem. 6 IDF medical corps, Ramat Gan. 7. Pediatric endocrine unit, Sheba, Ramat Gan. 8. Endocrinology, Sheba, Ramat Gan. Department of Military medicine, Hebrew university, Jerusalem. 10 Department of medicine, McMaster university, Ontario, Canada. 11Central Management, Sheba, Ramat Gan

Purpose: A correlation between myopia and insulin-resistance has been suggested. We investigated the association between myopia in adolescence and type 2 diabetes (T2D) incidence in young adulthood.

Methods: A population-based, retrospective, cohort study of 1,329,705 adolescents (579,543 women, 43.6%) aged 16-19 years, medically examined before mandatory military service during 1993-2012; and whose data were linked to the Israel National Diabetes Registry. Myopia was defined based on right eye refractive data. Cox proportional models were applied, separately for women and men, to estimate hazard ratios (HRs) for T2D incidence per person-years of follow-up.

Results: There was an interaction between myopia and sex with T2D (P<0.001). For women, T2D incidence rates (per 100,000 person-years) were 16.6, 19.2, and 25.1 for those without myopia, and with mild-to-moderate and high myopia, respectively. These corresponded to HRs of 1.29 (95%CI 1.14-1.45) and 1.63 (1.21-2.18) for women with mild-to-moderate and high myopia, respectively, compared to those without myopia, after adjustment for age at study entry, birth year, adolescent BMI, cognitive performance, socioeconomic status, and immigration status. Results persisted in extensive sensitivity and subgroup analyses. When managed as a continuous variable, every 1 diopter lower spherical equivalent yielded a 6.5% higher adjusted HR for T2D incidence (P= 0.003). There was no significant association among men.

Conclusions: For women, myopia in adolescence was associated with a significantly increased risk for incident T2D in young adulthood, in a severity-dependent manner. This finding may support the role of insulin resistance in myopia pathogenesis.

6 AC

Recovery of vision after optic nerve sheath fenestration in children and adolescents with elevated intracranial pressure.

Daphna Landau Prat [1,2,3], Grant T. Liu [1], Robert A. Avery [1], Gui-shuang Ying [4], Yineng Chen [4], Lauren A. Tomlinson [1], Karen E. Revere [1], James A. Katowitz [1], William R. Katowitz [1]
[1] Division of Ophthalmology, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA; [2] Goldschleger Eye Institute, Division of Ophthalmology, Sheba medical center, Israel; [3] Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [4] Center for Preventive Ophthalmology and Biostatistics, Department of Ophthalmology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA",

Purpose: The effectiveness of optic nerve sheath fenestration (ONSF) to treat vision loss has been demonstrated in adults; however, the literature regarding pediatric ONSF is sparse with only occasional case reports and few small cases series. Moreover, these studies did not evaluate: (a) the time course of visual recovery; (b) visual function from the non-operated eye; and (c) cases of non-IIH induced increased intracranial pressure (ICP). The purpose of the current study was to evaluate the effect of ONSF in children and adolescents with optic disc swelling due to increased ICP, and to determine the rate of vision function improvement in both the operated and non-operated eye.

Methods: Retrospective case series. Medical chart review of all pediatric patients who underwent ONSF between 2009 and 2020 at the Children Hospital of Philadelphia (CHOP). Visual function was assessed at pre- and postoperative visits. Main outcome measures were visual acuity (VA), color vision (CV), extra-ocular motility (EOM), visual field mean deviation (VF-MD), retinal nerve fiber layer (RNFL) thickness measured by OCT.

Results: Fourteen pediatric patients (10 females, mean (SD) age of 14 (2.6) years, range 8.5-17.5) were included. Five patients underwent bilateral surgeries. Ten patients were diagnosed with idiopathic intra-cranial hypertension (IIH). Of the 10 IIH patients, 3 had a previous history of weight gain and 2 of systemic steroid treatment; these can be referred to as pseudotumor cerebri (PTC). Mean (SD) follow-up length was 16.4 (12.3) months. VA improved from 20/138 to 20/68 in the operated eye (P=0.0003) and from 20/78 to 20/32 in the non-operated eye (P=0.02). CV improved in the operated eye (P=0.04), EOM improved in the operated and non-operated eye (P=0.002 and P=0.04 respectively). VF-MD improved in the operated (-23.4dB to -11.5dB, P<0.0001) and non-operated eye (-19.8dB to -6.8dB, P=0.02). RNFL thickness improved in the operated eye (349.1 to 66.2 um, P<0.0001). The postoperative improvement was observed as early as the postoperative day 1.

Conclusions: ONSF produces a rapid and persistent vision improvement in both the operated eye and the non-operated eye. In children and young adults with papilledema and elevated ICP causing vision loss that is severe at presentation or refractory to standard medical management, ONSF should be considered.

18,AC

Inter-session and inter-examiner reliability of the Mallett Unit associated phoria test.

Dmitriy Yehonathan Kurbet [1], Liat Laloum [1], Bruce JW Evans [2], Meira Zyroff [1] , Liat Gantz [1]

[1] Department of Optometry and Vision Science, Hadassah Academic College, Jerusalem. [2] The Institute of Optometry, London, UK

Background: The Mallett Unit test (MUT) measures the associated phoria (aligning prism, AP), the prism necessary to correct fixation disparity. This study examined the within-subject variability, inter-examiner and inter-session repeatability of the MUT.

Methods: Thirty-two optometry students with normal binocular vision (mean age: 25.59 ± 2.73, range: 22 - 33, 26 females) were recruited. The horizontal AP (measured in prism diopters, Δ) was measured three consecutive times using the MUT held at a regular reading angle with polaroid glasses, by two optometrists that were masked to each other's measurements. The measurement was repeated in 26 participants (mean age: 25.65 ± 2.84, range 22-33, 23 females) by one optometrist within two weeks of the initial session. Reliability was assessed using Wilcoxon test, Spearman correlation, and non-parametric Bland and Altman (B&A) analysis. Intra test repeatability was defined as the ANOVA within subject standard deviation (Sw), and test-retest repeatability (95% confidence interval (CI)) was defined as 2.77Sw, which indicated the interval within which 95% of the differences between measurements are expected to lie.

Results: The Sw was 1.27Δ with a mean standard deviation of the difference between consecutive measurements of 1.25Δ. The measurements of the two examiners were significantly correlated (Spearman R: 0.89, P< 0.0001) and not significantly different (P= 0.89). Sw was 1.15 and 2.77Sw was 3.18Δ. B&A analysis of the inter-examiner repeatability exhibited a mean difference of -0.04±0.44 Δ, with 93.75% of the observations falling between 0.83Δ and -0.91Δ. The inter-session measurements were significantly correlated (Spearman R: 1.00, P< 0.0001) and not significantly different (P= 1.00). Sw was 1.22 and 2.77Sw was 3.37Δ. B&A analysis of the inter-session repeatability exhibited a mean difference of 0.06±0.39Δ, with 96% of the observations falling between 0.70Δ and -0.83Δ.

Discussion: Differences lower than 1Δ are not considered clinically significant. The inter-session and inter-examiner differences were lower than 1Δ . They were also lower than the within-subject variability.

Conclusion: Results demonstrate that the Mallett unit has good intra-test, inter-session and inter-examiner repeatability, both lower than even 0.5Δ.

46,AC,

Surgical outcomes of medial rectus advancement for consecutive exotropia.

Ronen Spierer (1), Asaf Achiron (2), Ayat Qassoom (3), Anat Bachar Zipori (2), Oriel Spierer (3)

1 Bruce and Ruth Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel 2 Department of Ophthalmology, Tel Aviv Sourasky Medical Center, Affiliated to the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel 3 Department of Ophthalmology, E. Wolfson Medical Center, Affiliated to the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Purpose: To evaluate the surgical results of medial rectus muscle advancement for consecutive exotropia.

Methods: The medical data of patients that underwent reoperation between the years 2000-2020 were collected and reviewed retrospectively. Patients who underwent medial rectus advancement for consecutive exotropia were included. The exclusion criteria were follow-up period shorter than 6 months, past reoperations and restrictive or paralytic strabismus. Success was defined as alignment within 10 PD of orthophoria at last follow-up. The success group of patients was compared with the failure group.
Results: Twenty patients with mean postoperative follow-up from the second surgery of 34.7±29.2 months were included. On last follow-up examination, 9 (45.0%) patients had a successful result. Nine patients had undercorrection and 2 had overcorrection. The two groups were similar in the preoperative amount of mean exotropia, 23.3±9.9 PD in the success group and 29.8±14.0 PD in the failure group (p=0.261). On last follow-up examination, the amount of mean deviation was 2.7±2.6 PD exotropia in the success group and 13.4±23.6 PD exotropia in the failure group (p=0.163).

Conclusion: Medial rectus advancement for the correction of consecutive exotropia was successful in almost half of the cases. Failure was usually due to undercorrection.

65,AC

Improving Visual Function Following Temporal Perceptual Learning.

Auria Eisen-Enosh (1), Nairouz Farah (1), Uri Polat (1), Yossi Mandel (1,2)

(1) School of Optometry and Vision Science, Bar-Ilan University, Ramat-Gan, Israel. (2)Institute for Nanotechnology and Advanced Materials (BINA), Bar-Ilan University, Ramat Gan, Israel.

Purpose:
Numerous studies have shown that subjects with amblyopia can greatly benefit from Perceptual Learning (PL) leading to improvement in their visual function performance. The focus of these studies has mainly been on the spatial aspect of visual performance and little work has been done to evaluate the effect of PL on temporal performance. Here we aimed at studying whether PL can enhance temporal function performance and whether this enhancement is transferred to spatial functions in amblyopic subjects.

Methods:
Three amblyopic subjects underwent evaluation of baseline psychophysics spatial function performance (visual acuity, contrast sensitivity at various spatial frequencies and presentation durations), and psychophysics temporal function performance (critical fusion frequency (CFF) test), computerized flickering stereopsis test, and electrophysiological evaluation which included visual evoked potential (VEP) recorded in response to a sinusoidally flickering light at 15Hz. Next, subjects underwent daily training sessions for 5 days which included a task similar to the CFF test using the method of constant stimuli. After completing the training sessions subjects repeated the initial performance evaluation tasks to evaluate the change in the temporal and spatial visual performance.

Results:
All subjects showed improved temporal visual performance in the amblyopic eye (15%) and the fellow eye(7%) following temporal PL. In addition, spatial vision performance improvement was observed in the AE (30%) mainly contrast sensitivity at high spatial frequency and long display time tests. These results were further validated by an increase in VEP amplitude recorded in response to flickering light in the AE.

Conclusions:
Although further work is still needed to optimize this method for clinical applications, these results highlight the potential of PL for improving temporal and spatial visual performance.

66

Steroid-sparing maintenance immunotherapy for MOG-IgG associated disorder,A multicenter study: Immunoglobulin in Preventing Relapse in Adult MOGAD.

Hadas Stiebel-Kalish
Multinational

Purpose: To determine the effectiveness of maintenance IVIG in preventing relapses in a large adult cohort of MOGAD patients. Recent studies suggest that maintenance intravenous immunoglobulin (IVIG) may be an effective treatment to prevent relapses in myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD); however, most of these studies concern pediatric cohorts and IVIG has not been well studied in adults.

Methods: An international, multicenter, retrospective cohort study from 2010 through October 2021. The study included a total of 876 adult MOGAD patients who were screened for the following inclusion criteria: 1) history of ≥1 CNS demyelinating attack consistent with MOGAD; 2) MOG-IgG seropositivity tested by cell-based assay; 3) maintenance IVIG treatment. The main outcome measures were the relapse rates on maintenance IVIG compared to before initiation.

Results: Fifty-nine adult MOGAD patients were included; the median age at initiation of maintenance IVIG was 36 years (range, 18-69) and 56% were female. IVIG was initiated as first line immunotherapy in 15 (25%) patients, because of failure of prior immunotherapy in 37 (63%) patients, and intolerance to prior immunotherapy in 7 (12%) patients. The median annualized relapse rate (ARR) prior to IVIG treatment was 1.4 (range, 0-6.1), compared to a median ARR on IVIG of 0 (range, 0-3), $P<0.001$. Twenty (34%) patients had at least 1 relapse while on IVIG with a median time to first relapse of 1 year (range, 0.03 to 4.8 years). Seventeen (29%) patients were treated with concomitant maintenance immunotherapy. Only 5 of 26 (19%) of patients receiving ≥1g/kg every 4 weeks relapsed compared with 15 of 33 (45%) treated with lower or less frequent dosing (Cox model P=0.02). At final follow-up, 52 (88%) were still on maintenance IVIG with a median duration of 1.7 years (range, 0.5-9.9) of therapy. Seven patients discontinued IVIG for the following reasons: inefficacy=4, adverse effects=3, and trial off therapy following disease inactivity=1.

Conclusions and Relevance: This retrospective multicenter study of adult MOGAD patients provides class III evidence that maintenance IVIG is associated with a reduction in recurrent attacks. Less frequent and lower dosing of IVIG may be associated with treatment failure.

70 AC

Oculomotor Measures Of Visual Working Memory Load.

Kfir, Inbal [1] & Hadar, Snir [1]; Oren, Kadosh [1]; Yoram, Bonneh [1]

[1] Faculty of Life Sciences, Bar-Ilan University, Ramat Gan

Background: Involuntary eye movements occur constantly even during fixation and have been shown to convey information about cognitive processes. They are inhibited momentarily in response to external stimuli (oculomotor inhibition, OMI), with a time-course and magnitude that depend on stimulus saliency, attention and expectations or surprise. It has been recently shown that working memory load for numbers modulates microsaccade rate, but the generality of the effect and its temporal properties are yet unclear.

Purpose: Investigate the relation between OMI properties and working memory load for simple visual shapes, for both encoding and retrieval.

Methods: Participants (N=19) maintained central fixation and self-initiated trials in which they had to memorize and then match briefly flashed stimuli while their eyes were tracked. The stimuli consisted of three simple colored shapes, with small arrows indicating the shapes to be memorized: 1, 2, or 3 items, corresponding to low, medium, and high load. After a 1s retention period, one colored shape was briefly flashed, and the participants had to report if it matched any of the memorized colored shapes. The microsaccade event-related rate modulation and temporal properties were analyzed for the two separate events of memory encoding and recall.

Results: For both the encoding and recall stages, the microsaccade inhibition was longer and stronger when more colored shapes had to be remembered. This occurred even though the physical stimuli were identical in number in all conditions. The pupil dilation was also affected by load, but not the eye-blinks.

Conclusions: Similar to the OMI in response to oddballs, which is typically stronger and prolonged, encoding and recalling more items from working memory is also associated with longer and stronger inhibition. This suggests that event-related OMI is generally related to the associated processing time and load.

77 AC,

Heterophoria alters lateral cortical interactions.

Laura Benhaim Sitbon, Maria Lev, and Uri Polat (1)
School of Optometry and Vision Science, Faculty of Life Sciences, Bar-Ilan University, Ramat Gan

Purpose: Heterophoria (phoria) is a latent misalignment of the eyes, varying with distance, which is revealed under conditions that disrupt binocular vision (prevalence up to 30%) and may affect the quality of binocular fusion. Collinear facilitation (CF) is defined as improved detection (facilitation) of a target Gabor patch (GP) by the presence of GP flankers positioned in a collinear configuration. An abnormal pattern of CF has been observed in strabismic amblyopia. We hypothesize that phoria may affect CF on the horizontal meridian (HM), due to the latent eye misalignment and its influence on binocular fusion. We aim to investigate how phoria affects CF during binocular and monocular viewing.

Methods: 16 subjects (8 phoria and 8 controls) with normal or corrected-to-normal vision participated in the study. All participants had a full orthoptic examination and underwent a full optometric examination within the last six months. Inclusion principally required normal stereoscopic vision as well as the absence of strabismus, accommodative disorders, and ocular pathology. Subjects with horizontal phoria equal or superior to 6 Δ were included in the phoric group. Subjects were tested for CF at different target-flanker separations for both HM and vertical meridian (VM) during binocular viewing at three distances (0.4, 0.6, and 1m) and monocular viewing at 1m. Results: Heterophoric observers exhibited an abnormal pattern of CF only for HM at all distances for both binocular and monocular viewing, reminiscent of the pattern of amblyopic subjects.

Results: Heterophoric observers exhibited an abnormal pattern of CF only for HM at all distances for both binocular and monocular viewing, reminiscent of the pattern of amblyopic subjects.

Conclusions: Heterophoria impacts CF in a way that is reminiscent of meridional amblyopia without being attributed to abnormal refraction. The existence of an abnormal CF in monocular viewing suggests that phoria could be a binocular developmental disorder that affects monocular spatial interactions.

95

Visual tracking smoothness as a diagnostic marker of traumatic brain injury.

Shimrit Shani(1), Yaron Sacher(2,3), Yoram Bonneh(1)
(1) School of Optometry, Bar-Ilan University (2) Loewenstein Rehabilitation Hospital, Ra'anana, Israel (3) Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

Background: Patients with traumatic brain injury (TBI) present deficits in saccadic and smooth-pursuit eye movements, with longer latencies and reduced accuracy. In mild TBI, most of the saccadic and pursuit defects are subtle and can be missed during the clinical examination, therefore eye-tracking technology can be a simple and useful tool for detection of these defects. Disturbances in vision and eye movements may provide a measurable window for the disorder and possibly aid in predicting prognosis. In the current study, we conducted a detailed eye-tracking investigation of simple visual tracking in patients with TBI.

Methods: 25 patients with TBI with different degrees of impairment, from mild to severe, were tested on visual tracking in multiple testing sessions during recovery. We recorded eye movements while the patient tracked a white disc moving from the center outwards in a straight line with different directions in random order. We analyzed the data by computing separate tracking measures: (a) ""full pursuit"" speed computed from the full eye position traces including catchup saccades; (b) ""smooth pursuit"" speed computed by removing the catchup saccades and aligning the traces by the saccades start and end points; (c) "saccadic pursuit" speed computed as the difference between (a) and (b).

Results: The patients showed (1) faster "full pursuit", (2) slower "smooth pursuit" and (3) a significantly faster "saccadic pursuit" ($p<0.0001$), reflecting the extensive use of catch-up saccades. We further found that (4) this effect was larger for diagonal tracking, and (5) the patients had larger inter-ocular difference compared to controls.

Conclusions: These results demonstrate a strong deficit in the TBI patients for smooth tracking, which requires a tight closed-loop process, but a remarkable ability to compensate via catchup saccades or ""saccadic tracking"" that in some cases yielded high-speed gains. Our method is based on a simple tracking task and could potentially be used for a clinical assessment.

96

The spatial and chromatic attributes of the pupillary response to aversive patterns: towards the development of a screening tool for visual hyper-sensitivity.

Ron Meidan(1), Yoram Bonneh(1)
(1) School of Optometry and Vision Science, Faculty of Life Science, Bar-Ilan University, Ramat Gan

Background: Some observers find patterns of black and white stripes to be very unpleasant. These monochromatic high-contrast square wave gratings are known to give rise to visual discomfort, unpleasant sensation, glare, and illusory motion and at the same time. They are also known in their ability to induce pupillary size change with a smaller pupil for higher spatial-frequency - the so-called pupillary grating response (PGR). Here we linked the two phenomena and conducted a parametric study of the visual attributes of the stimuli that cause visual discomfort and its pupillary expression. Our end goal is to obtain objective measures for individual discomfort and investigate its principles.

Methods: observers (n=100) watched a slide show of flashed square wave gratings or text images with different spatial-frequency, contrast, and iso-luminant background color, and reported their subjective rating of aversion or free-view the images while their pupil size was recorded.

Results: Spatial-frequency, background color and total stimulus size had a significant effect on pupil size change as well as on the subjective aversion ratings. Importantly, these two measures were significantly correlated, consistent with the known tendency of the pupil to constrict following aversion or disgust. Moreover, a small but significant correlation ($r=-0.47$ $p=0.00$, $n=83$) was found between pupil size change and individual subjective rating of aversion, suggesting that it might be possible in the future to objectively screen for highly visual sensitivity. Different iso-luminant colors caused markedly different subjective sensations and a correlated pupil size change, while low plus-add lenses had no significant effect.

Conclusions: These findings are in line with suggestions that stripes patterns might give rise to an immediate aversive response, and how those sensations could be alleviated by color. They could lead to future development of a simple and objective screening tool for visual hyper-sensitivity.

97 AC

Studying Prosthetic and Natural Vision Cortical Interaction in V1 at the Population and Cellular Level.

Itay Shekel(1), Ori Carmi(2), Lamberto Lafranca(3) , Adi Gross(4), Nadav Ivzan(4), Nairouz Farah(4,5) ,Yossi Mandel(4,5)
(1)The Gonda Brain Research Center, Bar-Ilan University,Ramat Gan. (2)Faculty of Electrical Engineering, Bar Ilan University, Ramat Gan. (3)Department of Ophthalmology Vita-Salute San Raffaele University, Milan. (4)Faculty of Life Sciences, School of Optometry and Vision Science, Bar-Ilan University,Ramat Gan.(5) Bar Ilan's Institute for Nanotechnology and Advanced Materials (BINA), Bar-Ilan University ,Ramat Gan

Purpose:
With the advancements of retinal prostheses for vision restoration in patients with Age related Macular Degeneration (AMD), the need arises to address the intriguing question of the how the brain processes prosthetic and combined natural and prosthetic vision.

Methods:
Toward this end, we used voltage-sensitive dye imaging (VSDI) to record the visual cortex responses (population), and extracellular recordings using a multi electrode array (single cell), in rats subretinally implanted with a photovoltaic device. A customized projection system was utilized for projecting flexible spatial light patterns in both the visible (532nm) and the NIR (915nm) for stimulating the healthy peripheral retina and the implant simultaneously (pixel sizes of 140 and 280 μm), respectively. Using VSDI we generated retinotopic maps and investigated the persistence of the lateral inhibition phenomenon. Single unit recordings were used for the investigation of fundamental properties of V1 neurons such as receptive field, orientation selectivity induced by prosthetic stimulation.

Results:
VSDI revealed that cortical responses to the combined stimulus (visible flankers, and NIR target) were significantly reduced relative to the linear summation of the responses to its individual parts. This lateral inhibition effect declined as the distance between the target and the flankers increased. These results are in line with previous studies performed in humans and other species, showing non-linear target-flanker interactions. Moreover, we have successfully recorded single cell responses induced by both simple and complex visible light patterns and are in the process of isolating V1 responses induced by prosthetic stimulation.

Conclusions:
The tools presented here may prove to be highly useful for the investigation of prosthetic and combined prosthetic and natural vision information processing occurring in the visual cortex. This information might be important for design of prosthetic stimuli for high-resolution vision restoration.

103 AC

Visual crowding: a bottleneck for visual function acquisition after sight retrieval.

Noah, Rappeport, (1) Maria, Lev, (1), Ehud, Zohary (2), Uri, Polat, (1)
(1)School of Optometry and Vision Sciences, Faculty of Life Sciences, Bar-Ilan University, Ramat-Gan, (2) Neurobiology Department & The Edmond and Lily Safra Center for Brain Sciences, The Hebrew University of Jerusalem, Jerusalem

Background: BCC (bilateral congenital cataracts) in the developed world are generally diagnosed in early infancy and treated without delay. When treated early enough, children affected by BCC tend to develop normal visual processing. However, what happens when BCC are treated after the critical period?
Studies on late treated BCC, have examined visual processing development from low-level through to high-level. However, crowding has not yet been researched. Crowding is the failure to differentiate the target that one wishes to focus on from visual clutter surrounding it. Foveal crowding may be detected only for close target-flanker separations of ~0.5 letter spacing or less, and for a brief presentation time. However, it was found that amblyopes may have foveal crowding even at a much greater spacing, with strabismic amblyopes displaying significant crowding, and anisometropic amblyopes less.

Purpose: To investigate if crowding in the study group is significant, as found in strabismic amblyopes, or insignificant as found in anisometropic amblyopes. Additionally, such information may be indicative of what predated what, the strabismus or the cataract.

Methods: The study group (N=18) aged 8-18 were all born in Ethiopia with BCC and were only treated after years of visual deprivation. Three control groups (N=31) were included in this study: Early treated, Healthy age matched and congenital pathologies.
Each subject was seated at a distance calculated according to their visual acuity. The experiment included two parts: an uncrowded target (letter E) and a target within a crowded matrix. The latter condition included 4 blocks, each displaying a different letter spacing.
Results: The study group displayed significant crowding reminiscent of strabismic amblyopia, whereas the 3 control groups did not.

Conclusion: Almost all of those in the study group had strabismus, which could be indicative of the strabismus being present before the cataract. This could be the root cause of the crowding. During this research visual acuity improvements were recorded in the study group. This could suggest that visual processing can improve even if sight was deprived during the critical period.

111

The varied severity of motion sickness can be predicted by differences in audio-visual binding.

Revital Zilka and Yoram Bonneh
Visual Sciences at the Faculty of Life Sciences, Bar Ilan University, Ramt Gan

Motion sickness refers to the feeling of sickness that typically occur during travel. Current explanations focus on the sensory conflict in the perception of motion, primarily between the vestibular and the visual systems. One intriguing observation is that different people report very different levels of motion sickness under identical conditions for reasons that are currently unknown.
To account for these individual differences, we hypothesized that people feel motion sickness only when the conflicting stimuli are perceived as bound together. Accordingly, people with “persistent binding”, i.e. those who keep binding multi-sensory stimuli with large inconsistency will suffer more than those who “disconnect” the senses to ignore the mismatch.
To test this hypothesis, we measured the persistence of audio-visual binding using the McGurk effect in which a visual presentation of the moving mouth alters the auditory perception of phonemes. We examined the McGurk effect in 3 different tasks: syllable Identification (McGurk), simultaneity judgement, and syllable synchronization judgement.
To assess the severity of motion-sickness we used 2 subjective symptom questionnaires.
We found that the temporal binding window in two of the tasks, varied across individuals and was positively correlated ($R>0.8$) with the motion-sickness questionnaire severity scores. The highest correlations were found between Syllable synchronization and MSSQ- short questionnaire (adult): $R=0.96$, and between Syllable synchronization and our questionnaire: $R=0.94$.
These results support our hypothesis and explain for the first time the enigmatic differences between individuals in the susceptibility to motion-sickness. Our method could be used in the future to predict motion sickness and guide appropriate employment.

115 AC

The central visual field might mediate night vision in normally developed populations and Albino subjects.

Avital Moshkovitz, Maria Lev, and Uri Polat
School of Optometry and Vision Sciences, Faculty of Life Sciences, Bar-Ilan University

From a bright day to a dark night, extreme light levels may deteriorate our vision. Daylight vision is mediated by the cone's photoreceptor, accumulates in the center of the retina (fovea), and is responsible for maximal resolution and form vision. At low light levels, it is considered that vision is mediated by the rod's photoreceptors (spread in the retina's periphery) which are less sensitive to resolution. Studies suggest that foveal neuronal mechanisms are vital for low light levels. Albinism is a congenital heterogeneous group of disorders affecting melanin synthesis. Ocular albinism is an expression of the mutation which affects only the eyes. Oculocutaneous albinism affects the entire body: eyes, skin, and hair.
We explored the central visual processing underlying range of light levels in normally developed populations and albino subjects. The luminance levels were controlled using natural density filters (Rosco Laboratories) and measured using a photometer. The task was to identify the direction of an E target in a clutter (crowding) under daylight (50 cd/m2) and low luminance (0.003 cd/m2) for different target-flankers-spacing. The foveal crowding effect under daylight was significantly increased at a target-flanker spacing of half-letter for both groups. Interestingly, the crowding effect was abolished for normal subjects under low luminance and even performed with some facilitation, while the Albino patients had a strong crowding effect.
The absence of crowding in normally developed patients at low luminance levels suggests that crowding depends on the sensitivity to luminance level. Thus, under challenging visual conditions, such as low luminance, normally developed fovea exhibit central vision that may increase the excitatory level at the fovea rather than the periphery, but not in albino patients.

20 AC,

Neuroretinal rim thickness in optic disc edema.

Yakov Vega (1), Avishai Gavish (1), Lital Smadar (1), Sivan Elyashiv (1), Irit Moroz (1), Ruth Huna-Baron (1,2)
(1) Goldschleger Eye Institute, Sheba Medical Center, Tel-Hashomer, Israel. (2) Sackler School of Medicine, Tel?Aviv University, Ramat?Aviv, Israel.

Purpose: Many studies have examined the thinning of neuroretinal rim (NRR) in glaucoma, yet no data have been collected in patients with optic disc edema. The purpose of this study was to evaluate patterns of the NRR in cases of optic disc swelling resulting from different etiologies: ischemic optic neuropathy, raised intracranial pressure or inflammatory papillitis, using spectral-domain optical coherence tomography (SD-OCT).

Methods: We retrospectively analyzed data of 325 patients with disc edema, seen between 2012 and 2020. Data collected included age, sex, grade of edema, diagnosis, visual acuity, intraocular pressure and mean deviation of visual fields. In cases of elevated intracranial pressure, the opening pressure of the lumbar puncture was recorded. OCT data were collected by researchers blinded to the clinical data. OCT was performed with CIRRUS® OCT (Carl Zeiss Meditec, Dublin, CA, USA). The OCT parameters analyzed NRR thickness, NRR area and retinal nerve fiber layer (RNFL) thickness.

Results: One hundred sixty seven out of 325 patients matched inclusion criteria (51.2% female, age average 47.1±21.8), resulting on a total of 320 eyes. Our data show that the mean NRR thickness predict the presence of optic edema ($p<0.001$). There is significant correlation between the degree of edema and the mean thickness of the NRR ($p<0.001$). The NRR thickness can also significantly predict the etiology of the edema ($p <0.001$). In addition, the size of the NRR area predicts the existence of high-grade edema and distinguish the different etiologies ($p<0.05$). Furthermore, in the IIH group, a significant relationship ($p<0.01$) was observed between the degree of disc edema and the opening pressure in LP. There was a statistically significant relationship ($p <0.001$) between the mean RNFL thickness and the opening pressure in the LP.

Conclusions: The NRR can be used as a tool to diagnose presence of disc edema. The NRR correlates with degree of disc edema and differs between the various etiologies. In addition, there is significant correlation between the degree of edema in IHH patients and the LP opening pressure. It seems that measurements of NRR thickness and area, as well as longitudinal measurements, may add information regarding course and prognosis of disc edema.

2

Evaluation of distance stereoacuity in children with a novel digital application.

Guy Barnett-Itzhaki(1,2) Zohar Barnett-Itzhaki(3) Noa Ela-Dalman (1,2)

Department of Ophthalmology, Meir Medical Center, Kfar Saba, Israel (2) Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel (3) School of Engineering, Research Center for Health Informatics, Ruppin Academic Center, Emek Hefer, Israel

Purpose: Stereopsis is a fundamental skill in human vision and visual actions. There are serval ways to test and quantify distance stereoacuity: traditional and new digital applications are both valid ways to test the stereoacuity. The aim of this study is to compare the results obtained using standard tests for distance stereoacuity measurement with the new StereoTAB App.

Methods: A group of 120 children (69 females), aged between 4 and 17 years old (mean age 9.16), were tested using different tests for the quantification of stereopsis at distance. These tests were Distance Randot Stereotest, M&S random dots and the new developed StereoTAB App.

Results: Stereopsis at distance was better with M&S random dots (2.09) than with Distance Randot Stereo test (2.19) or StereoTAB (2.21), but not significantly (Kruskal Wallis,P= 0.117). A strong correlation was demonstrated between: M&S random dots and Distance Randot Stereotest(0.83,P<0.0001), M&S random dots and StereoTAB App(0.84,P<0.0001), Distance Randot Stereotest and StereoTAB App(0.88, P<0.0001). The limits of agreement (Bland–Altman) between M&S random dots and Distance Randot Stereotest was 0.54, between M&S random dots and StereoTAB App was 0.55, and between Distance Randot Stereotest and StereoTAB App was 0.45.

Conclusions: The distance stereoacuity based on random dots stereopsis showed that the better values were obtained in order by M&S random dots, Distance Randot Stereo test, and StereoTAB. However, the clinical significance of their values is similar, and they can be used interchangeably. The introduction of versatile, fast, and portable stereopsis test which can be used at different distances with children is of primary importance.

21

Development and validation of a questionnaire for assessing Parents' awareness and perception of vision screening and exams for children: a Delphi study.

Ahuva Ravid-Saffir(1,2), Shulamit Sella(1), Ariela Gordon-Shaag(1), Hadas Ben-Eli(1,3) (1) Department of Optometry and Vision Science, Hadassah Academic College, Jerusalem (2) Goldschleger Eye Institute, Sheba Medical Center, Tel-Hashomer, Ramat-Gan (3) Department of Ophthalmology Hadassah-Hebrew University Medical Center, Jerusalem

Purpose: Preschool vision screening is recommended to reduce the incidence of amblyopia. However, parent's perceptions regarding the importance of screening and early intervention may constitute a significant barrier to seeking eye and vision exams and pursuing treatment. The aim of this study was to develop and validate a questionnaire for assessing parent's awareness, perception and knowledge of children's vision tests and willingness to adhere to recommendations.

Methods: The questionnaire was developed using the Delphi method with experts from the fields of pediatric ophthalmology, optometry, orthoptics, pediatric medicine, social sciences and Mother Child Health Care centers. Experts were provided with drafts of the questions iteratively, in three-rounds until a consensus was reached independently on the relevant items that would be included in the questionnaire. The experts were also asked to point out and comment on poor wording or redundancies in the proposed questions and to suggest missing questions. Initial face and content validity were examined by calculating consensus between experts.

Results: The first, second and third stages of the Delphi process, 17, 15 and 13 experts participated in the panel, respectively. To enable the participation of international experts, the questions were composed and processed in English. Face and content validity were achieved by wide consensus among the panel on the relevance of each question, of 75%, 85% and 90%, for the three rounds, respectively. Furthermore, seven questions were added to the question pool after the first stage. At the end of the Delphi process, a questionnaire consisting of 31 questions was obtained. The final questionnaire consists of five demographic questions regarding the respondent, 12 questions that examine health literacy, perceptions and attitudes of parents regarding vision tests, 5 questions about the child and relevant family history, and 9 questions concerning the adherence of the parents with vision exams. The final questionnaire was translated into Hebrew by a professional translator and reliability of the translation was checked by two experts.

Conclusions: The Delphi process used in this study created a validated questionnaire for assessing parents' awareness and perception of and adherence to vision exams. The validated translation into Hebrew, allows the use of it for research in Israel as well. In the future, the questionnaire will be piloted on a sample group of parents of young children.

24

Variants of the Cloverleaf Pattern that are associated with Inattentiveness during automated perimetry.

Arie Maya [1], Elhanan Parnasah [2],Joshua M. Kruger [1]
[1] Department of Ophthalmology, Hadassah Medical Center; [2] Department of Internal Medicine, Hadassah Medical Center

Purpose: Loss of attention during conventional automated perimetry is associated with a cloverleaf pattern in the greyscale map. We sought to determine if there are other recognizable patterns.

Methods: Healthy volunteers were recruited for the study and familiarized with a sita-standard 24-2 algorithm on the Humphrey Field Analyzer. For each volunteer, testing was repeatedly performed on the right eye six times. During each test, the volunteer was instructed to stop responding to stimuli at one of the following six predetermined time points: 30 seconds, 45 seconds, 60 seconds, 75 seconds, 90 seconds, and 120 seconds.

Results: Six volunteers were recruited. The following findings were noted: 1) The first location to be quantified was always located at 9 x 9 degrees from fixation, but could be in any quadrant. 2) The next locations to be quantified were peripheral and adjacent to the 9 x 9 points. 3) The immediate paracentral points are not quantified before 90 seconds, and the nasal step was not evaluated during the entire 120 seconds. 4) The classic cloverleaf pattern requires at least 75 seconds of normal attention.

Conclusions: When patients lose attention before 75 seconds, distinct recognizable patterns occur which correspond to the specific duration of attention.

27

Reading Performance Improvement in Amblyopic Children Using Dichoptic Eye-tracking Training and an Eye- tracking Based- 30 Second Reading Test.

Tamara Wygnanski – Jaffe1, Michael Belkin2 , Avital Moshkovitz 3, Oren Yehezkel3
1. Goldschleger Eye Institute, Sheba Medical Center, Tel-Hashomer, Israel. 2. Goldschleger Eye Research Institute, Sheba Medical Center, Tel Hashomer, Israel. 3. Novasight Ltd, Airport city, Israel

Purpose: Reading is fundamental to academic achievement and child development. Strabismic and or anisometropic amblyopes were found to be slower readers when compared with controls. Poor reading among amblyopes is attributed to their fixation instability which causes them to have difficulties in planning and executing accurate forward saccades during reading.
An automatic diagnostic eye tracking based system (Eyeswift) was used to assess reading performance including speed, saccades and fixations during 30 seconds of overt binocular reading of age-appropriate texts.

Methods:
Ten subjects with amblyopia (8-16 years old) were treated for 12 weeks with the CureSight, a novel eye tracking-based dichoptic amblyopia treatment that overlaps the images perceived in both eyes while inducing dynamic foveal blur in the dominant eye, thus reducing interocular suppression.

Results:
Binocular reading speed improved significantly from 100±11 to 147±12 words per minute (an improvement of 47%; $P<0.005$, paired t-test). Average fixating duration decreased from 319±22 to 268±13 msec ($P<0.005$, paired t-test) and the average number of fixations during 30 seconds of reading increased from 62±7 to 72±8 ($P<0.005$, paired t-test). The resulting number of words read per fixation increased from 1.5±0.2 to 1.8±1 ($P<0.05$, paired t-test).

Conclusions:

The rapid automatic reading test was very effective in evaluating reading performance. This unique preliminary report indicates that dichoptic training improves binocular reading speed in amblyopic children. Furthermore, the ratio between the number of words read and fixations indicates that more efficient reading occurred. Most notably, this 30 second in office measurement of reading abilities can facilitate amblyopia treatment follow-up and provide additional data on functional improvement following treatment.

82 AC,

Chromatic Pupilloperimetry for Objective Diagnosis and Monitoring of Patients with Pseudotumor Cerebri.

Yossi Eshel, Ifat Sher, Ruth Huna-Baron, Ygal Rotenstreich
(1) The Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, Israel (2) Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel (3) Department of Ophthalmology, Hadassah-Hebrew University Hospital, Jerusalem

Purpose: To characterize rod-, cone- and melanopsin-mediated pupil responses (PLR) for small focal chromatic light stimuli presented in peripheral and central retinal locations in PTC patients before and after initiation of ICP reduction treatment.

Methods: 10 PTC patients (all females, Age: 29.1 ± 7.9 YO) and 17 age-similar healthy controls (all females, Age : 24.6 ± 6.3 YO) were enrolled. The pupil light responses (PLR) for small (0.43?) and short (1 second) red (624 ± 5 nm, 1000 cd/m2) and dim blue light stimuli (485 ± 5 nm, 170 cd/m2) presented at 54 locations of a 24-2 visual field were recorded and the PPC (percentage of pupil constriction) was calculated. In addition, the PLR for prolonged (8 seconds) bright blue light stimuli (485 ± 5 nm, 6000cd/m^2) presented at 4 central and 4 peripheral VF locations were recorded and the PPR (percentage of pupil recovery) was calculated. Patients underwent follow-up chromatic pupilloperimetry tests 7 days and 3 months after the ICP lowering treatment was initiated. All subjects underwent a complete ophthalmic exam, standard Humphrey automated perimetry (24-2), color vision test, BCVA test, and Optical Coherence Tomography (OCT) imaging.

Results: Two subgroups of PTC patients were identified: with reduced or surprisingly abnormally enhanced PLR. The "Reduced response" subgroup had lower rod and cone-mediated PPC (p= 4.29E-37, p= 1.94E-18, respectively) and higher melanopsin-mediated PPR (p= 4E-4). In contrast, the ""Enhanced response"" subgroup had higher rod and cone-mediated PPC (p= 1.68E-62, p= 2.9E-57, respectively) and lower melanopsin-mediated PPR (p=0.056) compared to controls. The "Enhanced response" subgroup showed statistically significant reduction in rod and cone-mediated PPC (toward the mean of healthy patients) during ICP reduction therapy on visit 2 (p= 0.005 and p= 1.1E-12, respectively) and a further decrease on visit 3 (p= 1.9E-19 and p= 1E-4, respectively). In contrast the "Reduced response" subgroup showed a further decrease (away from the mean of healthy patients) in rod and cone-mediated PPC on visit 2 (p= 0.016 and 5.9E-9, respectively) which remained unchanged on visit 3 (p= 0.2, p= 0.71, respectively).

Conclusions: PTC patients may present attenuated or surprisingly abnormally higher than normal pupillary responses. This heterogeneity may reflect different stages of pupil abnormality. The abnormal rod-, cone- and melanopsin-mediated pupil responses may present a highly sensitive surrogate functional biomarker for detection of PTC, and monitoring response to treatment.

86

Utility of eye tracking in a visual cortical prosthesis.

Avi Caspi
Jerusalem College of Technology, Jerusalem, Israel and Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, MD, USA

Restoring functional sight requires that the electrical stimulation should convey information to the brain that is associated with the correct spatial location in the scene. A visual cortex stimulator can bypass the eye and the optic nerve and create phosphenes, perception of light without light entering the eyes. Nonetheless, recently we demonstrated that eye movements dominate the perceived location of cortical stimulation-evoked phosphenes, even after years of blindness. In the current presentation we will present results from patients testing demonstrating the correlations between eye movements and the visual precept. Eye movement plays several roles in cortical visual prostheses. Eye position dominates the perceived location of the percent. Additionally, by instructing patients to conduct an eye movement toward the phosphene, eye tracking can be used as a marker to construct the spatial map of implanted cortical electrodes. Experiments were conducted with blind patients implanted with the NeuroPace Responsive Neurostimulator (RNS) and the Orion visual cortical prosthesis devices.

In a cortical visual, the layout of the implanted array does not match a retinotopic map and it is, therefore, necessary to find the location of the percept of each implanted electrode. To establish the spatial map of the electrodes, users were instructed to conduct an eye movement to the location of the phosphene generated by electrical stimulation of the occipital lobe. Two different schemes were compared. In the first, a brief stimulation was presented and the subject moved their eyes after the end of the stimulation toward the remembered phospene's location. In the second, a longer stimulation was presented and the subject moved their eye during the stimulation to track the phosphene's location. In the latter case, because the stimulation is continuously mapped based on eye position, an eye movement during the stimulation caused the phosphene to move. Results show that subjects were able to conduct a smooth pursuit motion as a result of constant stimulation.

These experimental setups demonstrate that the integration of eye-tracking recording can be used to create the spatial map of a cortical visual implant.

100

Objective measures of viewing behavior of myopic and non-myopic adults during near tasks.

Ravid Doron (1), Ariela Gordon-Shaag (1), Meira Zyroff (1), Lisa Ostrin (2) and Einat Shneor (1)
(1) Dept. of Optometry, Hadassah Academic College, Jerusalem (2) College of Optometry, University of Houston, Houston

Background: Evidence suggests that near working distance is associated with myopia. However, in most previous studies, near work distance and duration was assessed using questionnaires or proxies of near work such as education. The purpose of this study was to use an objective, continuously measuring range finding device to examine near work viewing behaviors in in non-myopic and myopic young adults.

Methods: Viewing distance was assessed in young adult men using the Clouclip, an objective rangefinder, during four 10-minute near tasks, including (a) passive reading and (b) active writing paper, (c) passive viewing of an iPad and (d) active engagement on an iPad. Visual acuity, autorefraction (VX130, Luneax) and axial length (Lenstar) were measured. Myopia was defined as spherical equivalent of ?-0.50 D. Continuous variables were compared using the Friedman and Mann-Whitney tests.

Results: Ten non-myopic (24.4 ± 2.8 years) and 27 myopic (24.0 ± 3.51 years) subjects participated in the study. Refractive error and axial length for the entire cohort was -1.69 ± 2.57D and 24.32 ± 1.47mm, respectively. Myopes had significantly higher refractive error (-2.56 ± 2.43D vs 0.55 ± 1.23D, $p<0.0001$) and axial length (24.72 ± 1.54 vs. 23.32 ± 0.49, $p<0.0007$) than non-myopes. For all subjects, the mean viewing distances significantly differed by task (41.73 ± 9.14, 34.80 ± 9.36, 44.02 ± 10.42 and 40.91 ± 9.24 for passive reading, active writing, passive viewing, and active engagement iPad, respectively, $p<0.0001$). Post-hoc analysis showed that writing on paper had a significantly shorter working distance than all other tasks ($p<0.002$). Furthermore, passive viewing of an iPad had a longer working distance than actively playing on the iPad ($p<0.005$). Viewing distance did not vary significantly in any of the tasks between myopes and non-myopes (41.10 ± 9.26 vs 43.37 ±9 .56, 34.57 ± 9.72 vs 36.06 ± 8.99, 43.53 ± 10.54 vs 46.58 ± 10.95 and 40.20 ± 8.94 vs 43.72 ± 10.66 for passive reading, active writing, passive viewing and active engagement iPad, respectively, $p>0.05$ for all).

Conclusions: Adults demonstrated differing viewing distances based on the type of near task they were performing. Viewing behaviors did not vary between myopic and non-myopic adults. Findings will contribute to a better understanding of how near viewing behaviors can be quantified objectively and relationships with myopia.

102,AC

Rod, cone and melanopsin mediated pupil responses to focal light stimuli in the central and peripheral retina in Fragile X carriers.

Dima Shbita (1,2), Ifat Sher (1,2), Ygal Rotenstreich (1,2)
(1) The Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, Israel; (2) Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Purpose: To characterize rod-, cone- and melanopsin-mediated pupil responses (PLR) for small focal chromatic light stimuli presented in peripheral and central retinal locations in Fragile X carriers.

Methods: 8 Fragile X carriers (all females, Age: 57.5 ± 18 YO) and 31 age-similar healthy controls (all females, Age : 55.5 ± 19 YO) were enrolled. The PLR for small (0.43 degrees) red and blue light stimuli presented at central (4.2 degrees) and peripheral (21 degrees) visual field locations were measured using a chromatic pupilloperimeter under mesopic light adaptation conditions. All subjects underwent a complete ophthalmic exam, Fransworth D15 color vision test, best-corrected visual acuity, refraction and Spectral-Domain Optical Coherence Tomography (SD-OCT) imaging And Montreal Cognitive Assessment (MoCA).

Results: Surprisingly, six of the eight carriers demonstrated mild- medium color vision defects.The rod-mediated maximal percentage of pupil contraction was significantly lower at central (7.1% ± 6.1% vs 14.2% ± 5.7%, p=0.008) but not peripheral retinal locations in Fragile X carriers compared with controls. In addition, the latency of maximal pupil contraction was significantly longer in Fragile X carriers compared with controls (1 sec ± 0.12 sec vs 0.54 sec ± 0.04 sec, p=8E-38). Melanopsin- and cone- mediated pupil responses did not significantly differ between groups.

Conclusions: For the first time we demonstrate mild - medium color vision defects in Fragile X carriers. The Fragile X carriers present attenuated rod mediated pupil light responses in the central retina specifically in the contraction arm of the reflex, suggesting that the rod- mediated PLR may present a potential objective functional biomarker for Fragile X carriers.

7 AC,

Outcome of primary monocanalicular stent placement in pediatric Down's syndrome patients with congenital nasolacrimal obstruction.

Daphna Landau Prat [1,2], Christiana E. Munroe [2], Karen E. Revere [2], Lama Khatib [2], Peiying Hua [3], Gui-Shuang Ying [3], Gil Binenbaum [2], William R. Katowitz [2]
[1] Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, Israel, affiliated to Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [2] Children's Hospital of Philadelphia, 3401 Civic Center Blvd, Philadelphia, PA, USA; [3] Center for Preventative Ophthalmology and Biostatistics, Perelman School of Medicine at the University of Pennsylvania, 3711 Market Street, Suite 801, Philadelphia, PA, United States

Purpose: Congenital Nasolacrimal duct obstruction (CNLDO) is a relatively common problem in children with Down Syndrome (DS). Probing and irrigation (PI) may be less successful with monocanalicular stent intubation (MSI), thus raising some concern regarding the preferred treatment in this population. The purpose of the current study was to describe the surgical outcome of PI along with MSI in children with DS compared with non-DS patients.

Methods: Retrospective comparative case series. Thirty-five consecutive eyes of 19 children with DS and 1,472 consecutive eyes of 1001 children without DS who underwent MSI as a primary treatment for CNLDO. All patients were operated on by a single surgeon at the Children's Hospital of Philadelphia between 2009-2020. Main Outcome Measure was Surgical success defined as resolution of symptoms after surgery.

Results: A total of 1020 patients participated in the study, 48% females; mean age of 1.9±1.4 years (range: 0.1 – 18.1). The mean follow-up time was 35.0 months. The DS patients group consisted of 19 patients, 12 females, with a mean age of 2.5±1.6 years (range: 0.7-6.23). A higher rate of right NLDO was observed in the DS group (100% vs. 73.2%, p=0.006). Patients with DS had more bilateral obstructions (84.2% vs. 46.8%, p=0.001) and had lower success rate (57.1% vs 92.4%,p<0.0001).

Conclusions: CNLDO in DS is more likely to be bilateral and to involve the right nasolacrimal system, less likely to resolve after initial MSI. Additional procedures may be considered if found to be more successful in future studies.

31

The role of thyroid stimulating immunoglobulin (TSI) in evaluating Thyroid Eye Disease.

Shiran Madgar 1, Guy Ben Simon 1 , Ayelet Priel 1, Daphna Prat 1, Oded Sagiv 1, Tali Cukierman-Yaffe 2, Amir Tirosh 2, Nancy Agmon-Levin 3, Tal Serlin 1, Ofira Zloto 1

1Goldschleger Eye Institute, 2Division of Endocrinology, Diabetes and Metabolism, and 3Clinical Immunology, Angioedema and Allergy Unit, Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer, Israel, affiliated to the Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel

Background: The most common blood tests to evaluated patients with Thyroid Eye Disease (TED) are: Thyroid Stimulating Hormone (TSH), T3, T4. However, it is known that those blood tests are not correlated with the severity of TED. In the last years, a new blood tests for Thyroid Stimulating Immunoglobulins (TSI) is in use. However, there is not enough evidence about the correlation between the TSI level to Thyroid Eye Disease (TED). Therefore, the purpose of this current study is to evaluate the correlation between TSI and TED and to examine if TSI is a good predictor for the severity of the disease.

Methods: A retrospective review of medical records of all patients who attended the TED clinic at Sheba Medical Center, Israel from January 2020 to December 2021 and had a TSI result was performed. The retrieved data included demographics, comprehensive ophthalmic examination findings, clinical activity scores (CAS), laboratory test results, and QOL assessments by the Graves' Orbitopathy QOL questionnaire (GO-QOL).

Results: 30 patients had a known TED and a documented TSI result. It was found that the TSI is correlated positively with eyelids involvement of TED (P=0.007) and IOP (P=0.027) while negatively correlated with HRR test (P=0.049) and Pattern standard deviation result (P=0.048). There was also an association between high TSI level and the need for steroid treatment according to the European Group on Graves' Orbitopathy (EUGOGO) protocol (P=0.037).

Conclusions: TSI value is correlated to the clinical features of the TED as well as for the treatment. Therefore, TSI can be considered as a good predictor factor for the severity of the disease. It is recommended to add this blood test to the panel of blood tests for patients with TED.

36 AC,

Why posterior approach ptosis surgery can fail.

Noa Kapelushnik, Ofira Zloto, Guy J. Ben Simon

1Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, Israel, affiliated to the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Purpose: Müller's muscle-conjunctival resection (MMCR) is commonly carried out in the treatment for upper eyelid ptosis, but the results are not always as good as expected. The aim of this study was to evaluate factors that may be associated with failed posterior approach ptosis surgery.

Methods: We retrospectively reviewed the medical records of all patients who underwent MMCR surgery in two medical centers between 1/2016 and 9/2018. Data on comprehensive ophthalmic and oculoplastic examinations were retrieved and analyzed. Margin-to-reflex distance (MRD) measurements were performed pre- and postoperatively on digital clinical photographs with ImageJ software. Only the right eye was included in the statistical analysis of bilateral surgeries. Functional outcome was defined as improvement of MRD1 and eyelid asymmetry <1 mm.

Results: In total, 79 patients [59 (74.7%) females, mean age 57.9±15.5 years, range 14.5-84.1 years] who underwent posterior approach ptosis surgery were included. Forty-seven (59.5%) patients underwent bilateral surgery, and 32 patients underwent unilateral surgery. Success was achieved in 71% of the patients. Failure was associated with unilateral surgery ($p<0.001$, chi square) and right upper eyelid surgery ($p=0.002$). Congenital ptosis was also associated with surgery failure, although to a lesser extent ($p=0.1$, Fisher Exact test). Sex, contact lens use and previous ocular surgery did not influence the outcome.

Conclusions: Successful posterior approach ptosis surgery is less predictive than commonly believed. Surgery failure, albeit minor or asymmetry-related, may be related to a congenital ptosis etiology and to unilateral surgery, especially when performed on the dominant right eye.

38 AC

The tobacco consumption effect on the clinical findings, treatment and prognosis of TED patients.

Lital Smadar 1, Guy Ben Simon 1, Ayelet Priel 1, Daphna Prat .1, Oded Sagiv 1, Tali Cukierman-Yaffe 2, Amir Tirosh 2, Nancy Agmon-Levin 3, Tal Serlin 1, Ofira Zloto 1

1Goldschleger Eye Institute, 2Division of Endocrinology, Diabetes and Metabolism, and 3Clinical Immunology, Angioedema and Allergy Unit, Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer, Israel, affiliated to the Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel

Background: The association between tobacco smoking and worsening of Thyroid Eye Disease (TED) was previously reported in the literature. However, the association between smoking and clinical and therapeutic parameters as well as long term prognosis is lacking. Therefore, the purpose of this current study is to examine the association between clinical findings, blood tests, treatment and long and smoking.

Method: A retrospective review of medical records of all patients who attended the TED clinic at Sheba Medical Center, Israel from 2016 to 2021 was done. The retrieved data included comprehensive ophthalmic examination findings, clinical activity scores (CAS), laboratory test results, drug therapy, surgeries and prognosis. The data compared between the tobacco consumers and non-consumer patients.

Results: Thirty-five TED patients (15 men, 20 women) were included in this study, with a mean age of 44.79 years. From them 15 (42.8%) were non-tobacco users and 20 (57.2%) were tobacco users.
In their first clinic in the clinic, tobacco consumers were presented with higher CAS compared to non-consumers (2.5 vs. 1.5, accordingly, p=0.043). Tobacco consumers had significantly more optic neuropathy compared to non-consumer patient (P=0.041, Chi-Square test).
TSH was significantly higher in tobacco-consumer patients vs. the non-consumer group (2.38 vs. 1.07, accordingly, p=0.045 ANOVA). The TSI mean was 1517% in tobacco-consumer patients, while it was almost 5 time less (391) in the non-consumer patients (p=0.046 ANOVA).
Seven tobacco consumers (35%) underwent decompression surgery while only 1 non-consumer patient (6.7%) underwent decompression surgery (p=0.048, Chi-Square test).
Five tobacco consumers (25%) got EUGOGO steroids treatment while only two (13.3%) non-consumer patients received this treatment (P=0.035 Chi-Square test).

Conclusions: Tobacco consumption proves to be negative prognostic factor for TED patients. Tobacco consumption are more likely to experience disease progression, to get more interventional treatments and they have poorer outcome. TED patients who consume tobacco should be encourage to stop it with the diagnosis of the disease.

51 AC

Reliability of Ptosis diagnosis on assessment via video consultation.

Ofira Zloto, Victor Paiusco, Fabiola Murta
Adnexal service, Moorfields Eye Hospital, London, England

Purpose: To examine the reliability of adult ptosis assessment in video consultation.

Methods: This is a retrospective, comparative, case series. The surgical waiting list for ptosis surgery between August 2020- January 2021 was checked and only cases listed for surgery via video consultation assessment, without any previous face-to-face consultation, were included.
The following data were collected for patients who underwent video consultation before surgery: Demographic data, date of video consultation, level of experience of clinician (Consultant/ Fellow/ Resident), side of ptosis, levator function, Cogan's twitch sign, fatigability test, eye motility, presence of lagophthalmos, questions to rule out Myasthenia Gravis or other myopathies, if the surgery was performed/cancelled, date of surgery, type of procedure, side and surgeon experience.

Results: 176 patients underwent ptosis surgery between 8/2020 to 1/2021. From them, 45 patients (25.6%) had a video assessment only prior to surgery when ptosis was diagnosed and patient was listed for surgery. Video consultation was done by: Consultant: 30 cases (67%); Fellow: 15 cases (33%). 36 patients (80%) eventually underwent ptosis surgery. Surgery was cancelled in 20% of the cases. It was due to: surgery no longer required due to misdiagnosis of ptosis confirmed on the day of surgery during pre-surgical face-to-face assessment in 2 cases (4.44%). Although ptosis was confirmed in the other 7 cases (15.55%) surgery was cancelled for other reasons. Reliability of ptosis assessment via video consultation was correct in 43 cases (95%) (p_value=0.156, chi_ square). In most of the cases ptosis assessment in video included: Judgment of levator function, eye motility and lagophthalmos check but not all cases had Cogan's twitch sign, fatigability test and questions to rule out Myasthenia Gravis performed.
Conclusions: Video consultation is an efficient and reliable way to assess patients with ptosis. Although an accurate and more thorough ptosis assessment is advised there was no difference between accuracy of diagnosing on those who did not do the full suggested assessment.

68 AC

Eyelid cysts over three generations.

Yakov Rabinovich (1), Inbal Man-Peles (1), Yoav Vardizer (1), Nitza Goldenberg-Cohen (1)
(1) Department of opthalmology, Bnai Zion Medical Center, Haifa

Introduction:

Cystic lesions of the eyelids are common, and usually secondary to infections or blepharitis. Genetic lesions are rare and difficult to diagnose. Here we present familial lid cysts with systemic manifestations

Case Description

Sixty-five years old grandmother with a history of rheumatoid arthritis, and her 12 years old generally healthy grandchild, presented to our clinic complaining of excessive tearing due to bilateral eyelid marginal cysts consisting with moniliform blepharosis. Symptoms were attributed to cystic lesions blocking the puncta orifice. The younger patient had the lesion surgically excised. Systemic manifestations included hoarseness due to vocal cord lesions. No neurological or psychiatric diseases were reported in the extended family including these members.

Results:

Biopsy results demonstrated marked fibrotic infiltrates with PAS positive stain, consisting with hyalin disposition. Abnormality in the ECM1 gene was detected in gene sequencing.

Discussion:

Here we present familial genetic eyelid cysts in the consanguineous family, diagnosed as the rare lipid proteinosis (LP) lesions. LP is also known as Urbach-Wiethe syndrome, an autosomal recessive disorder caused by mutations in the ECM1 gene, located on chromosome 1q21.2. This syndrome is a result of abnormal extracellular matrix deposition, ensuing in excessive amount of hyalin deposition in various tissues. Both mucocutaneous and neurological manifestations have been reported, notably dysphonia due to laryngeal cysts and cystic skin lesions. Surprisingly, albite neuropsychiatric symptoms are rare, hippocampal and amygdala calcifications can be found in at least half of the affected patients on radiological imaging. Further clinical and genetic analysis of the extended family may lead to better understanding of the pathogenesis underlying this syndrome.

112 AC

Outcomes of Mueller's Muscle Conjunctival Resection: Ethnic Considerations.

Zvi Gur,

Department of Ophthalmology, Hadassah Medical Organization and Faculty of Medicine, Hebrew University of Jerusalem, Jerusalem, Israel

Purpose: To compare outcomes of Mueller's Muscle Conjunctival Resection (MMCR) between 2 groups of patients with different anatomy due to ethnic heritage.

Methods: The medical records of patients who underwent MMCR between 2013 and 2018 were retrospectively reviewed. Patients who underwent additional procedures, such as upper blepharoplasty and browplasty, were excluded from the study. Patients were divided in 2 groups based on self-identified ethnic groups (Asian and Caucasian). Image J software was used to calculate MRD1 from digital images. The improvement of MRD1 (net MRD1) after surgery was evaluated and compared between 2 groups.

Results: Eighty-three eyes of 68 patients were included in this study. The Asian group consisted of 41 eyelids from 28 patients. The Caucasian group consisted of 42 eyelids from 40 patients. The average age was 52.18 (SD 20.176) in the Asian group compared with the 66.45 years (SD 9.22, $p< 0.005$) in the Caucasian group. The mean improvement of MRD1 was 1.96 ± 0.75 mm in Asian group and 2.05 ± 0.72 mm in Caucasian group, which was not statistically significant ($p = 0.62$). The incidence of ptosis overcorrection and undercorrection between the groups was also not statistically significant.

Conclusions: There was no statistically significant difference in the surgical outcomes among the 2 study groups. Despite differences in the anatomy of Caucasian and Asian eyelids, MMCR is a successful procedure in patients self-identified from both ethnic groups.

114 AC

Outcomes of Unilateral Mueller's Muscle Conjunctival Resection: Implication of Hering's Law.

Zvi Gur
Department of Ophthalmology, Hadassah Medical Organization and Faculty of Medicine, Hebrew University of Jerusalem, Israel

Purpose:
To determine the effect on unilateral upper eyelid ptosis correction by posterior approach conjunctival muellerectomy (MMCR) on the contralateral upper eyelid.

Methods:
The medical records of patients who underwent unilateral MMCR between 2013 and 2018 were retrospectively reviewed. Patients who underwent additional procedures, such as upper blepharoplasty and browplasty were excluded from the study. Image J software was used to calculate MRD1 of the operated and non operated eyelid from digital images.

Results:
Thirty-three eyes of 33 patients were included in this study. Average age was 51.7 ± 18.5 years. All the 33 cases had unilateral aponeurotic ptosis that did not require contralateral surgery. One patient experienced MRD1 drop of more than 1mm in the fellow eye. Another single patient exhibited MRD1 drop of 1.0mm. Eight cases showed decrease of 0.5-0.9 mm in the contralateral eyelid. Twenty-three patients showed less than 0.5 mm decrease in the non-operated eye. No additional surgeries we needed to be performed the neither of the eyelids.

Conclusion:
In mild to moderate case of unilateral upper eyelid ptosis, MMCR is a safe procedure with minor if any effect on the contralateral eyelid.

118,AC

The Correlation Between Chronic Usage of Topical Anti-Glaucoma Eye Drops and Lower Eyelid Increased Laxity.

Lital Smadar 1, Mordechai Rosner, 1, Noa Kapelushnik, 1, Guy Ben Simon, 1, Alon Skaat 1, Daphna Landau Prat,1 Ofira Zloto1

1Goldschleger Eye InstituteSheba Medical Center, Tel-Hashomer, Israel, affiliated to the Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel

Background: Ectropion in elderly patients is often assumed to be involutional, due to an increased horizontal and vertical lid laxity.
The first line of treatment in glaucoma patients is topical anti-glaucoma eye-drops, which are accompanied by a list of side effects caused by these agents and include ocular surface changes. In order to put those drops the patients stretch the lower eyelid. We hypothesis that this stretching may cause an ectropion. To the best of our knowledge this is the first time that this assumption is examined.

Method: A prospective, case-control comparison between glaucoma patients who use anti-glaucoma eye-drops vs. patients without glaucoma and that are not use eyedrops was done. All participants had gone through slit lamp examination and lower eyelid laxity tests and measurements.

Results: Fifty patients (26 men, 24 woman) were included in this study, with a mean age of 65 years. Out of those 20 (40%) glaucoma patients and 30 (60%) without glaucoma. In their clinical examination, glaucoma patients demonstrated higher lower eyelid laxity in both the Horizontal Laxity- Eyelid Distraction Test (3.125 mm vs. 1.98 mm, accordingly, $p<0.01$) and in Eyelid Distraction Test- Snap Back Test compared to the control group (4.65 mm vs. 2.25 mm, accordingly, $p=0.007$). Another finding in eye exam was the presence of Punctate Epithelial Erosions (PEE), that was significantly higher in the glaucoma group compared to the control group (1.6 vs. 0.06 accordingly, $p<0.01$).

Conclusions: In this study we found correlation between chronic usage of topical anti-glaucoma eye drops and increased lower eyelid laxity. Therefore, patients may need to be instructed to put the drops without stretching the lower eyelid. In addition, we found that the rate of PEEs in glaucoma patients was higher compared to control. Further studies should examine if this is due to the ectropion or to the anti-glaucoma drops side effect.

58 AC

Scleral Contact Lens Designed to Reduce Ptosis.

Zvi Gur (1), Nir Erdinest (1), Naomi London(2), Itay Lavy (1)

(1) Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem. (2) Private practice, Jerusalem.

Purpose: To explore whether scleral contact lenses can be designed to reduce ptosis effectively.

Methods: Eight patients, five males, with an average age of 39.3±14, were included in this study. All had monocular ptosis. Four had worn rigid gas permeable lenses, three post-trauma, one with an oculomotor palsy. To create a type of upper lid support, all these patients were fit with an asymmetrical scleral lens design with a superior limbal clearance of above 250 microns. The patients were also fitted with a soft lens. The upper lid marginal reflex distance (MRD) was measured without a lens, the soft lens, and the scleral lens using the Image Pro-Plus Software (Image Pro-Plus 6.0; Media Cybernetics, Silver Spring, MD, USA).

Results: The MRD did not change with the soft lens compared to without a contact lens. The MRD increased with the scleral lens compared with the soft lens with an average of +2.38±0.79 mm ($P<0.01$).

Conclusions: The superior excessive limbal clearance scleral lens design effectively decreased monocular ptosis in these patients.

15 AC

Ocular related emergencies at Hadassah Medical Center emergency department: a retrospective study.

Malak Sultan(1), Zena Mittwalli(1), Marina Abdallah(1), Einat Shneor(1), Hamzah Aweidah(2), Hadas Ben-Eli(1,2)
(1) Department of Optometry and Vision Science, Hadassah Academic College, Jerusalem (2) Department of Ophthalmology Hadassah-Hebrew University Medical Center, Jerusalem

Purpose: To determine the frequency of emergency department visits for ocular conditions presenting complaints and diagnosis for each of the non-urgent versus urgent ocular conditions.

Methods: An anonymous monocenter retrospective study included subjects presented to the ophthalmology emergency department (ED) at Hadassah Medical Center between January 2018 to June 2018. Data collected included age, gender, main ocular complaint, diagnosis, medical history, medical intervention and discharge status (hospitalization or sent to home). Diagnoses were categorized into eight main categories and their prevalence was calculated. A Chi square test was used to compare results by sex and age groups (adults ≥50, young people <50) for each category.

Results: A total of 906 subjects were included in the study with a mean age of 38.4 ± 23.1 years, (range 23 days - 96 years, 57% men, 35% adults >50). Eye pain was the most common complaint (21.2%) while viral conjunctivitis was the most common diagnosis (8.38%). Comparison by sex groups revealed that anterior segment disorders including trauma were more common in males ($p < 0.001$) while orbital and eyelid defects, retinal defects and optic nerve disorders were more common in females ($p < 0.0001$). Orbital and anterior segment disorders, optic nerve disorders and trauma were more common in young < 50 years ($p < 0.001$), while lens and retinal disorders were more common in adults ≥ 50 years ($p < 0.0001$). Surprisingly, 39.2% required medical/ surgical intervention and only 5.4% were hospitalized (59.2% of them were young, with no difference between age groups, P=0.06).

Conclusions: This study demonstrates that most ophthalmic ED presentations were related to anterior segment disorders while only a small proportion required hospitalization. This indicates the importance of regular emergency outpatient services in the community clinics to reduce ED congestion.

25

Uveal melanoma Patients reported outcomes (PROMS).

Vicktoria Vishnevskia-Dai1,2,3, Ido Didi Fabian1,2,3, Alex Galper2, Eyal Zimlichman2,3
1Goldschleger Eye Institute 2Sheba Medical Center, Tel Hashomer, Israel 3Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Purpose: To report on the Uveal melanoma Patients reported outcomes (PROMS) one year from the operation.
Design: prospective cohort study.
Participants: All patients with Uveal melanoma treated with brachytherapy at the Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, since Jan 2017 who signed an inform consent.

Methods: Patients were requested to fill validated and translated questionnaires on the general heath and ocular function at baseline (day of operation) and 3 months intervals.

Results: Forty patients were recruited. 57% were male gender; the average age was 64 years. Twenty-three patients completed 3 months questionnaire, 17- 6 months, 10 -12 months questionnaire and 4 completed 18 months questionnaire. All together 90 questionnaires were completed. The basic process demonstrated by the questionnaire: eye pain is resolving within 6 months. Driving ability is deteriorating with time. Far and near visual activities Deteriorate 3-6 months and improve but does not reach . baseline in 12 months. Social and mental functions are stable in 3 months but slightly deteriorating with time.

Conclusion: PROMS is a powerful tool that can assist us with understanding the healing process from the patient's point of view. It is an essential tool for physicians aiming to place the patients' needs in the center.

28

BAP1 immunohistochemistry in post-brachytherapy uveal melanoma,

Maya Eiger-Moscovich (1,2), Carol L. Shields (3), Ralph C. Eagle Jr. (2), Tatyana Milman (2,4)

(1) Department of Ophthalmology, Hadassah Medical Center, Jerusalem, Israel; (2) Department of Pathology, Wills Eye Hospital, Philadelphia, PA, USA; (3) Ocular Oncology Service, Wills Eye Hospital, Philadelphia, PA, USA; (4) Department of Ophthalmology, Wills Eye Hospital, Philadelphia, PA, United States

Purpose: BAP1 immunohistochemical (IHC) stain has emerged as a powerful and inexpensive prognostic tool in uveal melanoma (UM), correlating with UM molecular genetics and patient outcome. We aim to assess BAP1 IHC in irradiated UM eyes that ultimately underwent enucleation and to compare performance of BAP1 IHC with non-irradiated UM.

Methods: The medical records of all UM patients who underwent enucleation at the Oncology Service of Wills Eye Hospital from December 1st, 2007 to December 31st, 2014 with available paraffin-embedded tissue and either chromosome 3 (ch3) status or sufficient follow-up (>5 years or development of metastasis) were reviewed. Nuclear BAP1 (nBAP1) IHC was interpreted as intact (positive in >90% of nuclei), lost (positive in <5% of nuclei), or heterogeneous (positive in 5-90% of nuclei). Retina, intratumoral inflammatory cells, and blood vessels served as internal positive controls. Eyes without sufficient internal positive controls or with <5% viable tumor were labeled “non-interpretable”.

Results: There were 34 irradiated UM enucleated eyes compared to 47 non-irradiated UM eyes (controls). BAP1 IHC was non-interpretable in 7/81 (9%) eyes (4 irradiated and 3 non-irradiated). There was no significant difference between irradiated and non-irradiated UM with respect to nBAP1 IHC (lost in 41% vs 51%, p=0.19), ch3 status (monosomy 3 in 59% vs 60%, p=0.48), and outcome (metastatic disease in 44% vs 47%, p=0.8). Correlation of BAP1 IHC with disomy 3 (ch3D), monosomy 3 (ch3M), and outcome [intact BAP1:ch3D and/or no metastasis AND lost BAP1:ch3M and/or metastasis] in irradiated tumors was significantly lower when compared with non-irradiated tumors [21/30 (70%) vs 41/44 (93%), p=0.004*, Bonferroni correction 0.04*]. On re-evaluation of discordant cases, decreased or absent retinal staining overlying the tumor and weak intratumoral control were seen in six irradiated UM, pointing to a false-negative nBAP1 stain. With those cases excluded, the correlation of nBAP1 IHC with ch3 status and outcome was not significantly different in irradiated and non-irradiated UM [18/24 (75%) vs 41/44 (93%), p=0.017*, Bonferroni correction 0.15].

Conclusions: There are pitfalls in the interpretation of BAP1 immunostain in irradiated UM. This test should be used judiciously in tumors with prior plaque brachytherapy.

49,AC

Second-line therapy in young patients with relapsed or refractory orbital rhabdomyosarcoma.

Ofira Zloto, Veronique Minard-Colin, Helene Boutroux, Herve J Brisse, Christine Levy, Frederic Kolb, Stephanie Bolle, Matthieu Carton, Sylvie Helfre, Daniel Orbach
1- Goldschleger Eye Institute, Sheba Medical Center, Affiliated with The Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel. 2- Pediatric Adolescent Young Adult Department, Institut de Canc?rologie, Gustave Roussy Cancer Campus (GRCC), Villejuif, France.

Purpose: Localized orbital rhabdomyosarcoma (oRMS) has an overall favorable prognosis with more than 90% of survival. Little is known about the best strategy in recurrent/refractory (R/R) cases. The purpose is to examine the characteristics of patients with R/R-oRMS, focusing on local therapy.

Methods: This is a bicentric retrospective study. Analysis is of young patients (<30 years) with R/R-oRMS who were treated from 1989 to 2018 at the Institut Curie and Gustave Roussy Cancer Campus, France.

Results: Twenty-seven out of 162 patients (17%) with oRMS presented with R/R disease. 6 of these patients had alveolar RMS (22%), 3 of whom had initial parameningeal extension (11%). During first-line treatment, 18 patients (67%) had orbital radiotherapy. Median age at R/R was 10 years (ranges: 4-28) after a delay of 19 months from diagnosis (ranges: 3-40). Tumoral events were local-relapses (22 cases), local-progression (3 cases), or regional-relapses (2 cases). Second-line treatments included chemotherapy (27 cases), radiotherapy (16 cases), surgery (exenteration; 8 cases) and metastasis/ nodal removal (3 cases). After a median follow-up of 99 months (range: 10-306), 4 patients died and 23 are in complete remission (CR) without treatment. One patient had subsequent relapse treated with exenteration and brachytherapy until a new tumor remission. Five-year-Event-Free and overall-survivals after first tumor event are respectively 84.4% (95% confidence-interval: 71.5%- 98.8%) and 85.8% (95% confidence-interval: 72.1%-100.0%)

Conclusion: R/R oRMS is a rare situation. Second-line therapy is efficient in this location, sometime at the cost of lifesaving mutilating surgery. Second-line local therapy need therefore to consider local radiotherapy if possible or complete wide surgery.

50,AC

Periocular Presentation of Solitary Plasmacytomas and Multiple Myeloma.

Zloto, Ofira M.D. Vahdani, Kaveh M.D., F.R.C.Ophth, Stack, Rebecca F.R.A.N.Z.C.O. Verity, David H. M.D., F.R.C.Ophth, Rose, Geoffrey E. D.Sc., F.R.C.Ophth.
Orbital Service, Moorfields Eye Hospital, London, United Kingdon

Purpose:
To describe patients with periocular solitary extramedullary plasmacytoma (SEMP) and multiple myeloma (MM), together with an estimate of the risk of progression from SEMP to MM.

Patients and methods:
A retrospective case-note review for patients seen between 1978 and 2020, examining demographics, presentation, imaging, pathology, management, and outcome.

Results:
Twenty patients (10 male; 50%) presented at a mean age of 60.9 years, with an average symptom duration of 4.5 months. Ten (50%) patients had known systemic myeloma at ophthalmic presentation (the MM group) and, on average, they presented one decade earlier than those with occult MM discovered after orbital biopsy ($p = 0.06$); the majority (9/15; 60%) of patients with MM were female, whereas there was a male bias (4/5; 80%) with SEMP ($p = 0.30$). Most tumors (15/20; 75%) were within the anterior part of the orbit, especially superolaterally (16 patients; 80%), and the soft-tissue mass often appeared to “explode” from the frontal bone or greater wing of the sphenoid (16/20; 80%). Full treatment details were known for 19 patients: 6 (32%) had solely orbital radiotherapy, 4 (21%) chemotherapy, 6 (32%) combined chemoradiation, and 3 (16%) had combined chemoradiation with stem-cell transplant (Table 3). After an average follow up of 58 months, 1/5 (20%) patients with SEMP and 11/15 (73%) with MM had tumor-related death. The overall survival probability for all 20 patients with periocular plasmacytoma was 34% at 5 and 10 years, with MM patients having a worse outlook (27% 5-year, and 18% 10-year survival) compared with SEMP (53% survival at 5 and 10 years) ($p = 0.18$). None of the 5 patients with SEMP progressed to systemic MM over an average follow up of 9.1 years.

Conclusions:
Although 50% patients with periocular plasmacytoma appear to have a SEMP at ophthalmic presentation, a half of these patients were found to have occult MM within 6 months of biopsy. Of those without systemic disease around the time of biopsy, none developed MM over an average follow up of more than 9 years.

117 AC

PRIMA (PRegnancy In uveal Melanoma Analysis) Study - A European OOG MultiCenter Study.

Noa Jackson Amichay1, Jacob Pe'er1, Shahar Frenkel1 on behalf of the PRIMA study group
Hadassah Medical Center, Jerusalem, Israel

Introduction:
Uveal melanoma (UM) also affects women of childbearing age. However, little information exists on the risk of pregnancy hastening local recurrence or distant metastases.

Purpose:
In this European Ocular Oncology Group (OOG) multicenter trial, we aim to provide accurate information about the risks of pregnancy in UM patients: spread to the fetus, tumor re-growth, and metastases.

Methods:
A retrospective multicenter trial of European ocular oncology centers analyzes data of women of childbearing age diagnosed with UM. The pregnancy outcome, the fetus's fate, local recurrence events, and diagnosis of metastases were collected.

Results:
Out of the entire cohort of UM patients, we identified 76 patients of childbearing age at UM diagnosis ýime who had been pregnant: 64 women were diagnosed after having children, 17 were diagnosed while pregnant, and 13 became pregnant after treatment for UM, of which one became pregnant during treatment. Of which, one had a local recurrence during pregnancy. There were no immediate events of metastases within a year of pregnancy. No child contracted UM from the mother.

Conclusions:
Pregnancy appears safe for both women diagnosed with UM and their children.

120,AC

Elevated intraocular pressure following intravitreal methotrexate for vitreo-retinal lymphoma,

Noa Jackson Amichay-1, Zohar Habot-Wilner-2, Jacob Pe'er-1, Shahar Frenkel-1
1-Ocular Oncology Service, Division of Ophthalmology, Hadassah Medical Center, Jerusalem, Israel 2-Uveitis Service, Division of Ophthalmology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

Introduction:
Vitreoretinal lymphoma (VRL), part of the central nervous system lymphoma is the most common type of ocular lymphoma. VRL is treated with intravitreal injections of methotrexate (IVitM). Sustained elevation of intra-ocular pressure (eIOP) is a known side-effect of intra-ocular injections, including methotrexate injections for VRL.

Objectives:
We aimed to determine the extent of eIOP as a side effect of IVitM for VRL, by assessing its prevalence and severity. Furthermore, we wanted to assess the management of this side effect.

Methods:
This is a retrospective observational study. The study included a cohort of 81 patients who were diagnosed with VRL and treated by IVitM injections from 1997 to 2021. Collection of patients data was approved by the Hadassah IRB.

Results:
Out of 81 VRL patients we found 13 patients (16%, 8 of them women) with eIOP and a total of 15 eyes. Eleven patients had bilateral VRL (84.6%) and the rest had RE VRL, but only 2/11 developed IOP elevation in both eyes. eIOP was detected after a mean (±SD) of 14.5 (±3.8) injections. The mean (±SD) baseline IOP for eyes which later developed eIOP was 14.7 mmHg (±6.2). The mean (±SD) maximal IOP measured in these eyes was 40.5 mmHg (±5.5), representing a mean (±SD) IOP increase of 19.8 mmHg (±8.6) from the previous exam. Only two patients avoided surgery with prompt anti-VEGF treatment. Overall, 8 patients (9 eyes) needed surgery to control their IOP.

Conclusions:
IOP elevation is an uncommon side effect of IVitM for VRL, and most patients would eventually need surgical intervention.

121 AC

Responses to treatment of retinoblastoma in the IAC and IVitC era.

Abeer Hammod-1, Jacob Pe'er-1, Gal Goldstein-2, Jose Cohen-3, Shahar Frenkel-1
1-Ocular Oncology Service, Division of Ophthalmology; 2-Department of Children's Hematology and Oncology; 3-Neuro-intervention Unit, Hadassah Medical Center, Jerusalem, Israel

Introduction:
Treatment of retinoblastoma (Rb) progressed tremendously over the last decade with the addition of intra-arterial (IAC) and intravitreal chemotherapy (IVitC) to the intra-venous chemotherapy (IVC). Eyes that were previously quickly enucleated now undergo a long series of treatments which sometimes still end up in enucleation.

Objectives:
To evaluate the number of treatments, the chances of local recurrences and the time to enucleation, along with the influence of vitreal seeds on these parameters.

Methods:
A retrospective analysis of the electronic medical records of children diagnosed with Rb and treated for it since 2010 to 2021.

Results:
The study included 260 eyes (international groups: 29-A, 50-B, 31-C, 57-D, 93-E) of 180 children, 82 of them had bilateral Rb. 41% of the eyes survived (91%-B, 74%-C, 51%-C, 15%-E, $p<0.001$). Familial cases had less enucleations (38% vs. 62%, $p=0.04$). Presence of vitreal seeds at the time of diagnosis increased the risk of enucleation (64% vs. 44%, $p=0.015$) and hastened the mean time to enucleation (43 vs. 84 months). Patients treated with IVC had more treatment courses than patients treated without IVC (4 vs. 2, $p<0.001$). Some eyes received >10 treatments per eye. C and D eyes received the highest number of treatments ($p<0.001$).

Conclusions:
Despite the addition of newer delivery methods of chemotherapy and the increasing number of treatments per eye, many eyes still require enucleation.

Retina and AMD
14

Optical coherence tomography structural and angiographic assessment of retinal and choroidal crystals in Infantile Nephropathic Cystinosis.

Joel Hanhart (1), Eduardo Roditi (1) Ronen Rabinovich (1), Aya Altarescu (2), Lauren Wasser (1), Rinat Choni MD (2)
(1) Department of Ophthalmology, Shaare Zedek Medical Center, Jerusalem (2) Department of Nephrology, Shaare Zedek Medical Center, Jerusalem

Purpose: To describe the distribution of crystals in the retina and choroid in Infantile Nephropathic Cystinosis.

Methods: In this cross-sectional study, nephropathic cystinosis was diagnosed based on a typical clinical presentation and a leukocyte cystine concentration greater than 1.5 nmol half-cystine per milligram of protein, all of them were diagnosed several years ago. Apart visual acuity measurement, ophthalmological examination included slit lamp biomicroscopy for the anterior and posterior chambers, intraocular pressure measurements and corneal fluorescein staining.
Spectral domain OCT was performed, and pictures were reviewed by a retina specialist, unaware of the clinical severity of the condition and of its treatment protocol. On structural OCT, the presence of hyperreflective dots was qualitatively assessed in each layer in the retina and the choroid. It was then quantified on OCT en-face at the following selected retinal layers: retinal nerve fibre layer (RNFL), ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer nuclear layer (ONL), photoreceptor layer (PHR) and choroid. For each layer, the area of maximal crystalline density was identified and, in the 200 x 200 microns square corresponding to that area, the hyperreflective dots were quantified.

Results: This study included a total of 10 eyes from five patients (4 females and 1 male. Retinochoroidal cystine crystals were identifiable in the SD-OCT in the 9 eyes. Crystal deposition was identifiable in all layers of the neurosensory retina except the photoreceptor layers. The choroid had the denser concentration of crystals (100%), secondly the INL and the GCL. Enface analysis revealed that the crystals concentrated along retinal capillaries.

Conclusions: Our SD-OCT EnFace technique to image in vivo accumulation of crystals at selected retinal layers corroborate previous cystinosis mouse model studies that detected pronounced accumulation of cystine crystals in the choroid and INL using transmission electron microscopy.

Retina and AMD
26

Is Myopic Macular Degeneration a Choroidopathy?
Jonathan Li (1), Jacque Duncan (1), Ruikang Wang (2), Diana Zhou (2) Igor Mitrovic (3) (1) Dept. of Ophthalmology, University of California, San Francisco (2) Department of Bioengineering, University of Washington, Seattle (3) Department of Physiology, University of California, San Francisco

Purpose: Myopic macular degeneration (MMD) is a leading cause of irreversible vision loss. Overall choroidal thinning is associated with increased MMD severity. This cross-sectional study analyzed choriocapillaris (CC) alterations in MMD.

Methods: Axial length (AL), best corrected visual acuity (BCVA), fundus photos, and swept-source-optical coherence tomography angiography (SS-OCTA) were assessed in controls and high myopes (spherical equivalent ?-6 diopters). Myopic patients with Grade 2 MMD (macular diffuse chorioretinal atrophy[MDCA]), high axial myopia (AL?26.5 mm), and BCVA?20/40 were compared with controls without MMD. CC mean thickness was measured from 3mmx3mm SS-OCTA scans by identifying CC peaks in A-scan intensity profiles. CC flow deficit percent (CC FD%) was quantified using a fuzzy C-mean local thresholding method on enface OCTA images. Multivariate regressions compared CC thickness and CC FD% between myopic patients and controls, correcting for age and other confounders.

Results: Sixteen eyes with MDCA (AL 26.96-33.93mm; age 40-78 years) were compared with 51 control eyes (AL 21.65-25.84mm; age 19-88 years). CC thickness in patients with MDCA was 66% lower than controls (5.23±0.68µm [mean±standard deviation] versus 15.46±1.82µm, P<0.001). CC FD% in patients with MDCA was 237% greater than controls (26.5±4.3 versus 11.2±4.6, P<0.001).

Conclusions: Patients with MDCA with good visual acuity had thinner CC and increased CC FD%, or reduced CC flow, compared to controls. Patients with Grade 2 MMD and good visual acuity demonstrated significant choriocapillaris alterations, suggesting choriocapillaris perfusion defects contribute to the pathogenesis of MMD.

Retina and AMD
32,AC

Comparison of The Retinal and optic nerve head vascular networks using OCT-A between hypoxic and normal subjects.

Nadav Levinger1, Ayman Abu Rmeileh2, Eisa Mouallem3, Shadi Zahran4, Sheer Shabat5, Yotam Kolben6, Talmon Aviv7, Rottem Kuint2, Liran Tiosano1 and Samer Khateb1
1) Department of Ophthalmology, Hadassah Medical Center (2) Institute of Pulmonary Medicine, Hadassah Medical Center (3) Internal medical daycare, Hadassah Medical Center (4) Department of medicine B, Hadassah Medical Center (5) Department of Physical & Medical Rehabilitation, Hadassah Medical Center (6) Department of medicine A, Hadassah Medical Center (7) Department of medicine C, Hadassah Medical Center

Purpose: Chronic hypoxia had been shown to cause decrease in the choroidal and RNFL thickness. The purpose of this study is to examine whether patients with chronic and acute hypoxia have altered retinal and ONH capillary networks as seen by OCT-A.

Methods: Single center, open, prospective study. The study recruited 34 hypoxic patients and 23 in the control. All patients underwent full ophthalmology exam, OCT-A imaging and biometry (for AL). Angio images of the macula and ONH were obtained. The hypoxic patients were photographed with and without O2 supplementation.

Results: The study final analysis included 21 control patients and 20 hypoxic patients. The age was similar between the groups (p=0.487) but the hypoxic patinates had more CV disease.
The macular thickness was significantly thicker in the GCL and superficial slab in the control group as compared to the hypoxia patients in the inner nasal (p=0.041 and 0.042), inner superior (p=0.041 and 0.05) and circular 3 mm (p=0.036 and 0.05). the ONH Superficial peripapillary vascular density had a higher value in the control cohort as compared to the hypoxic patients (p=0.018). No retinal angiography difference was found between the groups.

Conclusion: Both macula thickness and ONH vasculature showed difference among hypoxic patients compared to age-matched healthy group.

Retina and AMD
34

Investigating the survival and function of retinal ganglion cells in an organotypic culture: An in-vitro model for studying synaptogenesis

Efrat Simon, Nairouz Farah
The Mina & Everard Goodman Faculty of Life Sciences Bar Ilan University

Background:
Stem cells replacement therapy is becoming a promising pursued avenue for vision restoration in people with degenerative diseases of the outer retina. However, the integration and survival of the transplanted cells and the formation of fully functioning synapses are a challenge. Our aim is to develop an in-vitro experimental paradigm which will allow us to address these issues while working under experimentally controlled conditions and avoiding immune system reactions faced in-vivo.

Methods:
As a first step, we are utilizing organotypic retinal cultures from transgenic rats expressing the calcium indicator GCaMP6f while monitoring the survival of the retinal ganglion cells (RGCs)using both extracellular recordings (multi electrode arrays), and calcium imaging at various time points.

Results:
Our calcium imaging revealed robust spontaneous activity of the RGCs up to 72hrs, albeit decreasing throughout culturing period. Concurrently with these experiments, we have successfully established the system for extracellular investigation of RGC electrical properties incorporating flexible light pattern stimulation and multiunit analysis of the light induced responses over 60 channels. We were able to observe various RGCs types e.g., ON, OFF, ON-OFF identified by 1sec flashes applied at 0.2Hz. Moreover, through the well-known white gaussian noise stimulus combined with spike triggered averaging we generated RGCs receptive field maps obtaining the expected results both spatial (160µm FWHM) and temporally.

Conclusions:
The experimental paradigm presented here can serve as a useful tool for the investigation of stem cell cells integration with the host retina, a main obstacle towards successful cell-replacement based vision restoration approaches.

Retina and AMD
45 AC

Long-term follow up on patients treated with laser for retinopathy of prematurity.
Dolev Dollberg [1,2], Karny Shouchane-Blum [1,2], Orly Gal-Or [1,2], Amir Sternfeld [1,2], Ruth Axer-Siegel [1,2], Idit Marshak [2,3], Rita Ehrlich [1,2]
[1] Department of Ophthalmology, Rabin Medical Center, Petah-Tikva [2] Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv [3] Department of Ophthalmology, Edith Wolfson Medical Center, Holon

Purpose: To evaluate the long-term functional and structural findings in eyes treated with laser photocoagulation for ROP.

Methods: Observational cross-sectional study on patients with ROP that were treated with laser photocoagulation between 1997 and 2004. All patients underwent best corrected visual acuity (BCVA) assessment, autorefraction, biometry evaluation (OA-2000, Tomy GmbH, Nagoya, Japan) for axial length (AXL), anterior chamber depth, corneal thickness (pachymetry) . We also retrieved from the patients' neonatal medical records disease characteristics including disease severity and the extent of laser treatment.

Results: Included 63 eyes of 33 patients with a mean follow up of 19 years. The mean BCVA was 0.133 (± 0.18) logMAR, and the BCVA was 6/12 or better in 92% of eyes. The refraction of the patients was between -19D to +3.5D with mean spheric equivalent of -5.04 (±5.13) D, the mean AXL was 22.97 (± 1.99) mm, mean ACD of 2.96 (± 0.41) mm and a mean corneal thickness of 533 (±32.14) µ. Mean keratometry values were 45.62 (± 1.96) D for flat K, 47.1 (± 2.28) D for steep K and 46.34(± 2.04) D for average K. The amount of laser energy delivered at baseline was negatively correlated with corneal thickness (r=-0.391, p=0.013). No correlation was found between amount of laser energy delivered and BCVA, refraction or keratometry readings at follow up.

Conclusion: Two decades after ROP treatment our patients demonstrated excellent long term visual acuity outcome and were moderately myopic on average. There may be a dose dependent relation between laser energy and corneal thinning.

The Association of Choroidal Thickness with Rhegmatogenous Retinal Detachment Surgery Outcomes.

Omer Trivizki (1) Ron Eremenko (1) Adrian Au (2) David Rabinovitch (3) Muhamad Abumanhal (1) Shulamit Schwartz (1) Ori Segal (2) Gilad Rabina (1),
1) Department of Ophthalmology, Tel Aviv Medical Center, University of Tel Aviv, Tel Aviv, Israel (2) Department of Ophthalmology, Meir Medical Center, Kfar Saba, affiliated to the Sackler Faculty of Medicine, Tel Aviv University, Israel (3) Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida, United States.

Purpose:
To compare the choroidal thickness before and after pars plana vitrectomy (PPV) for rhegmatogenous retinal detachment (RRD) repair.

Methods:
A retrospective case series of RRD patients presenting between January 2015 and September 2020. Sub-foveal choroidal thickness (SFCT) and anatomical success were measured in operated eyes and fellow eyes at presentation, 3 months and 6 months after PPV for RRD repair.

Results:
A total of 93 patients (males 59%) with a mean age of 61.8±15.2 years were included. Eighty-one patients were anatomically successful (Group 1), and 12 re-detached (group 2). Mean SFCT of operated eye at presentation was 258.3±82.0 μm in comparison to 257.5±83.7 μm in the fellow eye (p= 0.96). Group 2 presented with thicker SFCT than group 1 at baseline (309.2±56.2 versus 250.7±82.8 μm; p= 0.01). Both groups demonstrated thinning trend throughout follow-up. At 6-month follow-up mean SFCT was 225.6±75.5 μm (p= 0.05). Fellow eye SFCT was stable throughout follow-up (257±83.7 at baseline versus 255±80.2 μm at 6-months).

Conclusion:
Eyes with RRD demonstrated thinning in the SFCT after vitrectomy surgery. Eyes with recurrent retinal detachment presented with thicker choroid at baseline. Thicker SFCT at presentation may play a role in retinal re-detachment.

Screening for retinal pathologies via anomaly detection and localization in OCT scans.

Ya'acov Cna'any (1), Ron Abutbul (2), Rivkah Lender (1), Jaime Levy (1), Liran Tiosano (1), Itay Chowers (1), Yedid Hoshen (2)
(1) Department of Ophthalmology Hadassah-Hebrew University Medical Center, Jerusalem, Israel; (2) Department of Computer Science The Hebrew University of Jerusalem, Israel

Purpose: Retinal diseases affect millions of people worldwide, resulting in reduced VA and blindness. Timely diagnosis is crucial for optimal treatment and prevention of blindness, but disease bio-markers and lesions are difficult to detect in the early stages. Using anomaly detection combined with localization in retinal OCT scans can aid in the identification of anomalous scans and pinpoint abnormal areas in each scan. Such algorithms can support doctors in diagnosis of retinal diseases and clinical decisions, and may help reveal new bio-markers.

Methods: This work compared four state-of-the-art self-supervised frameworks which detect abnormal retinal OCT images and localize their abnormalities in a one-class anomaly detection setting. The backbone model of all the frameworks was a pre-trained convolutional neural network (CNN), which enabled extraction of meaningful features from OCT images. The frameworks were trained on a set of 5,000 normal OCT images, and tested on 10,000 normal and anomalous images (open-source dataset). Anomalous images included CNV, DME and drusen scans. ROC-AUC scores were compared in order to establish the accuracy of the different frameworks.

Results: All frameworks were shown to achieve high performance and generalized well for the different retinal diseases. Heat-maps were generated in order to visualize the quality of the frameworks' ability to localize anomalous areas of the image. Mean ROC-AUC scores ranged from 80% to 91% across the different frameworks.

Conclusions: We showed that with the use of pre-trained feature extractors, the frameworks tested in this work can generalize to the domain of retinal OCT scans and achieve high image-level ROC-AUC scores. The localization results of these frameworks are promising and successfully capture areas that indicate the presence of pathology. Moreover, such frameworks have the potential to uncover new bio-markers that are difficult for the human eye to detect. Frameworks for anomaly detection and localization can be integrated into clinical decision support and automatic screening systems that will aid ophthalmologists in patient diagnosis, follow-up, and treatment design. This work establishes a solid basis for further development of automated anomaly detection frameworks for clinical use.

Retina and AMD
85 AC

Foveal-Splitting Rhegmatogenous Retinal Detachment – a New Entity?

Dana Barequet, Dana Zvi, Ram Cohen, Shulamit Schwartz, Adiel Barak, Anat Loewenstein, Gilad Rabina
Division of Ophthalmology, Tel Aviv Medical Center, Tel Aviv, Israel

Purpose: To compare anatomical and functional outcomes of macula-on, macula-off and foveal-splitting rhegmatogenous retinal detachment (RRD) after pars plana vitrectomy during 6 months of follow-up.

Methods: Consecutive patients who underwent a successful PPV surgery for primary RRD over a 5-year period were included. Pre- and postoperative optical coherence tomography (OCT) were obtained for all patients. Patients diagnosed with a detachment extending to the edge of the fovea on OCT were termed foveal-splitting RRD. Main outcome variables were functional and anatomic outcomes 6 months after surgery.

Results: A total of 171 eyes were included, out of which 90 eyes presented with a macula-off, 51 with macula-on and 30 with foveal-splitting RRD. Preoperatively, mean visual acuity (VA) was 1.28±0.61, 0.3±0.37 and 0.67±0.55 for the macula-off, macula-on and fovea-splitting groups, respectively ($p<0.001$). Mean VA at 6 months follow-up significantly improved for the macula-off group to 0.62±0.49 ($p<0.001$ from baseline) and remained stable for the macula-on and foveal-splitting groups of 0.46±0.46 and 0.57±0.48, respectively ($p>0.05$ compared to baseline and $p=0.05$ between the groups). Preoperatively, a significant difference in central macular thickness (CMT) was observed (658.48±289.56, 306.96±45.94 and 463.76±173.67, $p<0.001$). However, mean final postoperative CMT was similar between the groups ($p=0.25$). Morphological changes in OCT in the macular regions which were significantly different between the groups included alteration of the outer retinal layers.

Conclusion: Eyes with foveal-splitting RRD had both a preoperative and final postoperative visual acuity between that of macula-on and macula-off eyes. Anatomical changes on OCT were similar between the groups, excluding alteration of outer retinal layers. This new entity of RRD warrants special preoperative and surgical considerations as well as different patient expectations for postoperative outcomes.

Retina and AMD
89

Abnormal Renal Profiles and Diabetic Eye Disease in Latino and African American Cohorts.

Jonathan Levine [1][2], Onelys Carrasquillo [2], Barton Levine [3]
[1] Department of Optometry, Hadassah Academic College, Jerusalem [2] Department of Ophthalmology, Bronxcare Hospital, Bronx NY [3] Department of Nephrology, VA Medical Center West, Los Angeles, CA

Purpose: To study the association between abnormal renal profiles and presence of diabetic retinopathy (DR) and diabetic macular edema (DME) in Latino (LA) and African American (AA) patients of our South Bronx community.

Methods: This is a retrospective chart review of adult diabetic LA and AA patients seen in our hospital's eye clinic within the last 5 years. Demographic information and most recent renal profiles including serum creatinine levels, eGFR, and urinary microalbumin to creatinine ratios (ACR) were recorded. In addition, we recorded hemoglobin A1C and cholesterol levels. Patients were stratified based on presence or absence of Diabetic Macular Edema and/or Diabetic Retinopathy. Log values of ACR were used for data analysis as the ACR values are not normally distributed. We also stratified ACR values into the following clinically defined categories of albuminuria ACR <30 (mild), 30-300 (moderate) and >300 mg/g (severe). Lab values were compared between groups and the unpaired Student's t-test was used to calculate statistical significance. Patients who did not have a recorded eye exam or relevant lab values within the past 24 months of the last eye exam were excluded.

Results: There were 1127 diabetic patients included in our study, 416 in the AA and 711 in the LA cohort. The prevalence of DR in the AA group was 26% (110/416) compared to 28% in the LA group (199/711). Both the AA and LA DR+ groups had a significantly higher mean log ACR compared to their respective DR- group cohorts. (1.798 vs 1.302 p <.0005; 1.852 vs 1.309 p <.0005 respectively). Patients in the AA and LA cohorts with moderate albuminuria (30<ACR< 300mg/g) were 1.5 and 1.7 times more likely to have DR than those with none to mild albuminuria. Patients in the AA and LA cohorts with severe albuminuria (ACR >300mg/g) were 5.8 times and 10.8 times more likely to have DR than those in the none to mild category.

Conclusions: Patients in our African American and Latino cohorts with abnormal ACR values were more likely to have diabetic eye disease than those with normal renal profiles. Other studies have proposed using abnormal ACR values as a prognostic indicator of future diabetic eye disease; perhaps future studies could evaluate this in our cohort as well.

Retina and AMD
92

Rapid distribution of bevacizumab throughout the posterior segment in rabbit eyes following suprachoroidal delivery using a novel injection system.
Ygal Rotenstreich (1,2), Zehavit Goldberg(1,2), Ettel Bubis (1,2), Ifat Sher (1,2)
(1) The Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, Israel. (2) The Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

Purpose: The aim of this study was to test the in-vivo bio-distribution and safety of bevacizumab delivery into the suprachoroidal space (SCS) using a novel injection system in a large eye model.

Methods: Bevacizumab (1.25 mg) was injected into the vitreous (IVT, 50µL, n=12) or the SCS, (150µL, n=37) of live rabbits. Bevacizumab biodistribution was assessed by immunofluorescence and ELISA analyses. Rabbits were monitored for intraocular pressure (IOP) measurements, SD-OCT and fundus imaging, electroretinogram (ERG), and histology analysis to determine the safety of SCS injection.

Results: Bevacizumab was observed throughout the choroid layers up to the retinal pigment epithelium (RPE), within 1 hour following SCS injection. The Cmax of bevacizumab in the retina/choroid was 1043 ± 597 µg/gr tissue (mean± standard error), 40-fold higher than in IVT injected eyes (p=0.03). One day following SCS injection, bevacizumab Cmax in the retina/choroid was reduced by 2-folds. One week post-SCS injection, bevacizumab concentration in the retina/choroid dropped to 2.36 ± 1.32 µg/gr tissue (p=0.03 vs. 1 hour), with a half-life of 20 hours. SD-OCT and fundus imaging demonstrated no suprachoroidal blebs, hemorrhages, inflammation, or retinal detachment up to 2 months following SCS injection. No adverse effects on retinal function by ERG were observed. IOP was elevated by 16 mmHg two minutes post-SCS injection and spontaneously returned to baseline levels within ten minutes.

Conclusions: The SCS novel injection system enabled a minimally invasive, safe, and consistent delivery of bevacizumab with rapid distribution throughout the choroid layers up to the RPE in large eyes in vivo. The high volume distribution enables the delivery of large volumes of anti-angiogenic in close proximity to the retina.

Retina and AMD
123

Intrinsic Expression of Coagulation Factors and Protease Activated Receptor 1 (PAR1) in Photoreceptors and Inner Retinal Layers.

Zehavit Goldberg (1,2), Ifat Sher (1,2), Lamis Qassim (3,4), Joab Chapman (3,4,5,6), Efrat Shavit-Stein(3,4), Ygal Rotenstreich (1,2,7)

Purpose: The aim of this study was to characterize the distribution of the thrombin receptor, Protease Activated Receptor 1 (PAR1), in the neuroretina.

Methods: Neuroretina samples of wild type C57BL/6J and, PAR1-/- mice were processed for indirect immunofluorescence, and western blot analysis. Reverse transcription quantitative real-time PCR (RT-qPCR) was used to determine mRNA expression of coagulation factor X (FX), prothrombin (PT), and PAR1 in the isolated neuroretina. Thrombin activity following KCl depolarization was assessed in mouse neuroretinas ex-vivo.

Results: PAR1 staining was observed in the retinal ganglion cells, inner nuclear layer cells, and photoreceptors in mouse retinal cross sections by indirect immunofluorescence. PAR1 was co-localized with rhodopsin in rod outer and inner segments but not in cone outer segments. Western blot analysis confirmed PAR1 expression. Factor X, prothrombin and PAR1 mRNA expression was detected in isolated neuroretinas. Thrombin activity was elevated by nearly 4-folds in mouse neuroretinas following KCl depolarization (0.012 vs. 0.044 mu/ml, p=0.0497).

Conclusions: PAR1 is expressed in cell bodies and outer segments of rods but not cones in the mouse retina. Intrinsic expression of coagulation factors in the isolated neuroretina together with a functional increase of thrombin activity following KCl depolarization may suggest a role for PAR1/thrombin pathway in retinal function.

Retina and AMD
13

Pseudophakia as a Surprising Protective Factor in Neovascular Age-Related Macular Degeneration,

Joel Hanhart(1), Rony Wiener(1), Hashem Totah(1) and David Zadok (1)
(1) Department of Ophthalmology, Shaare Zedek Medical Center, Jerusalem, Israel, affiliated to the Hebrew University, Jerusalem, Israel.

Purpose: To assess the impact of the lens status on macular function among patients treated for neovascular age-related macular degeneration (nvAMD) in whom scheduled intravitreal injections were delayed.

Methods: We reviewed demographic and clinical data as well as macular ocular computerized tomographic images of 34 patients (48 eyes) who did not follow their injection schedule during the first wave of COVID-19 in Israel. Functional worsening was defined as loss of at least 0.1 in decimal best-corrected visual acuity (BCVA). Morphological worsening was defined as new or increased subretinal/intraretinal fluids or new hemorrhage. OCT indexes of quality were used a measure for cataract density and progression.

Results: The planned interval between the intravitreal injections was 5.7 weeks, while the actual interval was 13.6 weeks (delay of 7.9 ± 5.2 weeks). Seventeen of the 20 eyes (85%) that maintained functional stability despite not receiving timely intravitreal injections were pseudophakic. Eighteen of the 28 eyes (64%) that functionally deteriorated were phakic (P = .001). Pseudophakia was associated with a better functional outcome than phakia: there was a loss of 0.06 ± 0.12 vs. 0.15 ± 0.10 decimal BCVA in the pseudophakic and phakic eyes, respectively (P = .001). A similar trend was observed for the morphological changes over the same period: there was an increase in macular thickness of 9 ± 26% vs.12 ± 40%, respectively (P = 0.79). During the first wave of COVID-19 the index of OCT quality remained stable for phakic eyes (26 ± 3.6 before the first wave of COVID-19, 26 ± 2.9 afterwards; P = 1) and pseudophakic eyes (30 ± 2.4 before the first wave of COVID-19, 30 ± 2.6 afterwards; P = 1).

Conclusion: nvAMD patients with pseudophakic eyes who missed their scheduled intravitreal injections experienced fewer morphological and functional complications than nvAMD patients with phakic eye.

Geographic atrophy area measurement: comparison between fundus autofluorescence and OCT.

Or Shmueli (1), Ilan Benhamou (2), Yahel Shwartz (1), Leo Joskowicz (2), Jaime Levy (1)
(1) Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel (2) School of Computer Science and Engineering, The Hebrew University of Jerusalem, Israel

Purpose: To compare geographic atrophy (GA) area and shape descriptors using fundus autofluorescence (FAF) annotation versus optical coherence tomography (OCT) annotation with complete retinal pigment epithelium and outer retinal atrophy (cRORA) criteria in cases of dry age-related macular degeneration (AMD).

Methods: Retrospective annotation of GA in FAF and OCT in a single timepoint.
Primary outcomes: GA area, focality, perimeter, circularity and minimal distance from the center. The primary outcomes were compared between both modalities. Correlations of the primary outcomes on OCT with the difference in GA area between both modalities were analyzed using univariate and multivariate regression analysis.

Results: 30 pairs of FAF and OCT scans from 30 eyes of 18 patients with dry AMD were included. The mean total GA area measured 8.77±4.38 mm2 with FAF and 2.78±3.39 mm2 with OCT ($P<0.0001$). The mean FAF-OCT area difference was 5.99±4.22 mm2. Multivariate regression analysis revealed a significant correlation between the FAF-OCT area difference and GA focality and minimal distance from the center on OCT (adjusted $r2 = 0.66$).

Conclusion: This study quantitatively measured and compared GA area using fundus autofluorescence as compared to OCT. The mean GA area measured on OCT was 3.15 times smaller than that on FAF. FAF-OCT area difference correlated with GA focality and minimal distance from the center on OCT. Further research is needed to establish the clinical application of these findings.

Retina and AMD
42,AC

Clinical outcome of a modified treat-and-extend protocol in the treatment of neovascular age-related macular degeneration.

Brice Vofo (1), Yaacov Cnaany (1), Itay Chowers (1)
1) Department of Ophthalmology, Hadassah – Hebrew University Medical Center and the Hebrew University – Hadassah School of Medicine, Jerusalem.

Purpose: Intravitreal injections of anti-vascular endothelial growth factor (VEGF) compounds overload retina clinics, and require considerable time investment from patients and caregivers. We compared outcomes of neovascular age-related macular degeneration (nvAMD) patients treated with a modified treat and extend protocol (MTAE) to that of those treated with a conventional treat and extend protocol (TAE).

Methods: A retrospective analysis of two consecutive groups of treatment naive nvAMD patients was conducted. The first group began anti-vascular endothelial growth factor (VEGF) therapy between January 2006 through December 2011and were treated using the conventional TAE protocol. The second group began anti-VEGF treatment between January 2016 and December 2017 and was treated using a MTAE. In the MTAE protocol, visual acuity (VA) and dilated fundus exams (DFE) were performed once in 3 visits, while during the other 2 visits, an OCT assessment was used to guide retreatment. The time spent per encounter, and the visual and anatomical outcomes were compared between the two groups after 36 months of follow-up.

Results: The TAE and MTAE cohorts included 135 eyes (116 patients, 41.4% female, mean age: 76.9±7.8 years) and 119 eyes (94 patients, 55.3% female, mean age 79.8±6.8 years), respectively. Both groups had similar baseline characteristics. At 36 months, the number of injections administered, (7.9±2.9 vs 8.1±2.3 injections, respectively, p=0.55), the number of eyes that gained ?15 Early Treatment for Diabetic Retinopathy Study (ETDRS) letters 31 (23%) vs 30 (25.2%), respectively (p=0.39) and lost ?15 EDTRS letters 29 (21.5%) vs 21 (17.7%), respectively, were similar in both groups (p=0.43). Anatomical outcomes per OCT were also similar in both groups. Both waiting time and service time were reduced during OCT-only assessments compared to full assessments (32±20 minutes vs 56±40 minutes, and 9±4 minutes vs 26±10 minutes, respectively, p<0.001 in each case). Saving an average of 41 minutes for each patient encounter.
Conclusion: MTAE and TAE protocols yielded comparable visual and anatomical outcomes. Applying MTAE leads to reduced number of full assessment visits which is associated with shorter time spent in the clinic during the OCT-only assessment visits. MTAE may further streamline anti-VEGF therapy, thereby, reducing patient, caregivers, and staff time allocated to treatment.

COVID-19 Pandemic Lockdowns Impact on Visual Acuity of Neovascular AMD Patients: A Large cohort.

Reut Shor (1) Michael Mimouni (2) Dinah Zur (1) Omer Trivizki (1) Shulamit Schwartz (1) Anat Loewenstein (1) Ori Segal (3) Gilad Rabina (1)
(1) Department of Ophthalmology, Tel Aviv Sourasky Medical Center, affiliated to the Sackler Faculty of Medicine, Tel Aviv University, Israel (2) Department of Ophthalmology, Rambam Health Care Campus and the Technion-Israel Institute of Technology, Haifa, Israel (3) Department of Ophthalmology, Meir Medical Center, Kfar Saba, affiliated to the Sackler Faculty of Medicine, Tel Aviv University, Israel

Purpose: To evaluate the impact of delayed care, secondary to COVID-19 pandemic lockdowns, on visual acuity and number of anti-VEGF injections in previously treated neovascular AMD (nAMD) patients.

Methods: A multi-center, retrospective, observational study of consecutive nAMD patients with previous treatment of anti-VEGF injections who were followed-up during 2019 (pre COVID-19) and compared to a nAMD patients who were followed-up during 2020 (COVID-19). Data collected included demographics, best-corrected visual acuity (BCVA), dates of anti VEGF injections and clinic visits.

Results: A total of 1,192 nAMD patients with a mean age of 81.5 years met the inclusion criteria. Of these 542 patients assessed during 2019 (pre COVID-19), 322 patients assessed during 2020 (COVID-19) and 308 patients assessed during both 2019 and 2020. There was no significant difference between the COVID-19 and Pre COVID-19 in terms of baseline and change in BCVA ($p=0.342$, $p=0.911$ respectively). During the COVID-19 period the mean amount of anti-VEGF injections was significantly lower than the corresponding pre COVID-19 period (5.55 Vs 6.13, $p<0.01$). A constant lower ratio of injections per patient is seen in 2020 comparing to 2019, with a notable decline during March and April ($p<0.01$). Baseline BCVA (0.859, $p<0.01$), number of injections (-0.006, $p=0.01$) and age (0.003, $p<0.01$) were significant predictors of final BCVA.

Conclusions: In a large cohort of previously treated nAMD patients, delayed care secondary to COVID-19 pandemic lockdowns has no significance impact on BCVA outcomes. Baseline BCVA, older age and decreased number of yearly anti VEGF injections are predictors for decrease final BCVA.

Retina and AMD
80,AC

The retinal toxicity of the pro-inflammatory and amyloidogenic S100A9 proteins.
Efrat Naaman(1), Amanda Qarawani(2,3), Rony Ben Zvi Elimelech(2,3) Chen Itzkovich(2), Michal Harel(2,3), Rami Khoury(2,3), Shadi Safuri(1), Shiri Zayit-Soudry(1,2,3)
1.Department of Ophthalmology, Rambam Health Care Campus, Haifa 2. Clinical Research Institute, Rambam Health Care Campus, Haifa 3. The Ruth and Bruce Rappaport Faculty of Medicine, Technion Israel Institute of Technology, Haifa

Purpose: Age-related macular degeneration (AMD) is a complex multifactorial disease in which inflammation is considered a key factor, but the exact underlying molecular mechanisms are unclear. The pro-inflammatory S100A9 proteins were amply found in drusen. These calcium-binding proteins have diverse signaling roles and can contribute to chronic inflammation, but their pathological and possibly physiological role in the retina is unknown. S100A9 were shown to be intrinsically amyloidogenic, possessing the capacity to self-assemble into amyloid structures in vitro and in vivo. Here, we hypothesized that the retinal effects exerted by S100A9 are related to their amyloid conformation.

Methods:
ARPE-19 cells were treated with monomeric or fibrillary S100A9 (0.1 nM- 0.1 μM) for 12 h. Cell viability was determined by the XTT assay. Wild type rats were treated with intravitreal injection (10μl) of monomeric or fibrillary S100A9 (0.1 μM) to right eye and vehicle in the left eye. Retinal function was assessed at baseline and through 28 days post injection. At each time point, electroretinography (ERG) measures were compared between eyes.

Results:
Cell viability assays and ERG in rats delineated distinct effects of S100A9 on the retina. The number of living ARPE-19 cells was increased by exposure to 0.1- 1nM fibrillar S100A9 but was decreased by treatment with 0.01- 0.1 μM of the S100A9 fibrils. Monomeric S100A9 had no significant impact on the cellular counts. Similarly, while retinal function remained normal in the eyes treated with monomeric S100A9, amplified ERG responses constituting increased amplitudes mostly of the b-wave were noted in the experimental eyes compared with their fellow (control) eyes through 14 days following injection of fibrillar S100A9 in rats. Thereafter, the retinal function became impaired, showing decreased ERG amplitudes in the treated eyes compared with controls.

Conclusions:
Fibrillar S100A9 exerted pronounced effects on the retina, which included cell proliferation in vitro and increased amplitudes of the ERG responses in rats. In contrast, exposure to higher doses of S100A9 fibrils induced cell death in vitro and prolonged exposure to these assemblies resulted in decreased retinal function in vivo. This complex behavior supports the importance of the amyloid conformation of S100A9 to its retinal implications, and suggests a clue both to the pathological and possibly physiological role of S100A9 in the human retina.

Retina and AMD
88,AC
PEDF-derived peptide inhibits Amyloid-β internalization and ameliorates retinal toxicity
Amanda Qarawani (2,4), Efrat Naaman (1,2), Rony Ben-Zvi Elimelech (2,4), Shadi Safuri (1,2,4), Chen Itzkovich (2,4), Michal Harel (2,4), Rami Khoury (2,4), Jack Henkin (3), Shiri Soudry (1,2,4)

(1) Department of Ophthalmology, Rambam Health Care Campus, Haifa, Israel. (2) Clinical Research Institute, Rambam Health Care Campus, Haifa, Israel. (3) Center for Developmental Therapeutics, Northwestern University, Evanston, IL, United States. (4) Ruth and Bruce Rappaport Faculty of Medicine, Technion Israel Institute of Technology, Haifa, Israel.

Purpose: Amyloid-beta (Aβ) has been implicated in the pathophysiology of age-related macular degeneration. We have shown that Aβ species possess differential retinal neurotoxicity, where oligomeric and fibrillar assemblies of Aβ42 mediated the primary retinotoxic effects. The mechanism of internalization of extracellular Aβ42 species in the retina is not well defined. In the brain, Aβ binding to the 67kDa laminin receptor (67LR) mediated the internalization of oligomeric Aβ42 and related neuronal cell death. We have found that PEDF335, a pigment epithelium-derived factor derived peptide, can bind to 67LR. Here, we hypothesized that 67LR mediates Aβ42 uptake in the retina, and PEDF335 may limit extracellular Aβ42 internalization, thereby inhibiting its retinal toxicity.

Methods: ARPE-19 cells were cultured with PEDF335 for 6h before treatment with oligomeric or fibrillar Aβ42 for 24 h. Cell viability was determined by XTT assay. The uptake of Aβ42 was assessed using immunostaining. Wild type rats were treated with intravitreal injection (10µl) of PEDF335 (3mM) in each eye two days prior to administration of oligomeric or fibrillar Aβ42 to the right eye. Retinal function was assessed at baseline and thereafter through 6 weeks post injection. At each time point, electroretinography (ERG) measures were compared between eyes. The retinal presence of 67LR was determined ex vivo by immunostaining.

Results: PEDF335 treatment blocked amyloid internalization into ARPE-19 cells and maintained their viability in the presence of oligomeric and fibrillar Aβ42. ERG responses in rat eyes treated with oligomeric or fibrillar Aβ42 assemblies were near-normal in eyes previously treated with PEDF335, whereas those measured in eyes treated with Aβ42 alone showed pathologic attenuation through 6 weeks. No adverse effects were noted in response to PEDF335. Retinal immunostaining demonstrated the expression of 67LR.

Conclusions: PEDF335 protects against oligomeric and fibrillar Aβ42 retinal toxicity, at least in part via binding to 67LR and inhibition of Aβ42 internalization. These observations provide evidence on the importance of extracellular versus intracellular Aβ42 in the retina and suggest that the mechanism of toxicity of fibrils possibly involves secondary release of oligomers. Such insights may promote the mechanistic understanding of the retinal pathogenicity of Aβ.

Retina and AMD
98,AC

Development of Blood Biomarkers for anti-VEGF Treatment Response in Neovascular Age Related Macular Degeneration.

Baty Rinsky; Sarah Elbaz-Hayoun; Itay Chowers,
Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel.

Purpose: Neovascular age related macular degeneration (nvAMD) is currently being treated with intravitreal anti-VEGF compounds. Treatment outcome vary among nvAMD patients and a meaningful portion of patients experience insufficient response. We aim to develop biomarkers for treatment outcome in nvAMD.

Methods: Peripheral blood was drawn from nvAMD patients with favorable (n=21; Group F) and insufficient response (n=25; Group IS) response for intravitreal anti-VEGF therapy. PBMC (peripheral blood mononuclear cells) were separated using a Histopaque gradient, and total blood monocytes, including the CD14+CD16+ subgroup of monocytes, were isolated using magnetic beads. Quantitative RT- PCR was performed for five genes whose expression was previously demonstrated to be associated with AMD (FOSB, TMEM176A, TMEM176B, TNFa and CD11b).

Results: TNFa mRNA expression in monocytes showed higher levels in group F vs. group IS (fold-2.43, p=0.05). Moreover, 43% of group F patients showed TNFa expression at the upper quarter of the expression level compared to only 12% of group IS patients (p= 0.057). The area under the curve value for TNFa mRNA levels in groups F and IS was 0.69. The other genes tested showed similar expression levels in both groups (FOSB; p=0.9, TMEM176A; p= 0.14, TMEM176B; p=0.143 and CD11b; p= 0.3).

Conclusions: Our results indicate that TNFa expression level in monocytes may be associated with favorable vs. insufficient response for anti-VEGF therapy in nvAMD. Further research is required to prospectively evaluate this parameter and to assess its usefulness to match therapy in nvAMD.

Retina and AMD
99

Intravitreal dexamethasone palmitate nanocapsules as a potential novel treatment for choroidal neovascularization.

Leslie Rebibo [1], Devora Potash-Miller [2], Tareq Jaouni [2], Taher Nassar [1], Itay Chowers [2] Simon Benita [1]
[1] Department of Pharmaceutics, The Hebrew University of Jerusalem, Jerusalem [2] Department of Ophthalmology, Hadassah-Hebrew University Medical Center and the Hebrew University–Hadassah School of Medicine, Jerusalem

Purpose: Inflammation has long been implicated in neovascular age-related macular degeneration (nvAMD) pathogenesis. Dexamethasone Palmitate (DXP), a lipophilic ester prodrug of dexamethasone (DXM) and a potent corticosteroid, is used to treat various ocular inflammatory diseases. However, it is only following the hydrolysis of DXP by esterases in the retina and choroid that free DXM can exert its anti-angiogenic and anti-inflammatory actions locally in these target tissues. Therefore, developing extended-release nanocarriers of DXP would decrease the risks associated with steroid applications in the eyes and the frequency of intravitreal injections.

Methods: DXP nanocapsules (NCs) were prepared via the solvent-evaporation method and were characterized by dynamic light scattering and cryo-TEM. The release of the free DXM from the DXP NCs was assessed in vitro in rat plasma. For CNV induction, a laser photocoagulation retinal injury model was performed on anesthetized C57BL/6 mice divided into two treatment groups: DXP NCs (n=13) or Blank NCs (n=10) that did not contain the drug. Immediately after laser injury, the different formulations were injected intravitreally. CNV area were measured seven days after injections using isolectin staining of RPE-choroid flat mounts.

Results: In invitro studies, DXP NCs exhibited a small average diameter (123 ± 2.5nm) with a low polydispersity index <0.1. The release of DXM from the DXP NCs was considerably extended (48h) compared to the DXP solution (8h). In addition, compared to the blank NCs, the CNV area was significantly reduced by our DXP NCs (fold-0.65697, p=0.0038).

Conclusions: These data suggest that DXP NCs administration could be an effective anti angiogenic compound in a model for CNV. The feasibility of applying DXP NCs in combination with anti-VEGF compound as a treatment for nvAMD should be further assessed.

Evaluation of HOBAM-11 as a Potential Novel Anti-angiogenic Therapy for Neovascular Age Related Macular Degeneration

Devora Potash Miller1; Sarah Elbaz-Hayoun1; Baty Rinsky1; Tareq Jaouni1; Itay Chowers1 and Ofra Benny2
Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel.

Purpose: Age-related macular degeneration (AMD) is a major cause of blindness worldwide. Anti-vascular endothelial growth factor (VEGF) injection is the main treatment offered for patients with neovascular AMD (nvAMD). However, incomplete or lack of response for anti-VEGF therapies is relatively common. We aim to assess the efficacy and the safety of a novel METAP2 inhibitor as a potential novel therapy for nvAMD.

Methods: Laser injury induced choroidal neovascularization (LI-CNV) was generated in C57BL/6J mice. Three treatment groups were evaluated: HOBAM-11(n=13), Aflibercept (n=5) and vehicle (n=8). Treatments were delivered via intravitreal injection immediately after the laser injury. Measurements of CNV size using isolectin staining of RPE-choroid flat mounts were performed 7 days after LI-CNV induction. The toxicity of HOBAM-11 was evaluated using electroretinogram (ERG) recording and histology analysis 7 days after intravitreal injections.

Results: Quantification of isolectin staining showed suppression of CNV area compared with vehicle treated eyes (fold - 0.592417, P value= 0.0194) and Aflibercept compared with vehicle treated eyes (fold-0.46810, p-0.0051) . ERG analysis showed similar response among the groups tested. Histology analysis demonstrated unaltered structure and similar outer nuclear layer (ONL) thickness among the groups.

Conclusion: The results show that this novel METAP 2 inhibitor is both effective and safe as a potential new anti-angiogenic treatment in the LI-CNV model. Further studies should evaluate the potential of this compound in nvAMD.

Retina and AMD

106 AC

Spatial modeling of variants in complement genes associated with age-related macular degeneration.

Michelle Grunin [1,2], Sarah de Jong [8], Ellen Palmer [1,3], Bowen Jin [1,3], David Rinker [4], Christopher Moth [5], John A. Capra [4,6], Jonathan L. Haines [1,3], William S. Bush [1,3], Anneke den Hollander [7]

[1] Population & Quantitative Health Sciences, CWRU, Cleveland, OH [2]Braun School of Public Health&CommunityMedicine, HUJI, Israel [3] Cleveland Institute for Computational Biology, CWRU, Cleveland, OH [4] Biological Sciences, Vanderbilt, Nashville, TN [5] Center for Structural Biology, Vanderbilt, Nashville, TN [6] Biomedical Informatics, Vanderbilt, Nashville, TN [7] Abb Vie Inc, Chicago, IL [8] Ophthalmology, Donders Institute for Brain, Cognition & Behavior, Radboud University Medical Center Nijmegen, Netherlands

Purpose: Genetic variants in complement genes are associated with age-related macular degeneration (AMD). However, the functional impact of the majority of missense variants is unknown. We evaluated spatial placement on protein structure, using the International AMD Genomics Consortium(IAMDGC) data(16,144 cases/17,832 controls).

Methods: The IAMDGC data was imputed using the HRC, with a 30% improvement over the original. Missense variants were extracted for CFH,CFI,CFB,C9,& C3 genes. We evaluated variants' placement in protein structure space: spatial proximity in the protein, and AMD association. We compared the spatial proximity of known AMD variants(KAV) to unassociated, assessed variants' likelihood of protein destabilization, and performed gene-based testing. Gene-based tests included: all variants; variants near KAV; and variants predicted to destabilize proteins. SKAT testing was used to confirm spatial associations. Logistic regression on KAV in CFI identified variants leading to >50% reduction in protein expression compared to wild type in vitro.These results were compared to functional impact scores, showing if a variant has a functional impact genome wide.

Results: Multiple destabilizing variants were found. Gene-based tests using all variants identified significant associations of the C3,C9,CFB,andCFH genes with AMD risk after controlling for age and sex(P=3.22x10- 5;7.58x10-6;2.1x10-3;1.2x10-31). Filtering on protein destabilization and SKAT-O tests found several missense variants in CFI and CFH associated with AMD(P=CFH:0.05,CFI:0.01, threshold<0.05).We identified spatial associations for AMD risk in structures for C3,C9,CFB,CFH,and CFI at P<0.05. Both structural and functional scores were predictive of reduced CFI protein expression, and ROC curve analyses suggest structural scores are a better predictor(AUCs of 0.76 and 0.69).

Conclusions: We demonstrate missense variants in complement genes cluster spatially and are associated with AMD status. Using this method, we can identify CFI and CFH variants previously classified as unknown significance, but are predicted to destabilize proteins. This method can predict in-vitro tested CFI protein expression changes, indicating that it is a useful tool for selecting variants for functional follow-up. Further investigation is needed to validate the models for additional variants in other complement and AMD-associated genes.

Genetics and Retinal Degeneration

40

Autosomal dominant retinitis pigmentosa with reduced penetrance due to an intronic mutation in PRPF31.

Tamar Ben-Yosef (1), Tahleel Ali Nasser (1), Shiri Zayit-Soudry (1,2), Eyal Banin (3), Dror Sharon (3)
(1) Rappaport Faculty of Medicine, Technion, Haifa, Israel (2) Department of Ophthalmology, Rambam Health Care Campus, Haifa, Israel (3) Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel

Purpose: To identify the molecular basis for autosomal dominant retinitis pigmentosa (adRP) with reduced penetrance in an Israeli Muslim Arab family.

Methods: Patients underwent a detailed ophthalmic evaluation, including funduscopic examination, visual field testing, optical coherence tomography and electroretinography. Genetic analysis was performed by a combination of whole exome sequencing and Sanger sequencing. Pathogenicity of the identified intronic variant was evaluated in silico using several web-based tools; in vitro, using a minigene-based assay; and in vivo, using reverse transcription-PCR analysis of lymphocyte-derived RNA.

Results: Affected individuals had childhood onset of RP, with night blindness as the initial symptom, followed by concentric restriction of the visual field. Funduscopic findings included narrowed retinal blood vessels and peripheral bone spicule pigmentation. Full-field electroretinography was non-recordable in the third decade of life. In these individuals we identified a novel heterozygous intronic variant, located at position +5 of PRPF31 intron 11 (c.1146+5G>T). The same variant was also detected in an unaffected family member. The variant was predicted to alter splicing of intron 11 by in silico analysis. In vitro splicing assay and reverse transcription-PCR analysis of lymphocyte-derived RNA revealed that the wt allele yielded both the expected product, harboring exon 11, and a shorter product in which exon 11 was skipped. The mutant allele yielded mainly the shorter product. Skipping of exon 11 is expected to cause a frameshift which yields an aberrant truncated protein (p.Tyr359Serfs*29). These results suggest that some degree of alternative splicing of exon 11 may occur normally, and that the c.1146+5G>T allele further weakens intron 11 donor splice-site and enhances the skipping of intron 11.

Conclusions: We report a novel intronic mutation in PRPF31 underlying adRP. This report expands the spectrum of pathogenic mutations in PRPF31 and further demonstrates the importance of intronic mutations. Moreover, it demonstrates the phenomena of reduced penetrance, previously associated with PRPF31 mutations.

Genetics and Retinal Degeneration

47 AC,

Dual mutational mechanism of the KIZ c.226C>T mutation as the cause of autosomal recessive retinitis pigmentosa.

Yogapriya Sundaresan (1), Maya Ross (2), Ron Ofri (2), Eyal Banin (1), Dror Sharon (1)
1) Department of Ophthalmology, Hadassah Medical Center, Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, Israel (2) Koret School of Veterinary Medicine, Hebrew University, Rehovot, Israel

Purpose: Mutations in the Kizuna (KIZ) gene, that encodes the centrosomal protein Kizuna, have been reported to cause autosomal recessive retinitis pigmentosa (ARRP), including a nonsense mutation (c.226C>T, p.R76*), located in exon 3. There is currently no approved treatment for KIZ-associated disease. Our aim is to characterize the expression pattern of KIZ in patient-derived skin fibroblasts as well as in normal mouse and sheep retinas by a novel method of alternative splicing analysis of RNA using next generation sequencing (NGS).

Methods: Skin biopsies were procured from four controls and three RP patients homozygous for KIZ-c.226C>T. In addition, retinas dissected from normal mice (n=6) and sheep (n=1) were included in the analysis. Primers for RT-PCR and NGS amplifying exons 2 to 5 were designed using Primer3. Following NGS, the aligned BAM files were analyzed using Integrative Genomics Viewer (IGV). In addition, potential exonic splicing enhancer (ESEs) sites were determined in WT and mutant human sequence using ESEFinder 3.0.

Results: RT-PCR and NGS-based analyses of RNA isolated from primary fibroblasts of patients and controls revealed the presence of four different transcripts: (i) the full-length transcript, (ii) skipping of exon 3, (iii) skipping of exon 3 and inclusion of an alternative exon, and (iv) skipping of both exons 3 and 4. Subsequent analysis of the expression pattern in the mouse and sheep retinas identified only two transcripts: (i) the full-length transcript and (ii) skipping of exon 4. The analyses revealed a lower expression level of the full-length transcript in patients compared to control (22% versus 58%). ESE analysis identified a 7 bp long sequence that includes the c.226 position with a higher score for the human WT sequence (4.411) compared to the mutant sequence (2.694).

Conclusions: KIZ- c.226C>T is a relatively frequent cause of ARRP in the Jewish population. Our data indicate that this variant might affect a putative ESE, that results in pronounced skipping of exon 3. Therefore, mutation-specific therapies, such as readthrough therapy and RNA editing, might show lower than expected efficacy since many transcripts do not contain this mutation. The KIZ nonsense variant is one of the few IRD mutations reported to affect an ESE, but we predict that ESE-affecting mutations are more common and need RNA-based analyses to be identified.

Genetics and Retinal Degeneration

59 AC

RNA Editing of Israeli Founder Nonsense Mutations causing IRDs using Site-Directed Adenosine Deaminase Acting on RNA.

Nina Schneider (1), Ricky Steinberg (2), Johanna Valensi (1), Amit Eylon (2), Eyal Banin (1), Erez Levanon (2), Shay Ben-Aroya (2), Dror Sharon (1)
(1) Department of Ophthalmology, Hadassah Medical Center, Faculty of Medicine, The Hebrew University of Jerusalem, Israel (2) Faculty of Life Sciences, Bar-Ilan University, Israel

Purpose: Targeted RNA editing utilizing the ubiquitous human adenosine deaminase acting on RNA (ADAR) enzyme is a possible new genetic therapeutic approach for the treatment of inherited retinal diseases (IRDs). Utilizing guideRNA (gRNA) to recruit the endogenously expressed ADAR enzyme to a mutated RNA and facilitating the deaminization of a specific adenosine to inosine (read as a guanine by the ribosome), allows for the correction of mRNA transcripts in a transient and tunable manner. According to our recent analyses, 40% of single nucleotide variants (SNVs)-causing IRDs are candidates for ADAR-directed editing. Our aim is to design and test gRNAs that induce targeted ADAR editing for 3 common Israeli mutations causing IRDs: TRPM1- p.K294*, FAM161A- p.R523*, and KIZ- p.R76*.

Methods: After determining Israeli IRD candidate mutations, we used a yeast model to identify candidate gRNAs for these mutations by measuring yeast survival and percent editing in next generation sequencing (NGS). Effective gRNA sequences were then assessed for appropriate chemical modifications and produced as single-stranded RNAs. We developed a fluorescence-expressing plasmid reporter system for ADAR editing by inserting a gene cassette harboring a nonsense mutation in between mCherry and EGFP, and subsequently transfected these plasmids into HeLa cells to test the candidate gRNAs. Successful editing of target gene RNA fragments produced by the reporter plasmid is measured through fluorescent microscopy, Sanger sequencing, and NGS.

Results: Our yeast model identified three possible gRNAs, one for each candidate mutation previously mentioned. In this yeast model, the gRNAs targeting mutations in TRPM1, FAM161A, and KIZ showed 9%, 1%, and 0.2% editing respectively of a relevant nucleotide flanking each mutation. Using our reporter system in HeLa cells, we found that the gRNA complementary to the target TRPM1 mutation induced RNA editing levels in our system of up to 55% in Sanger sequencing, 40% in NGS, and the treated cells expressed both mCherry and EGFP. Experiments utilizing the FAM161A and KIZ appropriate gRNAs are in progress.

Conclusions: Targeted RNA editing utilizing the ADAR enzyme could be the next frontier of genetic therapy for IRDs due to its ability to edit SNVs in a tunable manner. Next steps include applying this genetic therapy to the appropriate knock-in mouse models and retinal organoids.

Genetics and Retinal Degeneration

60 AC,

The gene networks regulating retinal pigmented epithelium differentiation are controlled by SWI/SNF complexes.

S. Ovadia*, G.Cui, M.Gulkar-Cohen, R.Elkon, N.Jing, R.Ashery-Padan
Tel Aviv University, Human Molecular Genetics and Biochemistry

Dynamic interplay between sequence-specific DNA-binding transcription factors (TFs) and chromatin-remodeling complexes controls the temporal differentiation of specific cell types during embryogenesis. We study these developmental transitions in the retinal pigmented epithelium (RPE), an essential tissue for retinal function and maintenance, which develops in a stereotypic spatial and temporal pattern during embryonic development. To delve into the global transcriptional changes that govern RPE differentiation and determine the roles of BAF (SWI/SNF) complexes in this developmentally regulated process, we combined conditional mutagenesis and geographical position sequencing (Geo-seq). We revealed the key TFs and downstream regulatory networks controlling the expression of over 2000 genes during RPE differentiation. Notably, a large fraction of these TFs and targets were dependent on the activity of the SWI/SNF complexes. Our study reveals the massive transcriptional changes in RPE cells during their differentiation, sheds light on the TFs that regulate this tissue differentiation and reveals a major role for the SWI/SNF complex in orchestrating the transition of progenitors to a highly specialized lineage of the central nervous system.

Genetics and Retinal Degeneration

64

Identification of autosomal recessive novel genes and retinal phenotypes in members of the solute carrier (SLC) superfamily.

Dror Sharon (1), Talya Millo (1), Antonio Rivera (1), Alexey Obolensky (1), Dvorah Marks-Ohana (1), Enosh Wilhelm (1), Prakadeeswari Gopalakrishnan (1), Menachem Gross (2), Boris Rosin (1), Mor Hanany (1), Anna Maria Tracewska (3), Ora Schueler-Furman (4), Susanne Roosing (5), Eyal Banin (1)

(1) Ophthalmology, Hadassah Medical Center, Faculty of Medicine, The Hebrew University of Jerusalem, Israel; (2) Otolaryngology-Head and Neck Surgery, Hadassah-Hebrew University Medical Center, Jerusalem, Israel; (3) Lukasiewicz Research Network – PORT Polish Center for Technology Development, Wroclaw, Poland; (4) Microbiology and Molecular Genetics, IMRIC, Faculty of Medicine, Hebrew University of Jerusalem, Israel; (5) Human Genetics, Radboud University Medical Center, Nijmegen, The Netherlands

Purpose: To study clinical and genetic aspects of solute carrier (SLC) genes in inherited retinal diseases (IRDs).

Methods: Ethical approval was obtained from the Hadassah Medical Center Institutional Review Board following the tenets of the Declaration of Helsinki. Ocular evaluation included a full ophthalmological examination, Goldmann perimetry, full field electroretinography, color vision testing, and various retinal imaging. Exome sequencing (ES) data were filtered to identify pathogenic variants in SLC genes. Analysis of transcript and protein expression was performed on fibroblast cell- lines and retinal sections.

Results: Comprehensive analysis of 433 SLC genes in ~900 ES IRD samples revealed homozygous pathogenic variants in six SLC genes including two novel ones: Two variants in SLC66A1 causing autosomal recessive retinitis pigmentosa (ARRP) and a variant in SLC39A12 causing AR mild widespread retinal degeneration with marked macular involvement. In addition, a splicing variant in SLC37A3, suggested previously to cause RP, was found in two ARRP patients resulting in enhanced exon skipping and reduced protein expression. Next generation sequencing analysis revealed a complex splicing pattern in which exon 6 is skipped in the vast majority of transcripts leading to no protein expression as verified by Western blotting. The recently reported SLC4A7 - c.2007dup variant was found in two ARRP patients resulting in the absence of protein. Finally, variants in SLC24A1 were found in four individuals with either ARRP or congenital stationary night blindness (CSNB). Immunohistochemical analysis of the human and mouse retinas using antibodies for four of the studies SLC proteins revealed expression in the outer nuclear layer.

Conclusions: We report on SLC66A1 and SLC39A12 as novel IRD genes, establish SLC37A3 pathogenicity, and provide further evidence of SLC4A7 as IRD genes. We extend the phenotypic spectrum of SLC24A1 and suggest that its ARRP phenotype may be more common than previously reported.

Genetics and Retinal Degeneration

74

Integrating gene regulation and single cell expression with genetic associations identifies genes and cell types contributing to primary open angle glaucoma.

Ayellet V. Segrè[1,2,3], Andrew Hamel[1,2,3], Jiali Wang[1,2,3], John Rouhana[1,2,3], Tavé van Zyl[4], Wenjun Yan[5], Alexi McAdams[1,5], Aboozar Monavarfeshani[5], Qingnan Liang[6], Rui Chen[6], Joshua R. Sanes[5], Janey L. Wiggs[1,2,3], International Glaucoma Genetics Consortium (IGGC)

[1] Ocular Genomics Institute and Department of Ophthalmology, Massachusetts Eye and Ear, Boston, MA [2] Department of Ophthalmology, Harvard Medical School, Boston, MA [3] Broad Institute of Harvard and MIT, Cambridge, MA [4] Department of Ophthalmology and Visual Sciences, Yale School of Medicine, New Haven, CT [5] Department of Molecular and Cellular Biology and Center for Brain Science, Harvard University, Cambridge, MA [6] Department of Molecular and Human Genetics, Baylor College of Medicine, TX

Purpose: Primary open-angle glaucoma (POAG), characterized by progressive optic neuropathy is a leading cause of irreversible vision loss. Yet, there is no cure for this disease, due to poor understanding of the molecular and cellular causes. Here we aimed to identify key genes and cell types that may contribute to POAG risk by integrating known genetic loci of POAG and its major risk factor, intraocular pressure (IOP), with genetic regulation of gene expression (eQTLs) and splicing (sQTLs) in bulk GTEx and retina tissues, and single cell expression in relevant ocular tissues.

Methods: We developed a method, ECLIPSER, that tests whether expression of genes mapped to genome-wide association study (GWAS) loci of a complex trait, based on e/sQTLs, is enriched in specific cell types. First, for each trait, tissue, and cell type combination, a GWAS locus is scored based on the fraction of cell type-specific genes (e.g. fold-change>1.3, FDR<0.1) mapped to the locus. Next, cell type enrichment of a traits' GWAS locus set is assessed against a null distribution of loci of unrelated traits taken from Open Target Genetics, using Bayesian Fisher's exact test. Genes were mapped to 127 POAG loci and 133 IOP loci found in large GWAS meta-analyses, by applying colocalization analysis (eCAVIAR and enloc) to the GWAS loci and all overlapping e/sQTLs from 49 GTEx tissues and retina (EyeGEx).

Results: ≥1 e/sQTLs significantly colocalized with 61.5% of POAG and IOP GWAS loci (Posterior Prob>0.01), suggesting 235 and 289 genes that may affect POAG and IOP, respectively. POAG genes were enriched in elastic fiber formation and extracellular matrix organization (P<6E-05, FDR<3E-05), while IOP genes in vasculature development (P=5E-05, FDR=0.13). By applying ECLIPSER to the mapped genes and single-nucleus RNA-seq of the anterior segment (AS), optic nerve head (ONH) and retina from healthy eyes, we found significant enrichment (P=0.01-4E-04, FDR=0.008-0.16) for POAG in astrocyte and Müller glia in ONH and retina, and ciliary and iris fibroblasts in the aqueous outflow pathway in AS. The IOP genes were enriched in smooth muscle, astrocyte, pericyte, and vascular endothelium in ONH, astrocyte in retina, and trabecular meshwork and ciliary fibroblasts in AS (P=0.001-0.009, FDR=0.02-0.15).

Conclusions: This integrative analysis suggests multiple regulatory mechanisms and genes that may affect POAG risk via specific cell types in the front and back of the eye. Experiments will be needed to validate these functional links, which could help guide novel therapies.

Genetics and Retinal Degeneration

75,AC

Novel mutation in COL9A1 causes autosomal recessive high myopia in Bedouin family.

Ofek Freund1, Ohad Wormser1, Yonatan Perez1, Libe Gradstein2,*, Ohad S. Birk1,3,
1 The Morris Kahn Laboratory of Human Genetics, National Institute for Biotechnology in the Negev and Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva. 2Department of Ophthalmology, Soroka Medical Center, and Clalit Health Services, Ben Gurion University, Beer Sheva 3Genetics institute, Soroka Medical Center, Ben Gurion University, Beer Sheva *Equal contribution

Purpose: To investigate the genetic cause of high myopia in consanguineous Bedouin family.

Methods: Affected individuals underwent complete ophthalmologic examination, including fundus photography and optical coherence tomography (OCT). Whole-exome sequencing (WES) for the proband, and homozygosity mapping using 750k SNP arrays for the nuclear family were performed, assuming autosomal recessive inheritance due to consanguinity. WES variants which passed a filtering cascade were screened using our in-house database of 500 ethnically-matched controls and validated using Sanger sequencing. Results were compared with up-to-date global databases to test prevalence and evaluate pathogenicity.

Results: Two siblings of a consanguineous Bedouin family were affected by high myopia since infancy. At the most recent exam at age 18 and 21 years, their refractive errors ranged from -8 to - 20 diopters. One of them also had anisometropia of 9 diopters, amblyopia, and strabismus. Fundus and OCT findings were compatible with high myopia. None of the affected individuals had facial deformities, hearing loss, skeletal anomalies, or any other systemic abnormalities. Linkage analysis unraveled several homozygous loci shared only by the two affected individuals. Using our in-house bioinformatics software to analyze the WES data, all variants within these loci were ruled out through segregation analysis within the kindred or population allele frequency, except for one variant: COL9A1 (NM_001851.4): c.1550G>A, p.G517E.

Conclusions: We report a novel COL9A1 mutation causing autosomal recessive myopia without systemic abnormalities. COL9A1 is responsible for the assembly of type IX collagen molecules and is expressed in various tissues including the eye and the brain. COL9A1 mutations have been previously reported mainly associated with Stickler syndrome, hearing loss and Multiple Epiphyseal Dysplasia. Our findings suggest that genetic evaluation of children with isolated severe myopia should include analysis for the presence of COL9A1 pathogenic variants.

78 AC

Structural variant analysis of a large set of whole exome sequencing data from Israeli and Palestinian patients with inherited retinal diseases.

Tamar Hayman [1], Talya Millo [1], Eyal Banin [1], Dror Sharon [1]
[1] Department of Ophthalmology, Hadassah Medical Center, Faculty of Medicine, The Hebrew University of Jerusalem, Israel

Purpose: Our patient database of Inherited Retinal Disease (IRD) patients consists of over 2000 families with the genetic cause unknown for ~30% of cases. Using a relatively small number of cases, we and others have reported that in 5-10% of IRD cases, the causative mutations are structural variants (SVs) which cannot be detected by routine whole exome sequencing (WES) analysis. The aim of this research was to perform an extensive analysis of SVs in 346 Israeli and Palestinian IRD WES samples using the Genoox® platform in the hopes of identifying SVs that explain the patient phenotype of our unsolved cases.

Methods: We utilized Genoox® SV analysis based on fastq files generated from WES analysis performed by the 3billion company. This was done through coverage analysis of each exon. The SVs indicated by the program were then confirmed by PCR followed by gel electrophoresis.

Results: We have done SV analysis on 346 cases and this analysis has allowed us to solve 22 cases (6.4%). SVs identified of 18 additional cases (5.2%) are suspected to cause or contribute to the patient phenotype but have yet to be confirmed. Most of the identified causative SVs (54.6%) are homozygous and the remaining are either X-linked (18.2%) compound heterozygous (13.6%) or heterozygous SVs of autosomal dominant variants (13.6%). In a few cases, the identified SV helped to better characterize the phenotype of the studied cases. For example, patient 1178-1 was diagnosed with Usher syndrome due to vision and hearing loss, but SV analysis revealed a large deletion on the X chromosome including 15 genes. Two of the deleted genes are known to cause hearing (POU3F4) and vision (CHM) loss indicating that this patient was misdiagnosed, and that each phenotype (choroideremia and congenital hearing loss) was caused by a deletion of a different gene. Patient 1728-1 was diagnosed with Stargardt disease, and SV analysis revealed a homozygous deletion of exons 17 to 26 of CACNA2D4, a previously reported founder mutation in Ashkenazi Jews. Some of the genes in which we have found SVs were previously known IRD-causing genes, but we have also identified some potential novel genes that may be the cause of disease. Further research is needed to confirm this.

Conclusions: Our analysis is the most extensive and large-scale SV analysis to date examining IRD causing genes in the Israeli and Palestinian populations. It has allowed us to identify the causative variant in 6-11% of analyzed IRD patients including some that have previously been misdiagnosed allowing for a more accurate clinical diagnosis.

Genetics and Retinal Degeneration

87 AC

abca4 c.859-25A>G,a frequent Palestinian founder mutation affecting the intron 7 branchpoint is associated with early-onset Stargardt disease.

Manar Salameh (3) (7),Zelia Corradi (1) (2),Mubeen Khan (1)(2),Elise Heon (4)(5)(6),Ketan Mishra (1)(2),Rebekkah Hitti-Malin (1)(2),Yaha AlSwaiti (3),Alice Aslanian (3),Eyal Banin (7),Brian Brooks (8),Wadih Zein (8),Robert Hufnagel (8),Susanne Roosing (1)(2),Claire-Marie Dhaenens (1)(9),Dror Sharon (7),Frans Cremers (1)(2),Alaa Talbishi (3)

(1) Dep. of Human Genetics Center,RUMC,Nijmegen,(2) Donders Inst. for Brain Cognition and Behaviour,RUMC,Nijmegen,(3)SJEH,Jerusalem,(4) Dep. of Ophth. and vision sciences,SickKids,Toronto,(5) Dep. of ophth. and vision sciences,U of T,Toronto,(6) Prog.of Genetics and genome biology,SickKids,Toronto,(7) Dep. of Ophth.,Had. Univ. Med. C.,HUJI,Jerusalem,(8) Ophth. Gen. and visual function branch,NEI,Bethesda,(9) Lille Neuroscience&Cognition,Univ. Lille,Lille

Purpose: The effect of noncoding variants is often unknown in the absence of functional assays. Here, we characterized an ABCA4 intron 7 variant, c.859-25A>G, identified in Palestinian probands with Stargardt disease (STGD) or cone-rod dystrophy (CRD). We investigated the effect of this variant on the ABCA4 mRNA and retinal phenotype, and its prevalence in Palestine.

Methods: The ABCA4 gene was sequenced completely or partially in 1,998 cases with STGD or CRD. In silico analysis of the effect of c.859-25A>G on splicing was performed using SpliceAI. The effect of c.859-25A>G was investigated using in vitro splice assays. The clinical phenotype was assessed using functional and structural analyses including visual acuity, full field electroretinography and multimodal imaging.

Results: smMIPs-based ABCA4 sequencing revealed c.859-25A>G in ten Palestinian probands living in, or originating from, Hebron and Jerusalem. SpliceAI predicted a significant effect of a putative branchpoint-inactivating variant on the nearby exon 8 splice acceptor site. Splice assays revealed exon 8 skipping and two upstream elongations of exon 8, each of which have a deleterious effect. Additional genotyping revealed another 46 affected homozygous or compound heterozygous individuals carrying this variant. Homozygotes shared a genomic segment of 59.6-87.9 kb, and showed severe retinal defects upon ophthalmoscopic evaluation.

Conclusions: ABCA4 variant c.859-25A>G disrupts a predicted branchpoint resulting in protein truncation due to different splice defects, and is associated with early-onset STGD1 when present in homozygosity. This variant was found in 52/1,203 Palestinian IRD probands, representing one of the most frequent inherited retinal disease-causing variants in Palestine.

124

Hermansky-Pudlak syndrome in a Bedouin family is caused by a novel splice-site mutation in HPS5.

Libe Gradstein[1], Ofek Freund[2], Ohad Wormser[2], Marjan Huizing[3], Michael Volodarsky[2], Marina Eskin-Schwartz[2,4], Ohad S. Birk[2,4]
[1]Department of Ophthalmology, Soroka Medical Center, and Clalit Health Services, Ben Gurion University, Beer Sheva [2]The Morris Kahn Laboratory of Human Genetics, National Institute for Biotechnology in the Negev and Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva [3]Medical Genetics Branch, National Human Genome Research Institute, National Institutes of Health, Bethesda, Maryland [4]Genetics Institute, Soroka Medical Center, Ben Gurion University, Beer Sheva

Purpose: To investigate the clinical characteristics and molecular genetic cause of Hermansky-Pudlak syndrome (HPS) in a Bedouin kindred.

Methods: Three children (2 brothers and a cousin) of an extended consanguineous Bedouin family with albinism and easy bruising underwent complete ophthalmologic examination and hematological evaluation. Presence of platelet dense bodies was assessed by a whole mount electron microscopy. Assuming autosomal recessive heredity due to homozygosity of a founder mutation, the proband's DNA was analyzed using SNP arrays looking for homozygosity in loci of known HPS genes. Relevant homozygous genes were analyzed by Sanger sequencing, followed by segregation analysis through Sanger sequencing.

Results: The three affected individuals exhibited mild hypopigmentation of skin and hair, nystagmus, epistaxis and easy bruising. One of them had heavy bleeding after an uneventful tonsillectomy requiring emergency reoperation. All patients had iris transillumination defects, foveal hypoplasia and fundus hypopigmentation of variable degree. Hematological evaluation revealed prolonged bleeding time and absence of platelets dense bodies on electron microscopy confirming HPS. Patients' visual acuity ranged from 6/12 to 6/120. Two patients had hyperopia and one myopia, and all had astigmatism of variable degree. Two patients had exotropia and one – esotropia. Analysis of SNP array of the proband focusing on genomic loci of all known HPS genes unraveled homozygosity only in the locus of HPS5. Sanger sequencing revealed a novel HPS5 (NM_007216: c.563-2A>G) splice-site mutation. The mutation segregated throughout the kindred as expected for autosomal recessive heredity, with homozygosity in the three affected individuals.

Conclusions: We report a novel homozygous HPS5 mutation causing HPS in extended Bedouin kindred. Affected individuals exhibited variable clinical presentation even within the same family. Although HPS is characterized by mild cutaneous hypopigmentation, it can be associated with profound visual loss and severe bleeding tendency following dental or surgical procedures. It is important for ophthalmologists to recognize this condition and to refer patients to genetic and hematological evaluation in order to prevent life-threatening bleeding complications.

Genetics and Retinal Degeneration

130

Micro-chromosomal deletions and NR5A2 gene involvement with autosomal dominant nystagmus.

Idan Hecht1,2,3, Chen Weiner2,3, Alina Kotlyar2,3, Nadav Shoshany1,2,3, Eran Pras1,2,3

1. Department of Ophthalmology, Shamir Medical Center (formerly Assaf-Harofeh), Tzrifin, Israel.
2. Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.
3. The Matlow's Ophthalmo-Genetics Laboratory, Department of Ophthalmology, Shamir Medical Center (formerly Assaf-Harofeh), Tzrifin, Israel.

Background: Nystagmus is an ocular condition characterised by bilateral involuntary ocular oscillation and can severely affect vision. When not associated with other ocular or systemic diseases, it is sometimes referred to as idiopathic or congenital motor nystagmus (CMN). Genome-wide linkage studies have previously identified several loci associated with CMN, however the genes responsible for some of these loci have yet to be identified. We have examined a large, three-generation family with autosomal dominant CMN. Our purpose was to characterise the clinical manifestations and reveal the molecular basis of the disease in this family.

Methods: Clinical evaluations included full ophthalmic evaluation, refraction and ocular imaging. Molecular analysis included linkage studies, whole genome sequencing (WGS) in select cases, and validation with Sanger sequencing.

Results: Of the 32 family members, 13 subjects in three-generations had CMN, in line with an autosomal dominant inheritance pattern. Molecular analysis was performed on 19 members, 10 of them affected by CMN. Linkage analysis revealed that the disease locus mapped to the NYS7 loci on chromosome 1. WGS on two samples revealed a large deletion spanning over 700,000 bp in the linkage interval. The boundaries of the deletion were confirmed with Sanger sequencing. No protein-coding genes exist within the deleted region, however, the deleted region has relative proximity to the gene NR5A2. We therefore hypothesised that the deletion might affect NR5A2 expression, and by so cause CMN. Interaction network analysis suggested that NR5A2 is strongly associated with other genes expressed in the retina such as PROX1, which in turn is also associated with genes related to nystagmus such as PAX6.

Conclusions: Among a large three-generation family with autosomal dominant CMN, a large deletion in the interval of NYS7 was linked with the disease. No protein-coding genes exist inside the deleted region, and so the mechanism in which CMN is caused is unclear. We suggest NR5A2, as a candidate gene involved in the pathogenesis.

Genetics and Retinal Degeneration

73 AC

FAM161A is expressed in rods and all cone types in the mouse and human retina.

Avigail Beryozkin (1), Chen Matsevich (1), Alexey Obolensky (1), Eyal Banin (1), Dror Sharon (1)
(1) Department of Ophthalmology, Hadassah Medical Center, Faculty of Medicine, The Hebrew University of Jerusalem, Israel

Purpose: We previously reported that FAM161A mutations are the most common cause of retinitis pigmentosa in the Israeli population. We also reported of two different mouse models that we developed for this gene, one of them is a KO which is currently undergo gene therapy. From previous studies we know that Fam161a is a ciliary protein, localized to the base of the connecting cilium, and also expressed in the inner segments of photoreceptor cells in the retina, the inner and outer plexiform layers and the ganglion cell layer. However, a detailed expression analysis in photoreceptors is lacking. The purpose of this study was to discover the exact expression pattern of FAM161A in the human and mouse retina.

Methods: Immunohistochemical staining was performed on slides originated from 1-month-old WT mouse eye, as well as KO mouse models and a human eye. Antibodies recognizing FAM161A, rods, cones and different types of cones were used in two different protocols of double staining and double labeling.

Results: Staining of a WT mouse retina with anti-Fam161a antibody revealed expression of the Fam161a protein mainly between the inner and outer segments of photoreceptors as well as in the outer plexiform layer (OPL). In addition, relatively low expression levels can be seen along the inner limiting membrane (ILM) and between the nuclei of the ONL towards the ILM. No staining at all was evident in the negative control and in KO mouse retina, as expected. Fam161a was identified in the cilia of rods, as well as blue and red/green cones in the mouse retina. In a retina originated from a human eye, expression of FAM161A was observed in cilia of rods as well as cones.

Conclusions: To the best of our knowledge, this is the first comprehensive immunolabeling study which reports the expression of FAM161A in different photoreceptor cell types in the mouse and human retina. Our results indicate that gene therapy in mouse and in human patients should target all types of photoreceptors, and therefore the therapy that is currently tested on mice and targets all photoreceptors, will be suitable for treating human patients in the future.

Genetics and Retinal Degeneration

91

Synthetic formulations of 9-cis beta carotene for treatment of retinitis pigmentosa.

Ifat Sher (1,2), Emily Praisman (1,2), Margalit Altman (1,2), Sara Pri-Chen (1,2), Elvira Haimov (3), Tamara Brider (3), Ehud Gazit (3,4,5), Ygal Rotenstreich (1,2)

(1) Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, Israel. (2) Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel. (3) BLAVATNIK CENTER for Drug Discovery, Tel Aviv University, Tel Aviv, Israel. (4) Shmunis School of Biomedicine and Cancer Research, George S. Wise Faculty of Life Sciences, Tel Aviv University, Tel Aviv, Israel. (5) Department of Materials Science and Engineering, Iby and Aladar Fleischman Faculty of Engineering, Tel Aviv University, Tel Aviv, Israel

Purpose: Retinitis Pigmentosa (RP) is an incurable retinal degeneration blinding disease. With a large number of RP causative genes, gene augmentation will not be efficient and reasonable for all patients, emphasizing the need to develop pharmaceutical interventions that target common disease pathways. In a series of preclinical and clinical studies we demonstrated that oral treatment with the 9-cis ?-carotene (9CBC)-rich Dunaliella alga significantly improved retinal function in RP patients and patients with mutations in RDH5, a visual cycle enzyme. Oral treatment with the alga rescued retinal function and promoted photoreceptor survival in RPE65/rd12 mice, suggesting that 9CBC, a 9-cis-retinal precursor, may present a promising safe treatment strategy for RP associated with visual cycle defects. The aim of this research was to develop new formulations of biologically active synthetic 9CBC.

Methods: Retinas from RPE65/Rd12 mice were incubated in media supplemented with synthetic 9CBC, all-trans-beta carotene or vehicle for 18 hours. Retinas were fixed and sections were stained with antibodies directed against S-cone opsin and M-cone opsin. Number of positively stained cells per retinal section was determined.

Results: Synthetic 9CBC at a concentration of 1 micromolar enhanced M- and S-cone survival in RPE65/rd12 eyecups in-vitro by 2 and 4 folds, respectively, compared to placebo. By contrast, supplementing the media with 1 micromolar all-trans beta Carotene resulted in nearly 2-fold lower cone survival compared with placebo treatment.

Conclusions: Synthetic 9CBC represents a promising drug candidate for treatment of retinal degeneration. Synthesis upscaling is the next step towards in vivo studies and clinical trials.

22

The effect of insulin degrading enzyme inhibitor drops on corneal wound healing (rat model).

Issac Levy (1,2), Dan Frenkel (3,4), Dolev Dollberg (1,2), Irit Bachar (1,2), Asaf Dotan M.D (1,2)
(1)Ophthalmology Division, Rabin Medical Center, Petach Tikva, Israel. (2)Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel. (3)Department of Neurobiology, School of Neurobiology, Biochemistry and Biophysics School, George S. Wise Faculty of Life Sciences, Tel Aviv University, Tel Aviv, Israel. (4)Sagol School of Neuroscience, Tel Aviv University, Tel Aviv, Israel.

Background:
Insulin degrading enzyme (IDE) is a protease that was first discovered due to its ability to break down the B chain of the insulin hormone. The ability to break down insulin by IDE has raised the possibility of controlling Insulin levels and treating diabetic patients with IDE inhibitors. High concentration of IDE may cause the breakdown of various growth factors in addition to insulin and thus impair wound healing.

Purpose:
To evaluate the effect of IDE inhibitor (IDEI) on corneal wound healing in a diabetic rat mode. The primary outcome measures of this study included the duration and rate of corneal wound healing.

Methods:
Our study consisted of 34 rats that were divided into two groups: diabetic and non-diabetic rats. An extensive corneal erosion of 4 mm was created. Half of the rats were treated with IDEI drops and the other half with NaCl 0.9% drops four times a day (sham). Follow up evaluation was conducted twice a day until a complete closure of the erosion was achieved.

Results:
Our result showed tendency over faster healing time with the IDEI drops regardless the diabetic condition of the rat. After 60 hours 85.7% of rats treated with IDEI and only 63.6% who treated with NaCl completely closed the erosion (P=0.19).
In the Non-diabetic rats, significant difference was found between treatments, after 60 hours - 100% of the rats treated with IDEI drops showed complete healing compared with only 57.1% percent of the rats treated with NaCl drops (P=0.038). In the diabetic rats - there was no significant difference in the percentage of rats who completely closed the erosion with either treatment, but faster healing was demonstrated under NaCl treatment.

Conclusions:
To our best knowledge it is the first study to test IDEI drops as a novel treatment for corneal wound repair. According to our preliminary results there may be a beneficial effect on corneal wound healing. Further studies are mandatory.

39 AC

Anti-inflammatory and retinal blood barrier stabilization activities of 3K3A-Activated Protein C in a murine model of acute ocular inflammation.

Dahlia Palevski(1), Rabeei Haj Daood(1), Gil Ben-David(1), Yehonatan Weinberger(1), José A Fernández (2), Ivan Budnik(3), Yael Nisgav(1) , Dov Weinberger(1,4), John H. Griffin(2), Tami Livnat(1,4,5)
(1) Rabin Medical Center, Ophthalmology Department and Laboratory of Eye Research Felsenstein Medical Research Center, Petah-Tikva, Israel (2) Department of Molecular Medicine, The Scripps Research Institute, La Jolla, CA, USA (3) Department of Pathophysiology, Sechenov First Moscow State Medical University, Moscow, Russia (4) Sackler Faculty of Medicine, Tel Aviv University, Tel-Aviv, Israel (5) Sheba Medical Center, The Amalia Biron Thrombosis Research Institute, Tel-Hashomer, Israel

Introduction: 3K3A-Activated Protein C (APC) is a recombinant variant of the physiological anticoagulant APC with distinct cytoprotective properties yet without bleeding risks. We recently showed that 3K3A-APC inhibits the growth and leakage of choroidal neovascularization (CNV). Furthermore, it reduces vascular endothelial growth factor in a murine model of CNV. 3K3A-APC's anti-inflammatory and endothelial barrier stabilizing activities were proven in various non-ocular studies. However, these beneficial properties are yet to be investigated in ocular pathologies.

Purpose: To study the ability of murine 3K3A-APC to inhibit inflammation and stabilize the blood-retinal-barrier (BRB) in a murine model of acute ocular inflammation.
Methods: The study was performed using the endotoxin-induced uveitis (EUI) mouse model. Intravitreal (IVT) injection of lipopolysaccharide (LPS) was applied immediately after IVT injection of 3K3A-APC. Leukocyte recruitment was assessed using flow-cytometry of myeloid markers in isolated retinas. Myeloid cell recruitment, extravasation, and microglial activation were assessed using immunofluorescence of retinal cryosections. Fluorescein isothiocyanate (FITC)-dextran perfusion followed by retinal flatmount staining with the leukocyte antibody anti-CD11B was used to assess inflammatory co-localization of cells to retinal vessels using 3D confocal imaging. Retinal blood barrier integrity was studied by tracing the tight junction protein Zonula Occludens 1 (ZO1). In-vivo capillary leakage was assessed by fluorescein angiography.

Results: LPS injection triggered robust inflammatory cell infiltration in both the anterior and posterior chambers of the eyes. 3K3A-APC treatment decreased the percentage of myeloid cells, specifically neutrophils and macrophages, 24 hours post-EUI induction. Immunostaining revealed that 3K3A-APC reduced leukocyte number and inhibited leukocyte extravasation from blood vessels into the retinal parenchyma. ZO1 clustering in blood vessels and the retinal pigment epithelium border, noted in 3K3A-APC treated eyes, suggests a barrier protective effect of 3K3A-APC on both the inner and outer BRB, respectively.
Conclusions: Our results indicate that 3K3A-APC treatment reduces inflammatory cell infiltration and extravasation into the retina. We hypothesize that 3K3A-APC’s barrier stabilizing properties contributed to the reduction of immune cell infiltration. Our results highlight the potential use of 3K3A-APC as a novel treatment for retinal disease associated with inflammation.

48 AC

Cannabinoid 2 (CB2) receptor upregulation in experimental autoimmune uveitis (EAU).

Gil Ben-David (1),Yael Nisgav (1), Yehonatan Weinberger(1), Michal Kramer (1,2)
(1) Department of Ophthalmology, Rabin Medical Center, and Laboratory of Eye Research, Felsenstein Medical Research Center, Petah?Tikva, Israel (2) Sackler School of Medicine, Tel Aviv University , Tel Aviv, Israel

Purpose:
To study the expression of CB2 receptor in the posterior segment of the eye and its response to intraocular inflammation (IOI).

Methods:
EAU was induced in 53 C57BL/6J mice as previously published using the uveitogenic 161-180amino acid fraction of human intra-retinal-binding-protein (hIRBP). Clinical and histopathological grading were performed on days 4, 10, 17, 21 and 24 post induction using indirect ophthalmoscopy and H&E staining respectively. CD4+ T Cells and CB2 receptor were stained in ocular sections and retinal whole flat mounts using immunofluorescence. Perfusion of Fluorescein isothiocyanate dextran conjugate (MW 500k, Sigma) was used for retinal blood vessels staining in flat retinas. Analysis was performed at different time points for cell volume and number using Confocal 3D microscopy and Imaris software.

Results:
IOI occurred in 44 out of 53 (83%) mice with induced EAU. Clinical signs of inflammation appeared at10 days, peaked at 17 to 21 days, and declined at 24 days, post EAU induction. Mice with high clinical scores exhibited more CD4+ cells and higher CB2 receptor positive cells in the vitreous, retina and choroid compared to mice with low grades of inflammation. In retinal flat mounts analysis, CB2 receptor was present in the retina of control mice and significantly upregulated on day 10 ($p<0.05$). CD4+ cells were located outside the retinal blood vessels, peaked on days 10-21 and diminished on day 24 post induction ($p<0.05$).

Conclusions:
EAU proved to be a robust and reproducible model in our laboratory. CB2 receptor peaked in the retina earlier than the appearance of CD4+ cells which paralleled the clinical appearance of IOI. These preliminary results suggest that cannabinoids may have a potential effect on EAU.

67,AC

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

Nitay Zuk-Bar, Shai Ovadia, Ruth Ashery-Padan [Tel-Aviv University], Ron Ofri, Eyal Banin, Alexey Obolensky, Chen Matsevich, [Hebrew University Jerusalem], Michal Simon, Keren ben Yaakov [Kaplan medical center]
Department of Human Molecular Genetics and Biochemistry, Sackler Faculty of Medicine, Tel-Aviv University], [Koret School of Veterinary Medicine, The Hebrew University of Jerusalem, Rehovot, Israel], [, Department of Ophthalmology, Hadassah Medical Center, Faculty of Medicine, The Hebrew University Jerusalem, Jerusalem, Israel], [Ophthalmology, Kaplan medical center, Rehovot, Israel]

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 transcription factors (TFs). The Baf155 (Smarcc1) and Baf170 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. To study the roles of Baf155 in retinal pigmented epithelium (RPE) differentiation, I have analyzed the phenotype of Baf155 conditional knockout in these cells (cKO; Baf155flox/flox;DctCre) compared to control. This analysis revealed unique importance of the Baf155 subunit in retinal function in old mice and for the development of the optic nerve. 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.

71 AC

Single cell profiling of non-neuronal retinal cells after optic nerve axotomy reveals tissue dynamics in CNS injury.

Inbal Benhar(1), Jiarui Ding(1), Wenjun Yan(2), Anne Jacobi(2,3), Irene E. Whitney(2), Malika Sud(1), Grace Burgin(1), Karthik Shekhar(1), Nicholas M. Tran(2), Chen Wang(3), Zhigang He(3), Joshua R. Sanes(2), Aviv Regev(1)
(1) Broad Institute of MIT and Harvard, Cambridge, MA 02142, USA (2) Department of Molecular and Cellular Biology, Harvard University, Cambridge, MA 02142, USA (3) F.M. Kirby Neurobiology Center and Department of Neurology, Boston Children's Hospital, Harvard Medical School, Boston, MA 02115, USA.

Purpose: It is increasingly clear that non-neuronal cells play key roles in determining how neurons of the central nervous system (CNS) respond to injuries. However, the dynamic and complex interplay between the different cell types has been challenging to analyze. We addressed this complexity at the systems level, using the mouse optic nerve crush (ONC) injury model.

Methods: We axotomized mouse retinal ganglion cells (RGCs) by crushing the optic nerve, then used single-cell RNAseq to generate transcriptomic atlases of immune, glial and epithelial cells at steady state and at six time points along the injury response. We experimentally validated results using immunohistochemistry, in situ hybridization and antibody-mediated monocyte depletion.

Results: We charted the heterogeneity, changes in composition and expression states of non-neuronal cells in the retina, finding that early glial reactivation was coupled with chemokine upregulation, and that a unique retinal pigment epithelial cell state emerged following injury. We resolved dynamic trajectories of resident and infiltrating mononuclear phagocytes in the retina, identifying distinct and previously undescribed resident subsets, and demonstrating that blood-derived monocytes gave rise to macrophages with overlapping signatures after injury. We further uncovered synchronized multicellular programs and interactions between RGCs, glia and immune cells, highlighting an interferon-response program that was augmented concurrently with the peak decline in RGCs. Finally, we analyzed expression of human retinal disease-related genes in our dataset, providing a species comparison as well as extra-neuronal insight.

Conclusions: CNS insult induces a coordinated response across the various cell types in the tissue. Our data provide a resource for further exploring the cellular circuitry, spatial relationships and molecular interactions governing post-injury tissue dynamics in the retina and CNS at large, with potential to highlight avenues for therapeutic intervention.

72

The effect of hemodialysis on intraocular pressure in dogs.

Dikla Arad (1), Hila Chen (2), Oren Pe'er (1), Lionel Sebbag (1), Gilad Segev (2), Ron Ofri (1)
(1) Department of Ophthalmology, Koret School of Veterinary Medicine, the Hebrew University of Jerusalem, Rehovot, Israel. (2) Department of Internal Medicine, Koret School of Veterinary Medicine, the Hebrew University of Jerusalem, Rehovot, Israel.

Purpose: In ISVER 2020, Maharshak I et al. reported that mean intra ocular pressure (IOP) is significantly reduced (by 1.32 mm Hg) during hemodialysis in humans. Our aim was to measure the effects of hemodialysis on IOP in canine patients.

Methods: Dogs undergoing hemodialysis treatment for acute kidney injury (AKI) were included in this study. Dogs that were sedated or had an ocular pathology that might influence IOP were excluded. IOP was measured at the beginning of hemodialysis (time 0) and hourly for 4 hours. Serum osmolarity was calculated at time 0, 2 and 4 hours, and blood pressure (BP) was measured hourly during the hemodialysis treatment. Data were analyzed using repeated measures MANOVA.

Results: Ten dogs underwent a total of 25 dialysis treatments. At 0, 1 and 2 hours mean ± SD IOP was 17.7 ± 3.8 mm Hg, 17.6 ± 3.7 mm Hg and 17.1 ± 3.7 mm Hg, respectively (P ? 0.13). IOP then decreased significantly (P ? 0.04) to 15.7 ± 3.7 mm Hg and 15.5 ± 3.4 mm Hg at 3 and 4 hours, respectively. Calculated serum osmolarity significantly decreased from 321.7 ± 14.5 mOsm/kg (time 0) to 301.8 ± 6.7 mOsm/kg (4 hours) (P < 0.0001). No consistent correlation was found between IOP and BP.

Conclusions: In humans, there are reports that IOP increases, decreases or is unchanged in hemodialysis. The present study shows significant IOP reduction in dogs undergoing hemodialysis for AKI, likely resulting from reduction in serum osmolarity. These preliminary findings suggest there is no risk for dogs with goniodysgenesis or glaucoma to undergo hemodialysis although further study is needed to confirm this recommendation.

81 AC

Cobalt trace elements injected to mice may cause retinal toxicity.

Basel Obied(1), Stephen Richard(1), Irit Mann(1), Alon Zahavi (2,5,6), Olga Girshevitz (3) Nitza Goldenberg-Cohen(1,4)
1. The Krieger Eye Research Laboratory, Technion, Hafia. 2. Rabin Medical Center, Sackler Faculty of medicine, Tel Aviv University, Tel Aviv. 3. Faculty of Engineering and Institute of Nanotechnology & Advanced Materials, Bar-Ilan University, Ramat Gan. 4. Department of Ophthalmology, Bnai-Zion Medical Center, Haifa. 5. Sackler School of Medicine, Tel Aviv University, Tel Aviv. 6. Laboratory of Eye Research, Felsenstein Medical Research Center, Petach Tikva.

Purpose:
Recent reports have described a specific toxicity including visual loss mediated by the high levels of cobalt released by metallic hip implants. The current study primarily aims to investigate cobalt toxicity following intravitreal or intravenous administration. Secondary goal is to define clearance time from the blood and possible presence in the tear film.

Methods:
Mice were divided into two groups: the first group (n=10) was injected intravenously with 0.1 ml cobalt chloride in different concentrations (15, 7.5, 1.5 mg/ml). The second group (n=10) underwent a single 0.3µl injection to the vitreous (concentration of 130ug/ml). Both groups underwent a baseline functional assessment by electroretinography (ERG) examination prior to intervention, followed by repeated ERG examinations after cobalt injection. At 21 days both groups underwent a final ERG recording prior to euthanization. Retinae and optic nerves were harvested and analyzed for cobalt presence by Particle induced x-ray emission (PIXE), histology and apoptosis staining (TUNEL). Blood, urine and tears were also analyzed for presence of cobalt by PIXE.

Results:
Intravenous injection of 0.1 ml 15mg/ml and 7.5mg/ml Cobalt led to 100% immediate mortality of the mice (10 mice). Instead, repeated 0.1 ml injections of 1.5mg/ml dose were well tolerated. Cobalt levels were elevated in body fluids (blood, urine) immediately following systemic injection. Intravitreal single injection was well tolerated but reduced ERG recording at 3 weeks, yet not at one day after the injection. No data yet available for the cobalt in retina nor tears.

Conclusions:
Our results demonstrate cobalt toxicity is lethal in high concentrations and may impair vision in repeated lower concentrations or direct intravitreal injection. Intravitreal injection affected retinal function as demonstrated by repeated ERG. Cobalt may be detected in tissues by PIXE, and cobalt toxicity should be suspected in patients presenting with unexplained systemic and visual symptoms with a medical history of hip replacement with cobalt containing implants.

104

Multimodal analysis of gadolinium in mouse tissues

Alon Zahavi (1,2,3), Olga Girshevitz (4), Yoav Vardizer (5), Hila Kreizman-Shefer (6), Jacob Bajar (6), Nahum Shabi (4), Dror Fixler (4), Nitza Goldenberg-Cohen (5,7)
(1) Ophthalmology Department, Rabin Medical Center, Petach Tikva (2) Sackler School of Medicine, Tel Aviv University, Tel Aviv (3) Laboratory of Eye Research, Felsenstein Medical Research Center, Petach Tikva (4) Faculty of Engineering, Institute of Nanotechnology, Bar-Ilan University, Ramat Gan (5) Ophthalmology Department, Bnai-Zion Medical Center, Haifa (6) Pathology Department, Bnai-Zion Medical Center, Haifa (7) The Krieger Eye Research Laboratory, Bruce and Ruth Faculty of Medicine, Technion, Haifa

Purpose: Gadolinium (Gd)-based contrast agent deposition disease (GDD) in the brain may occur in 0.03% of patients undergoing neuroimaging. This study aimed to investigate the applicability of multimodal imagining including Particle Induced X-ray Emission (PIXE) analysis, scanning electron microscopy, spectroscopy and immunohistochemistry to detect retention of Gd in mouse tissues following intravenous (IV) injections.

Methods: Forty-six C57Bl6 mice were divided into two groups: single or multiple IV injections of 0.12ml Gd (n=42), and a control of double IP injections of 0.2 ml saline (n=4). Double IP saline injections were given at three (n=2) and ten (n=2) days intervals, and mice were sacrificed immediately following the 2nd injection. Single IV injected mice were sacrificed immediately (n=5), between 30 minutes to 2.5 hours (30 minutes interval, n=25) and at 21 days (n=4). Six mice had weekly injections and were sacrificed at 7 days (2 injections, n=2) and 14 days (3 injections, n=4). Another 3 mice had a total of 4 injections and sacrificed a week after the last injection (35 days from 1st injection, n=1) and 21 days from last injection (60 days from 1st injection, n=2).
Analysis of tears, blood samples, urine, eyes, brain, kidney and spleen were performed by PIXE, scanning electron microscopy, spectroscopy and immunohistochemistry with metallothionein staining for metal detection.

Results: Blood samples were positive for Gd in 11 mice sacrificed up to 24 hours after IV injection. Urine excretion was in correlation with blood levels. Brain tissue was positive after 24 hours in 2 mice, 1 of which was negative in blood samples. Other tissues were negative for Gd. Electron microscopy did not detect Gd in tissues, but spectroscopy supported PIXE findings in mice brains.
Staining with metallothionein was positive for metallosis, but not specific for Gd in tissues.

Conclusions: We were able to detect Gd retention in mice brains in various methods. PIXE was demonstrated as the most sensitive method, supported by spectroscopy analysis. Electron microscopy and immunohistochemistry were less sensitive. The urine excretion rate was also calculated in correlation to blood levels. This analytical method enables quantitative detection of Gd in biological samples. Our results demonstrate good clearance rate within 24. However, the fact that Gd was detected by PIXE in the brain of 2 mice points to a risk of retention.

4 AC

Precorneal retention time of ocular lubricants: A fluorophtometric study in a large animal model (dogs).

Lionel Sebbag (1;2), Leila Bedos (2), Rachel A. Allbaugh (2), Jonathan P. Mochel (2)
(1) Koret School of Veterinary Medicine, Hebrew University of Jerusalem, Rehovot, Israel (2) Iowa State University, College of Veterinary Medicine, Ames, Iowa, USA

Purpose: To determine the precorneal retention time of selected artificial tears preparations in canine eyes, a species.

Methods: Six healthy Beagle dogs (n=12 eyes) were enrolled. Five different lubricants (Artificial Tears Solution®, Artificial Tears Ointment®, I-Drop® Vet Plus, Optixcare® Eye Lube Plus, and Systane® Ultra) were mixed with 10% sodium fluorescein to obtain 1% formulations. Following topical administration (35 mg) in each eye, tear fluid was collected with capillary tubes at selected times (0, 1, 5, 10, 20, 30, 40, 50, 60, 90, 120, 180 min) and fluorescein concentrations were measured with a computerized scanning ocular fluorophotometer. Data was analyzed with Kruskal-Wallis and two-way repeated measures ANOVA (post hoc Tukey).

Results: Tear fluorescence was significantly greater (P?0.009) with Artificial Tears Ointment® compared to other lubricants from 1 to 20min post- administration. Median (range) precorneal retention times were significantly different among the 5 lubricants (P=0.036), ranging from 40 minutes (20-90 min) for Artificial Tears Ointment®, 35 min (20-90 min) for Systane® Ultra, 30 min (10-60 min) for I-Drop® Vet Plus, 25 min (10-60 min) for Optixcare® Eye Lube Plus, and 10 min (10-20 min) for Artificial Tears Solution®. Precorneal retention time was significantly lower for Artificial Tears Solution® compared to the other 4 formulations (P≤0.028).

Conclusions: In dogs, ophthalmic ointment administration provided higher tear concentrations (first 20 min) and longer precorneal retention time compared to other topical lubricants. Precorneal retention time was also prolonged with formulations containing polyethylene glycol/propylene glycol (Systane® Ultra) and 0.25% hyaluronate (I-Drop® Vet Plus and Optixcare®) when compared to regular artificial tears solution (1.4% polyvinyl alcohol).

8 AC

Silicone sling frontalis suspension for congenital ptosis: outcome of 174 consecutive cases.

Daphna Landau Prat [1,2], Meera Ramakrishnan [2], Cindy Zhao [2], Karen E. Revere [2], William R. Katowitz [2], James A. Katowitz [2]
[1] Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, Israel, affiliated to Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [2] Children's Hospital of Philadelphia, 3401 Civic Center Blvd, Philadelphia, PA, USA.

Purpose: Frontalis suspension (FS) surgery is considered the treatment of choice in congenital ptosis with poor levator function. The frontalis muscle is surgically linked to the upper eyelid tarsal plate using an alloplastic or autogenous material. Eyelid position is improved in primary gaze, and eyelid elevation is facilitated through frontalis muscle contraction. Literature regarding frontalis suspension in the pediatric population is limited. The purpose of the current study is to report the surgical outcome of FS using a double triangle configuration of silicone slings in children with poor levator function.

Methods: A retrospective cohort study. Chart review was done of all pediatric patients with simple myogenic congenital ptosis repaired with FS over a 12-year period (2009-2020). Each silicone sling was secured by simple knots. Pre-and post-operative margin to reflex distance (MRD1) measurements were determined from clinical photographs using ImageJ Software. Main outcome measures were improvement in eyelid height, eyelid asymmetry, reoperation rate and timing.

Results: 139 patients (174 eyes) were included, 35 (25%) underwent bilateral surgery. Mean (±SD) age was 1.4±1.9 years. Mean follow up time was 32±20.5 months. Sixteen patients (11%) had a history of previous ptosis repair surgery. Mean MRD1 improved by an average of 1.5 mm. The final MRD1 in the successful group was a mean of 2.1 mm. The MRD1 difference between both eyes in all unilateral patients improved from 2.5 mm preoperatively to 1.2 mm at final visit ($p<0.001$). In the 123 cases without a history of previous ptosis surgery, repeat ptosis repair was performed in 37 (30%) patients, 34.9±19.9 months after the initial procedure. Overall, repeat repair was performed in 47 patients (34%).

Conclusions: Double silicone sling frontalis suspension has a favorable outcome in 2/3 of pediatric patients with simple myogenic congenital ptosis. Failed cases can be addressed with a second repair, using either fascia lata or repeat silicone slings.

9 AC

Patient-specific orbital implants vs. pre-formed implants for internal orbital reconstruction.

Daphna Landau Prat [1], Saeed Massarwa [2], Ofira Zloto [1], Ayelet Priel [1], Oded Sagiv [1], Assa Zohar [1], Guy Ben Simon [1]
[1] Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, Israel, affiliated to Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [2] Plastic Surgery Department, Hadassah Hospital, Jerusalem, Israel

Purpose: Orbital blowout fractures are encountered relatively commonly in the oculoplastic clinic. Selection of the type of surgery is based upon the fracture extent, ocular motility disturbances, and the presence of muscle entrapment. Several approaches for addressing and mitigating the challenges of traditional orbital fracture repair have been recently described, and advances in imaging techniques and associated technologies have led to improved preoperative planning. The purpose of this study is to compare the outcome of orbital blowout fracture repair by means of pre-formed porous-polyethylene titanium implants (PFI) vs patient-specific porous-polyethylene implants (PSI).

Methods: Retrospective cohort study. Baseline characteristics, ophthalmic examination results, ocular motility, fracture type, timing of surgery, implant type, and final relative enophthalmos of all patients operated for blow-out fractures in a single center were collected and analyzed.

Results: Twenty-seven patients (mean age 39 years, 9 females) were enrolled. Sixteen underwent fracture repair with PFI and 11 with PSI, 11 months (median) post-trauma. Follow-up duration was 1.1 years (mean). Both groups showed significant postoperative improvement in primary or vertical gaze diplopia (P = .03, ?2). Relative enophthalmos improved from -3.2 preoperative PFI to -1.7 mm postoperative PFI, and from -3.0 mm preoperative PSI to -1.1 mm postoperative PSI (P = .1). PSI patients had non-significantly less postoperative enophthalmos and globe asymmetry than PFI patients. Outcome was not influenced by previous surgery, age, sex, number of orbital walls involved in the initial trauma, or medial wall involvement (linear regression). Both groups sustained severe complications unrelated to implant choice.

Conclusions: PSI may be a good alternative to PFI in primary or secondary orbital blowout fracture repair with less enophthalmos and globe asymmetry, in spite of the possible disadvantages of production time, a relatively larger design, and challenging insertion. Since it is a mirror-image of the uninjured orbit, it may be beneficial in extensive fractures or secondary repair.

10 AC

Management of congenital nasolacrimal duct obstruction in Down syndrome

Daphna Landau Prat [1,2], Samuel Tadros [1], Karen E. Revere [1], James A. Katowitz [1], William R. Katowitz [1]
[1] Division of Ophthalmology, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA and the Edwin and Fannie Gray Hall Center for Human Appearance, The University of Pennsylvania, Perelman School of Medicine, Pennsylvania, USA; [2] Division of Ophthalmology, the Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, Israel; the Sheba Talpiot Medical Leadership Program.

Purpose: Congenital nasolacrimal duct obstruction (CNLDO) is common in Down Syndrome (DS), and more difficult to treat. Our purpose was to describe the management of CNLDO in pediatric patients with DS.

Methods: Retrospective cohort study including all DS patients diagnosed with CNLDO at the Division of Ophthalmology at the Children's Hospital of Philadelphia during a 12-year-period (2009-2020). The clinical records were reviewed and analyzed. Main Outcome Measures included surgical interventions, primary probing outcome, rate of dacryocystorhinostomy (DCR) and/or conjunctivodacryocystorhinostomy (CDCR), and overall success.

Results: 126 patients (236 eyes) were included, mean age of 1.8±2.1 years (range 0.1-11.3 y), 110 (87%) had bilateral CNLDO. Mean follow up time was 41 months. 84 patients (67%) underwent at least one surgical intervention; the mean number of surgical interventions in this group was 1.8±1.4 per patient (range, 1-6). The most common primary intervention was probing (n=74, 88%), mostly (n=57, 68%) with monocanalicular silicone intubation. Probing with or without intubation was successful in 59% of patients, while probing with silicone intubation had a higher success rate of 70% (P=0.002). 20 (24% of 84) patients underwent DCR/CDCR during the follow-up period. Complete resolution was achieved in 123 patients (98%).

Conclusions: CNLDO in Down syndrome is associated with high rates of bilateral obstructions and with less favorable surgical outcomes. Many patients ultimately require a more robust surgical intervention as DCR or CDCR. The use of monocanalicular stent in initial probing was associated with a higher success rate, and would appear to be appropriate in all CNLDO-DS cases.

19 AC

Oxidative stress facilitates exogenous mitochondria internalization and survival in retinal ganglion precursor cells.

Daniel Raz[1], Michal Aharoni-Simon[1], Keren Ben-Yaakov[1], Maya Sharvit-Bader[1], Yasmin Haim[1], Waleed Ghannam[1], Noga Porat[1], Avital. Eisenberg-Lerner[1], Hana Leiba[12], Arie Marcovich[12] and Ziv Rotfogel[12]
1. Ophthalmology Research Laboratory, Kaplan Medical Center, Rehovot, Israel 2. Faculty of Medicine, Hadassah Medical School, The Hebrew University of Jerusalem, Israel

Mitochondrial transplantation (MitoPlant) is a novel therapeutic modality for the treatment of ischemia/reperfusion insults. The mechanisms by which MitoPlant protect the cells, the survival rate and the faith of the exogenous mitochondria in the target cells is still obscure. The visual system is highly susceptible to impaired energy supply and indeed mitochondrial dysfunction contributes to various acute, chronic and genetic ocular diseases. It has been recently shown that MitoPlant temporarily protects retinal ganglion cells from cell death in an animal model of ocular ischemia. Here, we studied the dynamics of MitoPlant in retinal ganglion precursor cells, focusing on the effect of oxidative stress on mitochondrial uptake and survival.
We developed a method based on mtDNA detection for identification and continuous monitoring of transplanted mitochondria in recipient cells. We examined mitochondria content and survival following MitoPlant into 661W cells under basal conditions or following oxidative stress.
Interestingly, we found that exposure of recipient cells to moderate oxidative stress prior to MitoPlant dramatically enhanced mitochondrial uptake by more than three fold.
These findings demonstrate a beneficial effect of oxidative stress on MitoPlant into retinal ganglion precursor cells. Revealing mechanisms that mediate mitochondrial uptake will enable further developing MitoPlant as a novel therapeutic modality for treatment of chronic and genetic ocular pathologies, and beyond.

52,AC

Medical Cannabis Oil for Benign Essential Blepharospasm: A Prospective, Randomized Controlled Pilot Study.

Ofira Zloto, M.D.,1,2* Alon Weisman, M.D.,1,2* Inbal Avisar, M.D.,2,3 Tal Serlin, M.D.,1,2 Lihi Bar-lev, MSC, 4 Ayelet Priel, M.D.,1,2 Daphna Landau Prat, M.D.,1,2 Nira Granot, RN, BSN, MA,1 Iris Weisman, BSN RN,1 Guy Ben Simon, M.D.1,2
1Goldschleger Eye Institute, Sheba Medical Center, Tel-Hashomer, Israel 2 Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel 3 Rabin Medical Center, Petach Tikva, Israel 4 Tikun Olam NGO for Promotion of Medical Cannabis, Tel Aviv, Israel

Objective: To examine the efficacy and safety of medical cannabis in benign-essential-blepharospasm (BEB).

Methods: This is a prospective, double-blind, placebo-controlled study. All consecutive adult BEB patients who had been successfully treated with BTX-A injections between 3/2019 and 2/2020 were recruited. The study patients were randomly allocated into a treatment and a control (placebo) group in a 1:1 ratio. The treatment group used cannabis drops and the control group used cannabis oil drops during the first 6 weeks of the study, and both groups were treated with the medical cannabis drops during the second 6 weeks. The cannabis dose was gradually increased for each patient depending upon effect and tolerability.

Results: Three patients were included in each group. The mean duration of spasm attack during the first 6 weeks was 4.29 minutes in the treatment group and 73.9 minutes in the placebo group ($P < 0.01$). During the last 6 weeks, the treatment group used an average of 6.27 drops and the placebo group used an average of 5.36 drops ($P = 0.478$). There were 61 spasm events in the treatment group and 94 spasm events in the placebo group($P = 0.05$). The mean duration of spasm attack was 1.77 and 8.96 minutes, respectively ($P < 0.01$). The side effects were mild, and they included general fatigue, dry mouth, and insomnia.

Conclusions: Medical-cannabis can be an effective and safe treatment for BEB as a second line after BTX-A injections when used for 3 months. No significant ocular or systemic side-effects were associated with the treatment.

57 AC

Decreased effectiveness of 0.01% atropine treatment for myopia control during prolonged COVID-19 lockdowns.

Asaf Shemer(1), Nir Erdinest (2), Naomi London(3), Nadav Levinger(2,4), Itay Lavy(2), Eran Pras(1), Yair Morad(1)
(1) Department of Ophthalmology, Assaf Harofeh Medical Center, Zerifin, Israel. (2) Department of Ophthalmology, Hadassah-Hebrew University Medical Center. (3) Private practice, Jerusalem, Israel. (4) Department of Ophthalmology, Enaim Refractive Surgery Center, Jerusalem, Israel.

Purpose: To examine the possible impact of the lockdowns during the COVID-19 pandemic on the efficacy of atropine therapy for myopia control on children.

Methods: A clinic retrospectively reviewed chart data of children age 9-15 whom had not been in a frontal classroom and been socially restricted from March 2020 till March 2021. Fourteen of these children that had been under myopia control treatment which had been effective during the year prior to the pandemic were included, to learn if their myopia continued to stay under control, or if the unique environmental modifications affected their progression.

Results: The results showed that average increase in spherical equivalent refraction and axial length, measured with optical biometer OA-2000 (Tomey GmbH, Nagoya, Japan), during the year of lockdowns was -0.73±0.46D/0.46±0.31mm respectively, while the average increase in the year prior was -0.33±0.27D/0.24±0.21mm.

Conclusions: This study indicates a possible significant impact of the environment on myopia increase even in individuals under effective atropine treatment. These children's' progression suggests practitioners consider and address multiple aspects simultaneously when attempting myopia control.

62 AC

Behavior of Intravitreally Injected Drugs Simulated by Two Models of the Silicone Oil Filled Eye.

Anfisa Ayalon (1), Alexander Rubowitz (1), Pritam Kumar Roy (2), Shraga Shoval (2), Irina Legchenkova (2), Edward Bormashenko (2)
(1)Retina Service, Department of Ophthalmology, Meir Medical Center, Kfar Saba, Israel, and The Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel. (2) Engineering Faculty, Chemical Engineering Department, Ariel University, 407000, P.O.B. 3, Ariel, Israel

Abstract

Purpose: To obtain data on the intraocular migration and distribution of commonly injected ophthalmic drugs in eyes filled with silicone oil used as a retinal tamponade agent.

Methods: Novel in vitro and ex vivo models were created for studying the physical properties of the retinal surface. The behavior of several commonly used ophthalmic drugs injected into the medical-grade 1300 cSt silicone oil layer was studied, as well as their wetting properties, interaction with plasma-treated glass and animal retinas.

Results: In vitro experiments showed that droplets of all tested drugs sank rapidly in the silicone oil to contact with the glass, and then rapidly spread over the glass surface. In the ex vivo model, the migration phase was followed by contact with, and rapid spread/absorption by the retinal interface. The wetting behavior of drugs under contact with the glass substrate and retinas was similar. Characteristic time scales of spreading, controlled by the viscous dissipation, were close.

Conclusions: All tested drugs migrated to the retinal surface and rapidly spread across the retinal surface. This suggests that intravitreal drugs might be used effectively in eyes filled with a silicone oil tamponade, as they rapidly migrate to, and spread over the retinal surface. The rapid spread of these drugs in the small film of aqueous fluid present between the silicone oil and the retina may expose the retina to high drug concentrations and thus may introduce potential toxicity. A lower concentration or volume of drugs should possibly be considered for intra-silicone oil injections.

63 AC

Wetting of the Amphiphilic Retinal Surface and its Implications for the use of Silicone Oil as a Tamponading Agent in Retinal Surgery.

Alexander Rubowitz (1), Anfisa Ayalon (1), Pritam Kumar Roy (2), Shraga Shoval (2), Irina Legchenkova (2), Edward Bormashenko (2)
(1) Retina Service, Department of Ophthalmology, Meir Medical Center, Kfar Saba, Israel, and The Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel. (2) Engineering Faculty, Chemical Engineering Department, Ariel University, 407000, P.O.B. 3, Ariel, Israel

Purpose: Retinal detachment is a potentially blinding condition that requires prompt surgical intervention. Despite recent technological advances, retinal re-detachment remains a significant cause of morbidity and vision loss. The purpose of this research is to report on the static wetting of animal retina by water and organic oils and describe retinal interface properties that may potentially contribute to re-detachment of the retina even after successful surgery.

Methods: In order to test the wetting behavior of the retina as it occurs in a surgical situation in vivo, we studied the entire intact complex of retina-RPE-choroid-sclera in cow, sheep, and pig eyes. Wetting by water, silicone oils and castor oil, as well as experiments with double sandwich oil/water layers were performed.

Results: Both water and silicone oils demonstrated complete wetting of the retina, regardless of the viscosity of the silicone oil, whereas castor oil demonstrated a partial wetting regimen. Similar wetting regimens were observed for sheep, cow and pig retinas. The intact surface of animal retina was found to be both hydrophilic and oleophilic. The oils were rapidly replaced from the liquid/retina interface by added water.

Conclusions: The internal limiting membrane of the animal retina was found to be amphiphilic. At the same time, water demonstrated stronger affinity to the retina than oils. We believe that aqueous continuously secreted in the living eye may displace silicone oil from the retinal surface and contribute to retinal re-detachment.

69 AC

The association between pupil diameter and apparent chord mu length value.

Karny Shouchane-Blum (1,2), Olga Reitblat (1,2), Irit Bahar (1,2), Ruti Sella (1,2)
(1) Ophthalmology Department, Rabin Medical Center, Petah Tikva (2) Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv

Purpose: Chord mu length represents the distance between the pupil center and the visual axis. It is considered a new reference marker for evaluation before implantation of diffractive multifocal intraocular lenses (IOLs). Previous studies suggested that multifocal IOLs should be well considered in patients with an apparent chord mu length greater than 0.6, as it may be associated with a higher incidence of halos and glare. This value can be measured by a routine biometry prior cataract surgery, using the IOL Master 700 device (Carl Zeiss Meditec, AG). Pupil diameter can vary in different patients and measure differently for the same patient at different light conditions. The purpose of this study was to evaluate the correlation between apparent chord mu length and pupil diameter.

Methods: This prospective study evaluated patients scheduled for an elective cataract surgery at a single tertiary medical center between 2021-2022. Pupil diameter and Chord mu length, in photopic condition, before and after pupil dilatation (by administering a drop of mydramide 0.5% and a drop of cyclophentolate 1%, twice, 10 minutes apart), were measured using the IOL master 700. Exclusion criteria were visual acuity worse than 20/100 and pseudophakia. Wilcoxon signed-rank was used to compare the change in chord mu length.

Results: Forty-nine eyes of 49 patients were included. Mean ± SD pupil diameter, before and after pupil dilatation was 3.11 mm ± 0.83 and 6.66 mm ± 1.14 ($p<0.001$), respectively. Chord mu length increased from 0.322 mm ± 0.22 to 0.44 mm ± 0.25 ($p=0.001$), respectively.

Conclusion: Chord mu length significantly increases after pharmacological pupillary dilatation. This should be taken into consideration in preoperative planning, especially when the apparent chord mu value is taken into account for patient selection in cases of a planned multifocal IOL.

109

The neuroprotective effect of Phlomis viscosa Poiret and Ficus benjamina in the treatment of optic nerve crush.

Moria Oz (1), Alon Zahavi (2,3,4), Ludmila Yarmolinsk (1), Nitza Goldenberg-Cohen (5,6), Bat Chen R. Lubin (1,7)
(1) Eastern R&D center, Ariel (2) Ophthalmology Department, Rabin Medical Center, Petach Tikva (3) Sackler School of Medicine, Tel Aviv University, Tel Aviv (4) Laboratory of Eye Research, Felsenstein Medical Research Center, Petach Tikva (5) Ophthalmology Department, Bnai-Zion Medical Center, Haifa (6) The Krieger Eye Research Laboratory, Faculty of Medicine, Technion , Haifa (7) Department of Chemical Engineering, Biotechnology and materials, Ariel University, Ariel

Purpose: Stroke is one of the most important causes of mortality and morbidity in the world and is the third most common cause of death in Israel. About 67% are attributed to an ischemic stroke, caused by blockage of cerebral blood vessels. Apart from mortality, the main burden of stroke is the long-term disability caused by irreversible brain injury and subsequent focal neurologic deficits, which is evident especially in the elderly population.
Attention has currently turned towards approaches that include herbal drugs, which can be used in limiting the neurological damage. However, the strength of evidence to support the use of herbal drugs is unclear, mainly because the focus so far has been on traditional uses. The purpose of the study was to evaluate the possible neuroprotective effects of Phlomis viscosa Poiret and Ficus benjamina in vitro and in vivo.

Methods: In vitro analysis was performed in SH-SY-5Y cells which were treated with plant extract for 6 hours followed by H2O2 administration. Twelve hours post incubation cell viability was measured using XTT and annexin pi staining. Mitochondrial damage was measured using Seahorse analysis. Gene expression for oxidative stress neuronal bio markers and apoptosis gene was tested by real-time PCR.
In vivo analysis was performed in a mice model. Ten wild type C57Bl6 mice were pretreated with Ficus Benjemina extract for 2 hours followed by ONC induction. H&E and GFAP staining was performed.

Results: Our results demonstrate that Phlomis viscosa Poiret and Ficus benjamina have anti apoptotic, anti oxidative and neuroprotective effect on SH-SY-5Y cells as measured by XTT and FACS analysis for annexin Pi staining. Gene expression analysis showed increased expression of SOD and CAT levels (1.5 and 2.5-fold respectively) as well as the neuronal biomarkers BDNF 3-fold change and AADC 2-fold change.
Specific fraction from Ficuse Benjemina reversed the mitochondrial damage induced by H2O2 as measured by Seahorse analyzer.
Mice Crush model did not show RGC preservation. No reactive gliosis was noted on GFAP staining.

Conclusions: In this study we have shown potential neuroprotective effects of Phlomis viscosa Poiret and Ficus benjamina in an in vitro cell line model and in vivo in a mouse optic nerve crush model. Our results may lay the groundwork for identifying multi-target neuroprotective effects of herbal extracts.

11

SMAD7 miRNA delivery by NPCE exosomes Attenuate Wnt Signaling in Trabecular Meshwork Cells In Vitro.

Elie Beit-Yannai, Saray Tabak, Valeria Feinshtein, Sofia Schreiber-Avissar
Ben-Gurion University of the Negev

Primary open-angle glaucoma is established by the disruption of trabecular meshwork (TM) function. The disruption leads to increased resistance to the aqueous humor (AH), generated by the non-pigmented ciliary epithelium (NPCE). Extracellular vesicles (EVs) participate in the communication between the NPCE and the TM tissue in the ocular drainage system. The potential use of NPCE-derived EVs to deliver siRNA to TM cells has scarcely been explored. NPCE-derived EVs were isolated and loaded with anti-fibrotic (SMAD7) siRNA. EV's structural integrity and siRNA loading efficiency were estimated via electron microscopy and fluorescence. Engineered EVs were added to pre-cultured TM cells and qRT-PCR was used to verify the transfer of selected siRNA to the cells. Western blot analysis was used to evaluate the qualitative effects on Wnt-TGFβ2 proteins' expression. EVs loaded with exogenous siRNA achieved a 53% mRNA knockdown of SMAD7 in TM cells, resulting in a significant elevation in the levels of β-Catenin, pGSK3β, N-Cadherin, K-Cadherin, and TGFβ2 proteins in TM cells. NPCE-derived EVs can be used for efficient siRNA molecule delivery into TM cells, which may prove to be beneficial as a therapeutic target to lower intraocular pressure (IOP).

30

Assessment of the iCare Home 2, a New IOP Self-Measurement Tonometer.

Assaf Kratz (1,2), Rabia Zbidat (1), Kishner Rina (1), Michal Cohen (2), Walid Shalata (1)
(1) Soroka University Medical Center, Beer Sheva, Israel, (2) Faculty of Health Sciences, Ben Gurion University of the Negev, Beer Sheva, Israel

Purpose: To evaluate the accuracy, correlation and analysis of differences of intra-ocular pressure (IOP) measurements between the gold standard Goldmann tonometer and the new self measurement iCare Home 2 tonometer.

Methods: The study population included only glaucoma patients and glaucoma suspects. Patients referred to the glaucoma clinic had their IOP measured by the two instruments. For each patient a central corneal thickness (CCT) measurement was also taken. Eyes with any corneal morbidity were excluded. The measurements by the iCare Home 2 instrument (IOPi) were compared to measurements by the Goldmann tonometer (IOPG).

Results: A total of 135 eyes of 70 patients (40 males) were included in the study. The mean age of the patients was 68.2 years. The mean IOPi and IOPG were 16.5±7.3 mmHg (range 5-55) and 16.3±6.5 mmHg (range 3-56), respectively ($p=0.47$). IOPi and IOPG measurements showed a very strong correlation ($r=0.94$, $p<0.0001$). Bland-Altman plot demonstrated a proportional bias, in which IOPi readings tended to be higher than IOPG in higher IOP values. A positive proportional bias was also demonstrated towards thick corneas, as IOPi measurements tended to be higher than IOPG in thicker corneas.

Conclusions: Mean IOP readings in both instruments were equal and the differences in IOP were generally clinically insignificant. For the majority of eyes, the iCare home could be a reliable tonometer. Nevertheless, The iCare Home 2 tends to yield higher relative IOP measurements than Goldmann tonometer in higher IOP values and in thicker corneas.

43

Association between obesity and intraocular pressure in dogs.

Oren Pe'er, Michal Mazaki-Tovi, Ron Ofri
Koret School of Veterinary Medicine, Hebrew University of Jerusalem, Rehovot, Israel.

Purpose: The prevalence of obesity is increasing in the industrialized world, both in the human and canine populations. We hypothesize that as in humans, obesity in dogs, and its related metabolic disorders, is associated with elevated intraocular pressure (IOP) and thus might serve as potential risk factor for glaucoma. Therefore, our aim was to determine the association between body parameters of obesity and IOP in dogs.

Methods: This was a prospective, randomised, cross-sectional, observational study, conducted at the Hebrew University Veterinary Teaching Hospital (HUVTH). Healthy staff-owned dogs (n=37) admitted to the HUVTH for routine check-up examination were enrolled. Each dog underwent a complete physical and ophthalmic examination. Body condition score (BCS), body fat index (BFI) and body mass index (BMI) were recorded. IOP was measured using rebound tonometry three times in each eye in random order Blood pressure was measured and fasted blood samples were collected. Measurements of IOP were compared between lean-normal (3/9 < BCS < 5/9) and overweight (6/9 < BCS <9/9) dogs using the Student's t test. A general linear model was used to determine potential associations between IOP and BCS, BFI & BMI, including blood pressure, gender, and concentrations of triglycerides and cholesterol as covariates.

Results: IOP (mean ± SD) in lean-normal dogs (n=11, 14.2 ± 2 mm Hg) was significantly (P<0.00001) lower than in overweight dogs (n=26, 22.8 ± 2.4 mm Hg). In addition, IOP was positively associated with BCS (P<0.00001) and BMI (P<0.00001). For every one-point increase in BCS, or 1% increase in BFI and BMI, IOP increased by 1.53 mm Hg (95% Confidence Interval 0.95 - 2.1), 0.13 mm Hg (-0.08 - 0.26) and 0.32 mm Hg (0.21 - 0.42), respectively. Blood cholesterol and triglyceride levels were not correlated with IOP measurements (P=0.30 and P=0.51, respectively). Gender had no significant effect on IOP (P=0.83).

Conclusions: Just as in humans, obesity in dogs was associated with elevated IOP, and thus might serve as an important potential risk factor for glaucoma. Gender, blood pressure, cholesterol and triglycerides were not correlated with IOP.

17 AC

Validation of the cobra high definition meibographer in symptomatic and asymptomatic patients.

Reut Ifrah [1], Lluisa Quevedo [2], Liat Gantz [1]
[1] Department of Optometry and Vision Science, Hadassah Academic College, Jerusalem [2] Faculty of Optics and Optometry, Universitat Politecnica de Catalunya, Terrassa

Purpose: Meibomian gland (MG) loss may be quantified using non-contact infrared meibography, using a scale representing the severity of MG loss, progressing in steps of a minimum of 10%. This study examined the within-subject, inter- examiner, and inter-session repeatability of the Cobra HD meibographer in participants classified according to their Ocular Surface Disease Index questionnaire score (scores > 12 were considered symptomatic).

Methods: The inter-session and inter-examiner experiments had 64 (mean age: 23.3 ±4.7 years, range: 19-43, 14 male, 33 symptomatic) and 60 (mean age: 23.3 ±4.4 years, range: 19-39, 16 male, 30 symptomatic) participants, respectively. Meibography of the upper and lower right lids was measured 3 times, by 2 examiners. Within-subject repeatability was assessed using standard deviations and the within subject standard deviation (Sw). Inter-examiner and inter-session repeatability was assessed using correlation and Bland and Altman (mean difference, and 95% confidence intervals- CI) analyses, and differences between symptomatic and asymptomatic groups was assessed with a 2-factor repeated measures ANOVA.

Results: Mean MG loss in upper and lower lids and Sw was 12.9 ± 9.4%, 5.9 ± 4.1%, 9.5% and 12.3± 7.7%, 6.6± 4.7%, 7.9% for the 2 examiners, respectively. Inter-session measurements were significantly correlated (both R: 0.9) and not significantly different (pupper=0.1,plower=0.7). MG loss in the upper and lower lids was significantly different in both sub-groups (Fdf=1,62=47,p<0.001) without a significant interaction between sub-group and lid location (p=0.5), or session (p=0.6), or all factors (p=0.3). The inter-session Sw and mean difference was 8.5%, 0.85±3.5% (95%CI: -6.0-7.7) and 4.0%, -0.09±1.8% (95%CI: -3.7-3.5), in the upper and lower lids, respectively. Inter-examiner measurements were significantly correlated (Rupper:0.9; Rlower:0.8) and not significantly different (pupper=0.5;plower=0.1), with Sw and mean difference of 2.4% -0.30±3.4% (95%CI: -6.9- 6.3), and 2.1% and -0.70±2.9% (95%CI: -6.5-5.1), respectively. MG loss in the upper and lower lids was significantly different in both sub-groups (Fdf=1,58=45,p<0.001) without a significant interaction between examiner and sub-group (p=0.8) or lid location (p=0.4), or all factors (p=0.7).

Conclusions: The differences in consecutive measurements of each patient, between examiners, and between sessions were < 10%, demonstrating good repeatability and reproducibility. Additionally, no significant differences were found between symptomatic and asymptomatic participants.

61

Identification of murine limbal epithelial stem cell population dynamics, signature and niche.

Ruby Shalom-Feuerstein
Technion Israel Institute of Technology

Purpose: Previously, we combined mouse genetics and vital microscopy imaging to label limbal epithelial stem cells (LSCs) and follow the dynamics of individual stem cells in murine. However, LSC prevalence, heterogeneity and signature is poorly understood. Here, we aimed to identify LSC populations, characterize their genetic signature, regeneration dynamics and regulation by their niche.

Methods: We performed single-cell RNA sequencing, cell populations were identified in silico and validated by in situ hybridization and immunofluorescent staining. Quantitative lineage tracing and nucleotide incorporation assays were performed to follow clonal growth and pattern over time, and limbal niche cells and function were explored in immunodeficient mouse models and by injection of topical immune repressors.

Results: We report the identification of previously undescribed LSC populations that reside in separate and well-defined sub-compartments. In the “outer” limbus, we discovered a primitive widespread population of quiescent LSCs (qLSCs) that uniformly express Krt15/Gpha2/Ifitm3/Cd63 proteins that serve as SC reservoir and in boundary formation. In the “inner” peri-corneal limbus, we identified prevalent active LSCs (aLSCs) that express Krt15-GFP/Atf3/Mt1-2/Socs3 and maintain homeostasis. We propose that these SC populations are abundant, follow stochastic rules and neutral drift dynamics. Notably, we provide evidence that immune and the biomechanical properties of the murine limbus serve as niche for LSCs, regulating undifferentiated state, LSC proliferation and wound response.

Conclusion: This study provides a useful atlas that uncovers the main corneal epithelial cell populations, capturing the signature and the niche of quiescent and activated LSC states. These data open new research avenues for studying the mechanisms of cell proliferation and differentiation as well as the applications of LSCs in regenerative medicine.

90

Pupillary dilation and axial length in patients with high myopia.

Rita Zlatkin (1), Jennifer J Bu (2), Rebecca R Lian (2), Jenny Q Hu (2), Helena E Gali (2), Evan Walker (2), Eitan Livny (1,3), Irit Bahar (1,3), Natalie A Afshari (2), Ruti Sella (1,3)
(1) Department of Ophthalmology, Rabin Medical Center, Petah Tikva, Israel (2) Shiley Eye Institute, Viterbi Family Department of Ophthalmology, University of California San Diego, La Jolla, CA, United States (3) Sackler faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Purposes: To determine how high myopia impacts pharmacological pupillary dilation and to evaluate the relationship between the rate and extent of pharmacological pupillary dilation and axial length (AL).

Methods: Patients were recruited from Shiley Eye Institute at the University of California San Diego, and grouped into myopes, defined as one or both eyes having a spherical equivalent (SE) refraction greater than -6 diopters (D) or AL>26mm, and controls (SE less than -6 D and AL<26mm). Inclusion criteria were: phakic, ages 21 to 100, and planning to get pharmacological pupillary dilation as part of their eye exam. Exclusion criteria were current use of eye drops other than artificial tears, prior intraocular or refractive surgery, iris or angle abnormalities, history of eye inflammation, previous adverse reaction to dilating drops, or diabetes. Dilation was achieved with 1 drop of tropicamide 1% and phenylephrine 2.5% in each eye. Pupil size was measured utilizing a Colvard pupillometer and the Cirrus HD-OCT (manual measurement on anterior segment scans) at full and dim light prior to dilation, then 15 and 30 minutes after dilation. AL and keratometry were measured using the Zeiss IOLMaster 700. Two-sample t-test and generalized estimating equations (GEE) models were performed using R software.

Results: 34 patients (68 eyes) participated in the study. The average age was 49 years and 70.5% were females. 16 Patients were high myopes (average SE -7.14 D, range -4.75 to -11) and 18 were controls (average -1.06 D, range +2 to -5.5). Fully dilated pupil size at 30 minutes was significantly correlated with both SE refraction ($r=-0.59$, $p<0.001$) and AL ($r=0.44$, $p<0.001$), indicating eyes with higher myopia, as measured by both AL and refractive error, dilated more. When grouped by AL, 16 eyes had AL>26mm (range 26.03-28.58mm) and 48 eyes had AL<26mm (range 22.77-25.99mm), with eyes>26mm dilating to a greater extent than eyes<26mm at both 15 ($p=.05$) and 30 minutes ($p<.0005$).

Conclusions: Highly myopic patients dilate to a larger pupillary size compared to other patients. The positive correlation between dilation and axial length may be explained by the difference in elasticity of the sclera and thickness of the iris in highly myopic eyes. Predicting dilation based on extent of myopia could facilitate intraocular surgery planning and reduce clinic wait times for myopic patients.

93,AC

Identification of the role of immune cells in controlling limbal epithelial stem cells.
Shira Hadad-Porat, Ruby Shalom-Feuerstein
Department of Genetics and Developmental Biology, Technion, Haifa

Purpose: The limbal stem cell (LSC) microenvironment, “the niche”, is believed to influence LSC function. However, our knowledge on limbal niche components and mechanisms of niche – LSC regulation is poor. Here, we aimed to characterize the sub-populations of immune cell in the limbus niche and to uncover their potential function as niche cells.

Methods: Immunostaining of limbal/corneal wholemount and tissue sections was performed using antibodies against LSC and immune cell specific markers. LSC proliferation, marker expression and wound healing response was examined following inhibition of the immune cell activity and in immunodeficient mice.

Results: We identified significant numbers of dendritic cells and T cell populations including γδ and regulatory T cells in the outer LSC niche. Expression of outer LSC markers (GPHA2/CD63) was significantly affected by inhibition or absence of immune cells. Delayed corneal regeneration was observed in immunodeficient mice.

Conclusion: This study uncovers a new role for immune cells as LSC niche cells. Future studies are required in order to identify the mechanisms by which specific immune cell populations influence LSC function.

107 AC

Gadolinium detection in tears of humans and mice.

Mohammed Darawshe (1), Olga Girshevitz (2), Yoav Vardizer (3), Alon Zahavi (4,5,6), Nitza Goldenberg-Cohen (1,3)
(1) The Krieger Eye Research Laboratory, Bruce and Ruth Faculty of Medicine, Technion Institute of Technology, Haifa, Israel (2) Institute of Nanotechnology & Advanced Materials, Bar-Ilan University, Ramat Gan, Israel (3) Ophthalmology Department, Bnai-Zion Medical Center, Haifa, Israel (4) Ophthalmology Department, Rabin Medical Center, Petach Tikva, Israel (5) Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel (6) Laboratory of Eye Research, Felsenstein Medical Research Center, Petach Tikva, Israel

Purpose:
Gadolinium (Gd)-based contrast agent deposition disease (GDD) in the brain may occur in 0.03% of patients undergoing neuroimaging. This study aimed to investigate the applicability of tears as biomarkers for individuals at risk for Gd retention in the brain using Particle Induced X-ray Emission (PIXE).

Methods:
Ten C57BI6 mice and 17 humans undergoing MRI were investigated in this study. The recommended human dosage of macrocyclic Gd administered as an MRI contrast agent is 0.2 ml/kg. In mice, a single IV injection of 0.12 ml/kg Gd (Dotarem, 0.5 mmol/ml, Guerbet, Villepinte, France) that is 21.4 times more than the human dosage, was followed by euthanization within 2.5 hours. All blood and tears samples were collected up to 2.5 hours post Gd intravenous injection. Tears and blood samples were collected on Schirmer paper filter and elemental composition was analyzed by PIXE.

Results:
Blood samples of mice and humans were positive for Gd. However, the concentration of Gd in the human blood was minimal, though within the sensitivity of the analytical method. In addition, one of the human participants demonstrates the presence of Gd also in his tears (1 from 17) 45 minutes post injection; likewise, one of 10 samples of tears was positive in mice. This sample was taken 2 hours post injection.

Conclusions:
We were able to detect Gd in the blood of all participants, humans and mice. In the tears, 1/17 and 1/10 samples were positive, respectively, following a single IV injection up to 2.5 hours from the injection. This is the first report of Gd detection in human or animal tears, which was performed by PIXE analysis which is highly sensitive and uniquely suitable for small sample volumes. We suggest tears may be used as a biomarker to predict subjects at risk for Gd retention in the brain.

110

Do mineral dietary supplements affect the levels of trace elements in tears of athletes?

Tal Zobok (1), Yulia Sheinfeld (2), Yoav Vardizer (2), Alon Zahavi (3,4,5), Olga Girshevitz (6), Nitza Goldenberg-Cohen (2,7)
(1) Hadassah Hebrew University, Jerusalem (2) Ophthalmology Department, Bnai-Zion Medical Center, Haifa (3) Ophthalmology Department, Rabin Medical Center, Petach Tikva (4) Tel Aviv University, Tel Aviv (5) Laboratory of Eye Research, Felsenstein Medical Research Center, Petach Tikva (6) Faculty of Engineering and Institute of Nanotechnology & Advanced Materials, Bar-Ilan University, Ramat Gan (7) The Krieger Eye Research Laboratory, Technion Institute of Technology, Haifa

Purpose:
Physical activity has been shown to be associated with health-related quality of life. Participation in sports during leisure time is associated with change in diet and intake of nutritional supplements. Extreme and competitive athletes, as well as amateurs, use dietary supplements to improve their performance, build muscle, and improve their stability.
The associations between different sport activities and levels of electrolytes has been partially investigated, but the association with tear electrolytes levels is yet to be explored. In this study we aim to examine if tear composition is affected by intake of nutritional supplements by athletes, exercise intensity, or whether the activity is isometric or aerobic.

Methods:
In the study, 80 athletes were recruited from three fitness centers in Israel. Forty athletes trained at high intensity in Tel Aviv (boxing and CrossFit) and 40 training at moderate intensity in Haifa (studio-based exercise). Each participant was given a questionnaire regarding exercise intensity and dietary supplements. The tears were collected using Schirmer filter paper and analyzed by Particle Induced X-ray Emission (PIXE). Analysis was performed between the groups per gender, effort and supplement intake.

Results:
Mean tear magnesium levels for men and women were 18.87 µg/L and 62.07 µg/L, respectively. Mean sodium levels were 3343.5 µg/L and 2701.26 µg/L, respectively. Subjects practicing high intensity workouts (boxing or CrossFit) had iron levels of 234.18 µg/L in tears as compared to 11.12 µg/L in tears of studio trainers.

Conclusions:
PIXE results demonstrate significant differences in the composition of the metallic trace elements in tears of men and women, especially when highly intense effort was involved. Moreover, the correlation between composition of the tears and sport activity are negligible except iron. Surprisingly, magnesium intake did not increase the magnesium levels in tears. Despite gender related differences, nutrition-related tears levels were not affected by supplement intake.

116,AC

Uncovering mechanisms of corneal healing following catastrophic limbal stem cell loss.

Shalini Dimri [1] and Ruby Shalom-Feuerstein [1]
[1] Department of Genetics & Developmental Biology, The Rappaport Faculty of Medicine & Research Institute, Technion - Israel Institute of Technology, Haifa, Israel

Purpose: Recently, we discovered that the murine limbus contains two discrete population of limbal stem cells (LSCs). Interestingly, we reported that upon total surgical limbal epithelial removal, peripheral corneal committed cells rapidly migrate to heal the denuded limbus and undergo reprogramming into LSC-like cells. The purpose of this study is to explore whether the two LSC populations are recovered and if LSC-like cells can heal the injured corneal epithelium.

Methods: We used K15-GFP transgenic (GFP under K15 promoter to label active LSCs) mice to monitor LSC recovery. Limbal epithelium removal was performed using Algerbrush in live mice under binocular microscope. K15-GFP recovery was recorded at different time points and on day 30, corneas were subjected to wholemount staining for quiescent (Gpha2, IFITM3) and active (K15-GFP) LSC markers. For wound healing assay, the central corneal epithelium of mice that recovered from limbal epithelial ablation (day 30 post limbal depletion) was injured using Algerbrush and after 30 days of recovery period, a second debridement was repeated. Corneal wound closure by native LSCs or LSC-like cells was followed using Fluorescein dye staining and imaging using cobalt blue filter under binocular microscope.

Results: We discovered that the two LSC-like compartments were seemingly re-established, namely, the inner limbus that host active LSC-like cells (K15-GFP+), and the outer limbus that consists of quiescent LSC-like cells (IFITM3+ and Gpha2+). Remarkably, the LSC-like cells could successfully regenerate the injured corneal epithelium. Moreover, the LSC-like cells exhibited a significantly faster wound healing response, as compared to the wound closure of corneas with native limbus. Additionally, the LSC-like cells also efficiently repaired consecutive corneal injuries maintaining higher scores of corneal transparency for up to 60 days post damage.

Conclusion: Following total LSC loss, corneal committed cells successfully restore the limbus and reorganize into normally appearing limbal subcompartment of outer and inner limbus. The dedifferentiated LSC-like cells behave as bona fide LSC in terms of marker expression, corneal maintenance in homeostasis and possess a superior wound healing ability.

119,AC

Pathophysiology and rescue of P63-related limbal stem cell deficiency.
Waseem Nasser (1), Shalini Dimri (1), Anna Altshuler (1), Lior Strinkovsky (2), Swarnabh Bhattachariya (3), Aya Amitai-Lange (1), Caterina Missero (4), Daniel Aberdam (5), Colin Willoughby (6), Yonatan Savir (2) and Ruby Shalom-Feuerstein (1)
(1) Department of Genetics and Developmental Biology, Technion, Haifa, Israel; (2) Department of Physiology, Biophysics and System Biology, Faculty of Medicine, Technion, Haifa, Israel; (3) Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA, US; (4) CEINGE Biotecnologie Avanzate, Napoli, Italy; (5) INSERM U976, Paris, France; (6) Department of Eye and Vision Science, Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, United Kingdom

Purpose: To generate an in-vivo mouse model for genetically induced LSCD, characterize its phenotype relevance to human disease, and examine new therapeutic approaches.

Methods: We discovered L514F mutation in P63 gene leads to LSCD in humans. To gain more insight into the disease progression, we generated a new conditional P63L514F mouse model that explicitly expresses the mutation in limbal and corneal cells. To test the relevance of our new mouse model to human disease, we first examined its eye and corneal phenotype at different ages by brightfield microscopy. We performed H&E staining to examine the corneal histology and RNA-sequencing of corneal epithelium to identify the altered pathways in the mutant. Immunofluorescent-staining (IF) was conducted to explore the expression of stemness and differentiation markers. To examine the impact of L514F mutation on limbal stem cell dynamics, proliferative capacity and clonal growth patterns over time, we performed quantitative lineage tracing and nucleotide incorporation assays. Finally, we utilized our new mouse model to examine the therapeutic potential of PRIMA-1MET in vivo.

Results: P63L514F/+ mice displayed multiple eye abnormalities reminiscent of defects found in patients who carry the same mutation, hallmarked by neovascularization and loss of corneal transparency. Furthermore, mutant mice showed impaired wound repair. RNAseq analysis revealed enrichment of mucus secretion, vascularization, and immune response pathways. Inline, histological analysis showed thickening of the corneal epithelium and the presence of goblet cells. IF stainings showed altered expression of limbal, conjunctival markers, and enrichment of immune cells in the cornea. In addition, mutated corneal cells displayed significantly higher proliferative capacity. Analysis of the properties of confetti labeled mutant clones displayed abnormal size, orientation, and survival. PRIMA-1MET could substantially prevent the development of the LSCD phenotype in homeostasis and alleviate its aggravation following injury.

Conclusions: Altogether, we propose that P63 plays a crucial role in regulating corneal morphogenesis and that P63-related pathology involves a developmental failure. In addition, this study demonstrates that P63 controls limbal stem/progenitor cell state while mutations in P63 disrupt epithelial homeostasis, leading to loss of corneal transparency and blindness. Furthermore, PRIMA-1MET showed promising therapeutic potential for human disease."
122,AC

Changes in tears or sweat elements levels before and after physical activity in athletes may predict dehydration.

Yulia Sheinfeld (1), Tal Zobok (2), Yoav Vardizer (1), Alon Zahavi (3,4,5), Nahum Shabi (7), Olga Girshevitz (7), Yael Nisgav (5), Nitza Goldenberg-Cohen (1,6)
(1) Ophthalmology Department, Bnai-Zion Medical Center, Haifa (2) Hadassah Hebrew Medical School, Jerusalem (3) Rabin Medical Center, Sackler Faculty of medicine, Tel Aviv University, Tel Aviv (4) Sackler School of Medicine, Tel Aviv University, Tel Aviv (5) Laboratory of Eye Research, Felsenstein Medical Research Center, Petach Tikva (6) Krieger Eye Research Laboratory, Ruth and Bruce Rappaport Faculty of medicine, Technion, Hafia (7) Institute of Nanotechnology & Advanced Materials, Bar-Ilan University, Ramat Gan

Purpose:
Accurate evaluation of training athletes hydration status is paramount for maintaining homeostasis and health. Hydration estimates are commonly based on sampling blood or urine, while the potential of tears or sweat was not studied. The broad aim of the study was to evaluate the potential of tears or sweat to serve as biomarkers for hydration status influenced by fluid restriction or physical activity.

Methods:
The study included 2 groups of athletes: 10 subjects regularly training at moderate intensity in fitness centers, provided tears samples prior to and following exercise and 10 high intensity training marathon runners who provided tears and sweat samples following exercise. Each participant filled a questionnaire, including demographic information, effort type, duration and dietary habits. Tears and sweat samples were collected using Schirmer filter paper and analyzes by Particle Induced X-ray Emission (PIXE).

Results:
Elemental analysis by PIXE showed a significant decrease in cupper levels, and a mild decrease in aluminum and calcium levels following physical exercise. A significant increase was noted in iron levels, with a mild increase in silicone levels. Mean Na and K did not change in the tears before and after effort.

Conclusions:
The novel approach to analyze tears and sweat using PIXE quantitative method make possible to detect a subject prone to dehydration during extreme effort. This may prevent and guide training log in military activities in the future. The using of Schirmer paper filter simplifies the collection process of the ultra small amount of samples and may spare blood or urine tests for diagnosis of dehydration.