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

PROGRAM & ABSTRACTS
39th Annual Meeting

Kfar Maccabiah
6th-7th March, 2019

תכנית ותקצירים
הכינוס השנתי ה-39
כפר המכבייה

6-7 במרץ, 2019

עריכת התוכנית: דר׳ מיכל קרמר, דר׳ יגאל רוטנשטרייך, דר׳ יוסי מנדל
פרופ׳ איתי חוברס

כלים שלובים
כנסים, ארגון והפקות בע"מ

הפקת הכינוס:

עיצוב והבאה לדפוס: דבורה מרקס או

ISRAELI SOCIETY FOR VISION AND EYE RESEARCH

The 39th Annual Meeting, March 6-7, 2019

Program at a glance

Wednesday, March 06 , 2019

Session	Location	Time
Coffee & Exhibition	Exhibition Hall	08:00 – 08:30
Opening remarks	Rayman Center	08:30 – 08:35
Rapid fire I	Rayman Center	08:35 – 09:25
Neuro-ophthalmology and Visual function	Rayman Center	09:25 – 10:30
Coffee & Exhibition	Exhibition Hall	10:30 – 11:00
Retina I	Rayman Center	11:00 – 12:10
Keynote speaker - Jeffrey Goldberg	Rayman Center	12:10 – 12:50
Lunch break	Dining Room	12:50 – 13:50
Keynote speaker – Jeffrey Goldberg	Rayman Center	13:50 – 14:30
Cornea	Rayman Center	14:30 – 15:25
Coffee & Exhibition	Exhibition Hall	15:25 – 16:00
Imaging	Rayman Center	16:00 – 17:00

Thursday, March 07 , 2019

Coffee & Exhibition	Exhibition Hall	08:00 – 08:30
Retina II	Rayman Center	08:30 – 09:40
Anterior segment	Rayman Center	09:40 – 10:35
Coffee & Exhibition	Exhibition Hall	10:35 – 11:10
Awards & ISVER update	Rayman Center	11:10 – 11:30
Retina III	Rayman Center	11:30 – 12:35
Lunch break	Dining Room	12:35 – 13:35
Start-up and innovation	Rayman Center	13:35 - 15:05
Coffee & Exhibition	Exhibition Hall	15:05 – 15:40
Rapid fire II	Rayman Center	15:40 – 16:45
Concluding remarks	Rayman Center	16:45 – 17:00

יושבי-ראש של האגודה הישראלית לחקר העין והראייה

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Prof. Dror Sharon	**2015-2018**	**פרופ' דרור שרון**
Prof. Itay Chowers	**2019**	**פרופ' איתי חוברס**

חברי ועד האגודה הישראלית לחקר העין והראייה
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ARVO CHAPTER AFFILIATE

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

הכנס ה-39 של האגודה הישראלית לחקר העין והראיה
בחסות:

מרצים המקבלים השנה פרס על עבודות שהוצגו בכנס השנה שעברה (הכנס ה-38, 8-7 במרץ 2018)

Award Recipients for the Best Papers Presented at the Previous Annual Meeting (the 38th Meeting, March 7th-8th 2018)

מלגות נסיעה ל- ARVO ניתנות בעזרת מענקים שנתרמו באדיבות:
משפחת מרין לזכרו של פרופ' שאול מרין ז"ל
משפחת דברת לזכרה של פרופ' אהובה דברת ז"ל
משפחת מנדלס לזכרם של מיכה שוקן ז״ל ושמעון מנדלס ז״ל
באדיבות עמותת "לראות".

Nano-drops for correcting refractive errors

David Smadja (1,2), Moshe Lellouche (1), Mark Krauthammer (3), Yifat Harel (1), Adi Abulafia (2), David Zadok (2), Zeev Zalevsky (1)
(1) Bar-Ilan University, Institute of Nanotechnology and Advanced Materials, Ramat Gan; (2) Shaare Zedek Medical Center, Ophthalmology Department, Jerusalem, (3) Ophthalmology Department, Tel Aviv Sourasky Medical Center

Electrophysiological characterization of Human Embryonic Stem cells-derived photoreceptor precursors

Revital Schick (1), Nairouz Farah (1), Amos Markos (1), Yossi Mandel (1,2)
(1) Mina and Everard Goodman Faculty of Life Sciences, (2) Optometry and Visual Science ,Faculty of Life Science. Bar-Ilan University

Azithromycin as a possible neuroprotectitive drug following optic nerve crush induction in mice

Ofira Zloto (1,2), Moran Fridman (2,3), Shirel Weiss (2,3), Nitza Goldenberg-Cohen (3,4,5)
(1) Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, (2) Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, (3) Krieger Eye Research Laboratory, Felsenstein Medical Research Center, Petach Tikva, (4) Department of Ophthalmology, Bnai Zion Medical Center, Haifa, (5) The Ruth and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa

Ataluren-mediated read-through of a nonsense mutation in the FAM161A gene which causes retinitis pigmentosa

Avigail Beryozkin (1), Ananya Samanta (2), Samer Khateb (1), Eyal Banin (1), Dror Sharon (1), Uwe Wolfrum (2), Kerstin Nagel-Wolfrum (2)
(1) Ophthalmology Department, Hadassah-Hebrew University Medical Center, Jerusalem, (2) Inst. of Molecular Physiology, Johannes-Gutenberg University of Mainz, Germany

מרצים המקבלים השנה פרס על עבודות שהוצגו בכנס השנה שעברה (הכנס ה-38, 7-8 במרץ 2018)

Award Recipients for the Best Papers Presented at the Previous Annual Meeting (the 38th Meeting, March 7th-8th 2018)

Clinical and genetic characterization of Pseudoxanthoma Elasticum patients

Iyar Sheps (1), Chen Weiner (2), Nadav Shoshany (1), Eran Pras (1)
(1) Ophthalmology Department, Assaf Harofe Medical Center, Zeriffin, affiliated to Tel Aviv University (2) Matlow's Ophthalmogenetic laboratory, Assaf Harofe Medical Center, Zeriffin

Worldwide Carrier Frequency Analysis of Mutations Causing Autosomal Recessive Inherited Retinal Diseases

Mor Hanany, Segev Meyer, Dror Sharon
Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem

Genetic diagnosis of Stickler syndrome caused by deep intronic mutation in COL2A1 in 10 family members

Shirel Rossenwasser Weiss (1,2), Naama Orenstein (3), Nitza Goldenberg-Cohen (1,2,5)
(1) The Krieger Eye Research Laboratory, Felsenstein Medical Research Center, Tel Aviv University, (2) Sackler School of Medicine, Tel Aviv University, (3) Pediatric Genetics, Schneider Children Medical Center of Israel, Petah Tikwa, (4) Rappaport Faculty of Medicine, Technion, Haifa, (5) Ophthalmology Department, Bnai Zion Medical Center, Haifa

Effect of Histone Deacetylase Inhibitor (AN-7) on Vascular Permeability in the Retina

Elinor Megiddo-Barnir (1), Mor Dahbash (2,3), Yael Nisgav (2), Dov Weinberger (1,2,3), Ada Rephaeli (3,4), Tami Livnat (2,3,5)
(1) Department of Ophthalmology, Rabin Medical Center, Petah Tikva, (2) Laboratory of Eye Research, Felsenstein Medical Research Center, Rabin Medical Center, Petah Tikva, (3) Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, (4) Laboratory of Experimental Pharmacology and Oncology, Felsenstein Medical Research Center, Rabin Medical Center, Petah Tikva, (5) National Hemophilia Center, Sheba Medical Center, Tel Hashomer

Keynote speaker ISVER 2019

Dr. Jeffrey Goldberg

Inaugural speaker of the

Dr. Stephen and Susan Fichman

Annual Lecture in Clinical Ophthalmology

Wednesday March 6th 2019

12:10

Retinal Ganglion Cell Differentiation and Transplantation

13:50

Glaucoma Biomarkers and Neuroprotection: Clinical Trials

Dr. Jeffrey Goldberg is Professor and Chairman of Ophthalmology and Director of the Byers Eye Institute at Stanford University. His clinical effort is focused on patients in need of medical or surgical intervention for glaucoma and other retinal and optic nerve diseases, as well as cataract. His research is directed at neuroprotection and regeneration of retinal ganglion cells and the optic nerve, a major unmet need in glaucoma and other optic neuropathies, and his laboratory is developing novel molecular, stem cell and nanotherapeutics approaches for eye repair.

Dr. Goldberg received his B.S. magna cum laude from Yale University, and his M.D. and Ph.D. from Stanford University where he made significant discoveries about the failure of optic nerve regeneration. He did his clinical training in ophthalmology and then in glaucoma at the Bascom Palmer Eye Institute, and was awarded a fellowship from the Heed Foundation. He was named the 2010 Scientist of the Year by the Hope For Vision foundation, and received the Cogan award from the Association for Research in Vision and Ophthalmology in 2012. He was elected in 2010 to the American Society of Clinical Investigation, an honorary society of physician scientists. He directs an NIH-funded research laboratory and is one of the scientists funded by the National Eye Institute's Audacious Goals Initiative. In addition, he has developed significant expertise with implementing FDA clinical trials for optic nerve neuroprotection and regeneration. His goal is to translate scientific discoveries to patient therapies.

Wednesday, March 6th 2019

Coffee and Exhibition 8:00 – 8:30

Opening remarks 8:30 – 8:35
Prof. Itay Chowers

Rapid fire I 8:35 – 9:25

Moderators:

Irit Bahar and Hani Levkovitch-Verbin

1 8:35 AC

Corneal topography followed pars plana vitrectomy and transscleral 4-point suture fixation of Akreos AO60 intraocular lens (IOL)

Rabeea H.Daood (1,2) , David Barash (1,2) , Yoav Nahum (1,2) , Assaf Dotan (1,2)
(1) Department of Ophthalmology, Rabin medical center, Beilinson Campus (2) Sackler Medical School , Tel Aviv

2 8:38 AC

Postoperative Position Effect on DSAEK graft Adhesion

Margarita Safir, Biana Dubinsky-Pertzov, Lior Or, Assaf Rozenberg, Eran Pras, Adi Einan-Lifshitz, Yakov Goldich
Assaf Harofeh Medical Center

3 8:41 AC

Punching DMEK graft on a contact lens versus punching the graft on the donor stroma: preserving more endothelial cells at the graft margin

Asaf Achiron, Yoav Nahum, Irit Bahar, Eitan Livny
Department of Ophthalmology, Rabin Medical Center and the Sackler School of Medicine, Tel Aviv University

4 8:44 AC

Evaluation of the neuroprotective effect of Azithromycin in a mouse glaucoma model

Alon Zahavi (1,2), Shirel Weiss (2,3), Moran Fridman (2,3), Tal Sela (4), Yaniv Barkana (5), Ron Ofri (6,7), and Nitza Goldenberg-Cohen (3,8,9)
(1) Department of Ophthalmology, Rabin Medical Center, (2) Sackler Faculty of Medicine, Tel Aviv University, (3) Krieger Eye Research Laboratory, Felsenstein Medical Research Center, Petach Tikva, (4) Israel Defense Forces, (5) Teleglaucoma Unit, Baruch Padeh Medical Center, (6) Faculty of agriculture, Rehovot, (7) The Hebrew University, (8) Department of Ophthalmology, Bnai Zion Medical Center, (9) The Ruth and Bruce Rappaport Faculty of Medicine, Technion

5 8:47 AC

Laser peripheral iridotomy with and without anti-inflammatory drops after

Ari Leshno, Reut Zinger, Hila Goldberg, Mordechai Goldenfeld, Yair Rubinstein and Hani Levkovitch-Verbin
Goldschleger Eye Institute, Sheba Medical Center, Tel-Hashomer; Sackler Faculty of Medicine, Tel-Aviv University, Tel-Hashomer

6 8:50

Marked Variability in Visual Field Interpretation Among Israel Neuro-Ophthalmologists

Josh Kruger
Department of Ophthalmology, Hadassah Medical Center

7 8:53

Patients with progressive NAION have no distinguishing clinical characteristics

Omer Y. Bialer (1,2), Hadas Stiebel-Kalish (1,2)
(1) Neuro-Ophthalmology Unit, Ophthalmology Department, Rabin Medical Center, (2) Sackler School of Medicine, Tel-Aviv University

8 8:56 AC

Technically Reliable, but Falsely Positive Automated Visual Fields – A Report of 7 Cases from a Neuro-Ophthalmology Practice

Pablo Galarza (1), Elchanan Parnasa (2), Noah Guttman (1), Joshua M. Kruger(1)
(1) Department of Ophthalmology, Hadassah Medical Center, Jerusalem (2) Hebrew University-Hadassah School of Medicine

9 8:59

Osseous Metaplasia (Cataracta Ossea) of Lens Remnants in Chronic Uveitis

Amir Hadayer (1), Ahmet Ozkok (2), Henry J Kaplan (2), Shlomit Schaal (3)
(1) Rabin Medical Center , (2) University of Louisville, KY, USA, (3) UMASS Medical School, MA, USA

10 9:02

Mutations in two different genes cause a complex phenotype of high myopia and corneal dystrophy in the same family

Ohad Wormser (1), Zach Ashkenazy (2), Yonatan Perez (1), Tova Lifshitz (2), Ohad S. Birk* (1,3) and Libe Gradstein* (2)*
(1) The Morris Kahn Laboratory of Human Genetics at the National Institute of Biotechnology in the Negev, Ben-Gurion University, (2) Department of Ophthalmology, Soroka Medical Center and Clalit Health Services, Faculty of Health Sciences, Ben-Gurion University (3) Genetics Institute, Soroka Medical Center, Beer Sheva] *Equal contribution

11 9:05

Case Series of Bilateral Idiopathic Multiple Pigment Epithelial Detachments

Boris Rosin and Eyal Banin
Center for Retinal and Macular Degenerations, Department of Ophthalmology
Hadassah-Hebrew University Medical Center,

12 9:08 AC

The Effect of Q Score on Macular Thickness and Volume and Peripapillary RNFL Thickness Measurements Using OCT Spectralis

Assaf Gershoni (1), Igor Vainer (2), Raviv Allon (2), Roy Yavnieli (3), Yinon Shapira (2), Michael Mimouni (2), Ori Segal (3,4)
(1) Department of Ophthalmology, Rabin Medical Center, (2) Department of Ophthalmology, Rambam Health Care Campus, (3) Department of Ophthalmology, Meir Medical Center, (4) Sackler School of Medicine, Tel Aviv University

13 9:11 AC

Recombinant Adeno-Associated Virus [rAAV9-7m8] Injected in the Peripheral Subretinal Space Spreads Beyond the Bleb Borders in Sheep

Maya Ross (1), Eyal Banin (2), Deniz Dalkara (3), Melissa Desrosiers (3), Alexey Obolensky (2), Raaya Ezra-Elia (1), Hen Honig (4), Esther Yamin (2) Alexander Rosov (4), Hay Dvir (4), Edward Averbukh (2), Elisha Gootwine (4), Ron Ofri (1)
(1) Koret School of Veterinary Medicine, Hebrew University of Jerusalem, Rehovot, (2) Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, (3) Institute de la Vision, Paris, France, (4) ARO, The Volcani Center, Rishon LeZion.

14 9:14

The Effect of Reduced Contrast Sensitivity on Color Vision Testing

Gad Dotan (1), Lior Lipsky (2)
(1) Ophthalmology Unit, Schneider Children's Medical Center of Israel, Petah Tikva, (2) Ophthalmology Department, Tel Aviv Medical Center

15 9:17 **Familial encephalopathy and ophthalmoplegia responsive to thiamine treatment**

Libe Gradstein (1), Ohad Wormser (2), Marina Eskin-Schwartz (3), Ilan Shelef (4), Iris Noyman (5), Yair Sedaka (5), Zamir Shorer (5) and Ohad S. Birk (2,3)

(1) Department of Ophthalmology, Soroka Medical Center and Clalit Health Services, Faculty of Health Sciences, Ben-Gurion University, (2) The Morris Kahn Laboratory of Human Genetics at the National Institute of Biotechnology in the Negev and Faculty of Health Sciences, Ben-Gurion University, (3) Genetics Institute, Soroka University Medical Center, (4) Department of Imaging, Soroka University Medical Center, (5) Pediatric Neurology Unit, Soroka Medical Center and Faculty of Health Sciences, Ben-Gurion University.

9:20 **Discussion**

Neuro-ophthalmlogy and Visual perception

9:25– 10:30

Moderators:

Hadas Stiebel-Kalish and Hadas Newman

16 9:25 **Optic nerve crush causes increased damage to diabetic mice**

Tamar Azrad Lebobitz (1,2), Moran Friedman (1,2), Shirel Weiss (1,2), Nitza Goldenberg-Cohen (1,3,4)

(1) The Krieger Eye Research Laboratory, FMRC, Rabin Campus (2) Sackler School of Medicine, Tel Aviv University, (3) Ophthalmology Department, Bnai Zion Medical Center, (4) The Ruth and Bruce Rappaport Faculty of Medicine, Technion Institute of Technology

17 9:32 AC **Glial fibrillary acidic protein (GFAP) and Aquaporin 4 (AQP4) expression are increased in the optic nerves of experimental autoimmune encephalomyelitis (EAE) induced NOD mice**

Judith Brody (1,2)*, Katia Pozyuchenko (3)* , Katie Lazdon(3), Yael Nisgav (4), Dan Frenkel (3,5), Hadas Stiebel-Kalish (1,2).

(1) Ophthalmology Department, Rabin Medical Center, Petach Tikva (2) Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv (3) Department of Neurobiology George S. Wise Faculty of Life Sciences, Tel Aviv University, Tel Aviv (4) Laboratory of Eye research Felsenstein Medical Research Center, Rabin Medical Center, Petah Tikva, (5) Sagol School of Neuroscience, Tel Aviv University, Tel Avi

18 9:39
An optimized treatment for ocular organophosphate nerve agent insult
Ariel Gore (1), Uri Nili (1), Ettie Grauer (1) and Inbal Egoz (1)
Dept. Of Pharmacology, Israel Institute for Biological Research, Ness-Ziona

19 9:46 AC
A Novel Method for Automated Visual Field Testing on Eyes with Severe Central Vision
Binyamin Stern, Yaara Forer, Idit Gabay, Josh Kruger
Department of Ophthalmology, Hadassah Medical Center

20 9:53
Sensorimotor information and negative BOLD in the deprived visual cortex of congenitally blind
Or Yizhar (1) and Amir Amedi (1,2)
(1) The Hebrew University of Jerusalem, (2) UPMC Univ Paris 06, Paris, France

21 10:00 AC
The Effect of Irrelevant Environmental Noise on the Performance of Visual-to-Auditory Sensory Substitution Devices Used by Blind Adults
Galit Buchs (1), Benedetta Heimler (2,3) and Amir Amedi (1,2,3,4)
(1) Department of Cognitive Science, Faculty of Humanities, Hebrew University of Jerusalem, Hadassah Ein-Kerem, (2) The Edmond and Lily Safra Center for Brain Research, Hebrew University of Jerusalem, Hadassah Ein-Kerem, (3) Department of Medical Neurobiology, Institute for Medical Research Israel-Canada, Faculty of Medicine, Hebrew University of Jerusalem, Hadassah Ein-Kerem, (4) Sorbonne Universités UPMC Univ Paris 06, Institut de la Vision Paris, France

22 10:07 AC
Inter-ocular Changes in Visual Temporal Resolution Alters Binocular Summation
Auria Eisen-Enosh (1), Nairouz Farah (1), Zvia Burgansky-Eliash (2,3), Uri Polat (1), Yossi Mandel (1,4)
(1) School of Optometry and Vision Science, Bar-Ilan University (2) E. Wolfson Medical Center, Holon (3)Sackler School of Medicine, Tel-Aviv University (4) Institute for Nanotechnology and Advanced Materials (BINA), Bar-Ilan University

22 a. 10:14
Eye tracking control in visual prostheses
Avi Caspi (1-3)
(1) Department of Electronic Engineering, Jerusalem College of Technology, (2) Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, MD, USA. (3) Second Sight Medical Products, Inc. Sylmar, CA, USA.

10:21 **Discussion**

Coffee and breakfast

10:30– 11:00

Retina I

11:00– 12:10

Moderators:

Shahar Frenkel and Tamar Ben-Yosef

23
11:00
AC

Study the roles in eye development of BAF155 and BAF170 - the subunits of the chromatin remodeling Swi/Snf complex

Shai Ovadia and Ruth Ashery Padan
Tel Aviv University, Sackler Faculty of Medicine

24
11:07
AC

The role of the LIM homeodomain 2 (Lhx2) in differentiation of the Mammalian Retinal-Pigmented Epithelium (RPE)

Ahuvit David (1), Mazal Cohen (1), Maria Idelson (2), Benjamin Reubinoff (2), Ran Elkon (1) and Ruth Ashery-Padan (1).
(1) Department of Human Molecular Genetics and Biochemistry, Sackler Faculty of Medicine, Tel-Aviv University (2) The Hadassah Human Embryonic Stem Cell Research Center, The Goldyne Savad Institute of Gene Therapy & Department of Gynecology

25
11:14
AC

Carbon nano tubes as a scaffold for hESC differentiation into photoreceptor precursor cells

Yoav Chemla (1),Efrat Shawat (2), Amos Markus (1), Yulia Kostikov (2) Daniel Nessim (2), Yossi Mandel (1)
(1) Faculty of life Sciences, Optometry Track and Bar-Ilan Institute for nanotechnology and Advanced Materials (BINA), Bar Ilan University (2) Department of Chemistry and the Bar-Ilan Institute for Nanotechnology and Advanced Materials (BINA), Bar-Ilan University

26
11:21

A Putative Missense Mutation in *TUB* in Druze and Arab Patients with Autosomal Recessive Retinitis Pigmentosa

Tamar Ben-Yosef (1), Yasmin Tatour (1), Tzipora Falik-Zaccai (2), Eyal Banin (3), and Dror Sharon (3)
(1) Rappaport Faculty of Medicine, Technion (2) Institute of Human Genetics, Galilee Medical Center, Naharia, (3) Department of Ophthalmology, Hadassah-Hebrew University Medical Center

27 11:28 AC

The Complex Expression Pattern of FAM161A which is the most Common Cause of Retinitis Pigmentosa in Israel

Prakadeeswari Gopalakrishnan (1),AvigailBeryozkin-Muniz (1), Eyal Banin (1), Carlo Rivolta (2), Dror Sharon (1)
Institution: (1) Department of Ophthalmology, Hadassah-Hebrew University Medical Center (2) Department of Medical Genetics, University of Lausanne, Lausanne, Switzerland.

28 11:35 AC

A *Drosophila* model for a Dehydrodolichyl Diphosphate Synthase (DHDDS) mutation causing Retinitis Pigmentosa in humans

Reut Ifrah(1), LIliana Mizrahi-Meissonnier(2), Tal Brandwine(1), Dror Sharon(2), Offer Gerlitz(1) and Baruch Minke(1)
(1) Department of Medical Neurobiology, Faculty of Medicine and the Edmond and Lily Safra Center for Brain Sciences (ELSC), Hebrew University (2) Department of Ophthalmology, Hadassah University Hospital, Ein Kerem

29 11:42

SCAPER localizes to primary cilia and its mutation causes human ciliopathy syndrome.

Ohad Wormser (1), Libe Gradstein (2), Yuval Yogev (1), Inna Goliand (3), Yair Sadka (4), Hagit Flusser (5), Dikla Nachmias (3), Roni Gat (3), Uri Abdu (3), Natalie Elia (3), Ohad S. Birk (1,6).
(1) The Morris Kahn Laboratory of Human Genetics, National Institute for Biotechnology in the Negev and Faculty of Health-Sciences,(2) Department of Ophthalmology, Soroka Medical Center and Clalit Health-Services, Faculty of Health-Sciences, (3) Department of Life-Sciences and National Institute for Biotechnology in the Negev, (4) Child Developmental Center, Beer-Sheva Mental-Health Center, (5) The Zusman Institute for Child Development, Division of Pediatrics, Soroka Medical Center (6) Genetics Institute, Soroka Medical Center. All at Ben-Gurion University of the Negev, Beer-Sheva.

30 11:49 AC

Infectious knockdown of CREB and HIF-1 for the treatment of metastatic uveal melanoma

Maria Gimmelshein (1,2), Ana Voropaev (1,2), Dudi Shneor (1,2), Alik Honigman (2), Shahar Frenkel (1)
(1) Division of Ophthalmology, Hadassah-Hebrew University Medical Center (2) Department of Biochemistry and Molecular Biology, IMRIC, The Hebrew University-Hadassah Medical School

31 11:56 **Distinct biological types of ocular adnexal sebaceous carcinoma: HPV-driven and virus-negative tumors arise through non-overlapping molecular-genetic alterations**

Oded Sagiv,(1) Michael T. Tetzlaff,(2,3) Jonathan L Curry,(2,4) Jing Ning,(5) Thomas Kandl,(1) Bo Peng,(5) Diana Bell,(2) Mark J Routbort,(6) Courtney W Hudgens,(3) Doina Ivan,(2,4) Tae-Beom Kim,(5) Ken Chen,(5) Agda Karina Eterovic,(7,8) Kenna R Mills Shaw,(7) Victor G. Prieto,(2,4) Anna Yemelyanova,(2) Bita Esmaeli (1)

(1) Orbital Oncology and Ophthalmic Plastic Surgery, Department of Plastic Surgery, University of Texas MD Anderson Cancer Center.(2) Department of Pathology, University of Texas MD Anderson Cancer Center, (3) Department of Translational and Molecular Pathology, University of Texas MD Anderson Cancer Center, (4) Department of Dermatology, University of Texas MD Anderson Cancer Center, (5) Bioinformatics and Computational Biology, University of Texas MD Anderson Cancer Center, (6) Department of Hematopathology, University of Texas MD Anderson Cancer Center, (7) The Sheikh Khalifa Bin Zayed Al Nahyan Institute for Personalized Cancer Therapy, The University of Texas MD Anderson Cancer Center., (8) Department of Systems Biology, The University of Texas MD Anderson Cancer Center.

12:03 **Discussion**

Guest lecture - Jeffrey Goldberg 12:10 - 12:50

Retinal Ganglion Cell Differentiation and Transplantation

Lunch break 12:50 - 13:50

Guest lecture - Jeffrey Goldberg 13:50 - 14:30

Glaucoma Biomarkers and Neuroprotection: Clinical Trial

14:30 - 15:25

Cornea

Moderators:

Avi Solomon and Yoav Nahum

32
14:30
AC

In vivo keratometric changes in rabbit eye induced by topical 17β-estradiol

Ari Leshno (1, 2), Noa Avni (1, 2), Katalin Prokai-Tatrai (3), Ygal Rotenstreich (1, 2), Asaf Magid (2), Ettel Bubis (1,2) and Adiel Barak (4, 3)
(1) Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer (2) Sackler Faculty of Medicine, Tel Aviv University (3) Department of Pharmacology and Neuroscience, and the Institute for Healthy Aging, University of North Texas Health Science Center, Fort Worth, TX, United States; (4) Department of Ophthalmology, Tel-Aviv Medical Center

33
14:37

Ocular Magnetic Neurostimulation Promotes Healing of the Corneal Epithelium in Dry Eye Patients

Abraham Solomon (1), Hadas Ben Eli (1), Denise Wajnstajn (1), Hagay Avizemer (2), Lilly Karmona (2), David Zadok (3)
Departments of Ophthalmology, (1) Hadassah Medical Center, (2) Wolfson Medical Center and (3) Shaarei Zedek Medical Center

34
14:44
AC

MicroRNA-184 controls corneal stromal thickness, epithelial cell proliferation, adhesion and response to injury

Sara Nagosa (1), Swarnabh Bhattacharya (1), Aya Amitai-Lange (1), Friederike Leesch (1), Daria Putin (1), Daniel Aberdam (2) and Ruby Shalom-Feuerstein (1)
(1) The Ruth and Bruce Rappaport Faculty of Medicine, Technion – Israel Institute of Technology, (2) Hopital St-Louis, Paris, France

35
14:51

Loss of the entire limbal stem cell compartment can be repaired by dedifferentiation of corneal committed cells if the niche is intact

Ruby Shalom-Feuerstein (1), Waseem Nasser (1), Aya Amitai-Lange (1), Eran Bercovic (2), Beatrice Tiosano (2))
(1) Technion Israel Institute of Technology (2) Hillel Yafe Medical Center

36 14:58 AC

P63 plays a key role in corneal development, homeostasis and disease

Waseem Nasser (1), Sara Nagosa (1), Caterina Missero (2), Colin Willoughby (3), Ruby Shalom-Feuerstein (1)
(1) Technion - Israel Institute of Technology, (2) CEINGE Biotecnologie Avanzate, Napoli, Italy, (3) Department of Eye and Vision Science, Institute of Ageing and Chronic Disease, University of Liverpool, United Kingdom

37 15:05

A comprehensive analyses of corneal mRNA level, during sulfur mustard induced ocular late pathology in the rabbit model, using RNA-sequencing

Vered Horwitz, Inbar Cohen-Gihon, Inbal Egoz, Shlomit Dachir, Maayan Cohen, Liat Cohen, Hila Gutman, Rellie Gez, Tamar Kadar, Ariel Gore(1), Adi Beth-Din, Anat Zvi, Galia Zaida, and Ofir Israeli
Israel Institute for Biological Research, Ness-Ziona

38 15:12 AC

The Outcomes of Descemet Membrane Endothelial Keratoplasty for Secondary Penetrating Keratoplasty Graft Failure

Khaled Safadi, Itay Lavy
Hadassah Medical Center

15:19 **Discussion**

Coffee and exhibition 15:25-16:00

Imaging

16:00 – 17:00

Moderators:

Jaime Levy and Adiel Barak

39 16:00 AC

Mechanical analysis of Epiretinal membranes studied by A 3D geometrical computer-aided design model

Assaf Gershoni (1), Keren Della Rocca (2), Amir Hadayer (1), Orly Gal-Or (1), Anat Ratnovsky (2), Sara Naftali (2), Rita Ehrlich (1)

(1)Department of Ophthalmology, Rabin Medical Centerl (2)Afeka- Tel Aviv Academic College of Engineering

40 16:07 AC

Retinal thinning in Gaucher patients as a predictive test for developing Parkinson's disease

Yishay Weill (1), Michal Becker-Cohen (2), Joel Hanhart (1), Shoshana Revel-Vilk (2), Lauren Wasser (1), David Zadok (1), Ari Zimran (2)

(1) Ophthalmology department, Shaare Zedek Medical Center (2). Gaucher unit, Shaare Zedek Medical Center

41 16:14 AC

Imaging of the retinal and choroidal vasculature in rodents using swept source OCT angiography and fluorescein angiography

Chen Matsevich, Hamzah Aweidah, Ayala Ejzenberg, Tareq Jaouni, Eyal Banin, Alexey Obolensky

Center for Retinal and Macular Degenerations, Department of Ophthalmology, Hadassah- Hebrew University Medical Center

42 16:21 AC

In vivo imaging of the fibrillar architecture of the posterior vitreous and its relationship to the premacular bursa, Cloquet's canal, prevascular vitreous fissures and cisterns

Orly Gal-Or (1,2), Quraish Ghadiali (1) and Michael Engelbert (1)

(1)Vitreous Retina Macula Consultants of New York, New York, New York, USA, (2) Rabin Medical Center, Department of Ophthalmology

43 16:28 AC

In vivo MRI assessment of bioactive magnetic iron oxide/human serum albumin nanoparticle delivery into the posterior segment of the eye in a rat model of retinal degeneration

Hadas Ketter Katz (1)*, Adi Tzameret (1,2)*, Victoria Edelshtain (1,2), Ifat Sher (1), Enav Corem-Salkmon (3), Itay Levy (3), David Last (4), David Guez (4), Yael Mardor (2,4), Shlomo Margel (3), Ygal Rotenstrich (2).
(1) Goldschleger Eye Institute, Sheba Medical Center, Tel-Hashomer, (2) Sackler Faculty of Medicine, Tel-Aviv University, (3) Department of Chemistry, Bar-Ilan Institute of Nanotechnology and Advanced Materials, (4) Advanced Technology Center, Sheba Medical Center, Ramat-Gan.
* Equal contribution

45 16:35 AC

Optical density ratio – a prognostic marker for chronicity in Central Serous Chorioretinopathy

Ari Leshno(1, 2), Noam Brakin (2), Adiel Barak (2, 3), Dinah Zur(2, 3), Anat Loewenstein(2, 3), Iris Moros(2, 3), Meira Neudorfer(2, 3)
(1) Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, (2) Sackler Faculty of Medicine, Tel Aviv University, (3) Department of Ophthalmology, Tel-Aviv Medical Center

46 16:42 AC

Why FA when you can OCTA proliferative diabetic retinopathy patients?

Michal Schaap Fogler (1,2), Mathen Mathen (2), Richard Leicht (2), Ravi Dookeran (2), Andre Jastrzebski (2), Joshua Manusow (2) and Frank Stockl (2)
(1) Rabin Medical Center, (2) University of Manitoba, Winnipeg, Canada

16:49 **Discussion**

Thursday, March 7th 2019

Coffee and Exhibition 8:00 -8:30

Retina II 8:30 – 9:45

Moderators:

Shiri Zayit-Soudry and Yossi Mandel

47 8:30 AC

Studying the biocompatibility and 3D cell-scaffold interface of photoreceptor precursors in a microwells array

Amos Markus (1), Yoav Chemla (1), Gal Shpun (1), Nairouz Farah (1), Yossi Mandel (1,2,3)
(1) Mina and Everard Goodman Faculty of Life Sciences, Ramat-Gan (2) School of Optometry and Visual Science, Faculty of Life Science, Bar-Ilan University. (3) Institute for Nanotechnology and Advanced Materials (BINA) Bar-Ilan University.

48 8:37 AC

Oligomeric and fibrillar assemblies of Amyloid-B 42 are highly retinotoxic: Implications for the pathophysiology of Age-Related Macular Degeneration

Efrat Na'aman (1), Sarah Ya'ari (2), Lior Liba (3), Shadi Safuri (1), Michael Mimouni (1,3), Irit Mann (3), Lihi Adler-Abramovich (2), Ido Perlman (3), Shiri Soudry (1,3)
(1) Department of Ophthalmology, Rambam Health Care Campus, (2) Department of Oral Biology, The Goldschleger School of Dental Medicine, Sackler Faculty of Medicine, Tel Aviv University, (3) Ruth and Bruce Rappaport Faculty of Medicine, Technion, Israel Institute of Technology

49 8:44

Photovoltaic Restoration of Sight in Atrophic Age-related Macular

Daniel Palanker (1), Yannick Le Mer (2), Ralf Hornig (3), Guillaume Buc (3), M. Deterre (3), Jose A. Sahel (2,4)
(1) Ophthalmology, Stanford University, CA, USA (2) Ophthalmology, Foundation Rothschild, Paris, France (3) Pixium Vision, Paris, France (4) Ophthalmology, University of Pittsburgh, PA, United States.

50 8:51 AC

The relevance of Ccr1 receptor in a model of retinal degeneration.

Sarah Hayoun, Batya Rinsky, Shira Hagbi-Levi, Michelle Grunin, Itay Chowers
Department of Ophthalmology, Hadassah-Hebrew University Medical Center, and the Hebrew University – Hadassah School of Medicine

51 8:58 AC

Retinal stimulation through a DLP based projection system enables the generation of high-resolution VSDI retinotopic maps

Adi Gross (1), Nadav Ivzan (1), Nairouz Farah (1) Yossi Mandel (1,2)
(1) Faculty of Life Sciences, School of Optometry and Vision Science, Bar-Ilan University, (2) Bar-Ilan Institute for Nanotechnology and Advanced Materials (BINA), Bar-Ilan University

52 9:05 AC

MSCs Encapsulation within Thermo-Responsive Hydrogel as Regenerative Therapy for Retinal Degeneration

Dorit Eliyaev (2,3), ·Itay Nakdimon (2,3), Moshe Benhamou (2,3), Noam Azmon (2), Anat Lowenstein (2,3), Adiel Barak (2,3), Tal Dvir (1) and Aya Barzelay (2,3)
(1) School of Molecular Cell Biology and Biotechnology, Tel Aviv, (2) Division of Ophthalmology, Tel Aviv Sourasky Medical Center, (3) Sackler Faculty of Medicine, Tel Aviv University

53 9:12

Metabolite Amyloids in Human Disease: Oxalate Nanofibrils Induce Comparable Retinopathy in Hyperoxaluria Patients and Treated Animals

Shiri Zayit-Soudry (1,2), Shira Shaham-Niv (3), Michael Mimouni (1,2), Dor Zaguri (3), Efrat Naaman (1), Daniella Magen (2,4), Shirley Pollack (4), Topaz Kreiser (3), Rina Leibu (1), Ido Perlman(2) and Ehud Gazit (3)
(1) Department of Ophthalmology, Rambam Health Care Campus (2) Ruth and Bruce Faculty of Medicine, Technion Israel Institute of Technology, (3) Department of Molecular Microbiology and Biotechnology, Tel Aviv University, (4) Pediatric Nephrology, Rambam Health Care Campus

54 9:19

Allele Frequency Analysis of Variants Reported to cause Autosomal Dominant Retinal Diseases Revealed that 17% of Genes and 9% of Mutations are Unlikely Pathogenic

Mor Hanany, Dror Sharon
Department of Ophthalmology, Hadassah-Hebrew Univ Medical Center

55 9:26 **Cortical response to combined prosthetic and visible stimuli exhibits similarities to natural visual processing**

Tamar Arens-Arad (1,2), Farah Nairouz (1,2), Moshkovitz Avital (1,2), Rivkah Lender (1,2), Thomas Flores (3), Daniel Palanker(3,4), Mandel Yossi (1,2)
(1) Faculty of Life Sciences, School of Optometry and Vision Science, Bar-Ilan University, (2)Bar-Ilan Institute for Nanotechnology and Advanced Materials (BINA), Bar-Ilan University, (3) Hansen Experimental Physics Laboratory, Stanford University, Stanford, USA, (4) Ophthalmology, Stanford University, Stanford, USA

9:33 **Discussion**

Anterior segment

Moderators: 9:40 – 10:35

Alon Skaat and Ehud Assia

56 9:40 **Microarchitecture of Schlemm's Canal Before and After Cataract Extraction Surgery**

Reut Singer, Miri Fogel-Levin, Hani Levkovitch Verbin, Yair Rubinstein, Ari Leshno and Alon Skaat
Goldschleger Eye Institute, Sheba Medical Center, Tel-Hashomer; Sackler Faculty of Medicine, Tel-Aviv University, Tel-Hashomer.

57 9:47 AC **Non-Pigmented ciliary epithelium deliver oxidative stress alert via exosomes**

Natalie Lerner, Sofia Schreiber-Avissar, Elie Beit-Yannai
Ben-Gurion University of the Negev

58 9:54 **First-in-Human clinical study to establish the safety and efficacy of automatic Direct Laser Trabeculoplasty (DSLT)**

Mordechai Goldenfeld (1), Sharon Blum Meirovitch (1), Ari Leshno (1), Zachary Sacks (2), Masha Dobkin-Bekman (2), Arieh Kisos (2), Yuval Yohai (2), Emil Abramov (2), Daniel Elkayam (2), Daria Lemann-Blumenthal (2), Alon Skaat (1), Michael Belkin (1,3)
(1) Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, (2) BELKIN Laser Ltd, Yavne, (3) Goldschleger Eye Research Institute, Tel Aviv University, Tel Hashomer

59 10:01 AC

Rosmarinic Acid Restores Complete Transparency of Human Cataract Ex Vivo and Delays Cataract Formation In Vivo

Michael Mimouni (1), Marina Chemerovski-Glikman (2), Yarden Dagan (2), Esraa Haj (2), Lihi Adler-Abramovich (2), Daniel Segal (2), Ehud Gazit (2), Shiri Zayit-Soudry (1)
(1) Department of Ophthalmology, Rambam Health Care Campus, Technion- Israel Institute of Technology, (2) Department of Molecular Microbiology and Biotechnology, Tel Aviv University

60 10:08 AC

SOX2 regulates P63 and stem/progenitor cell state in the corneal epithelium

Swarnabh Bhattacharya (1), Laura Serror (1), Eshkar Nir (1), Dalbir Dhiraj (2), Anna Altshuler (1), Maroun Khreish (3), Beatrice Tiosano (3), Peleg Hasson (1), Lia Panman (2), Daniel Aberdam (4), Ruby Shalom-Feuerstein (1)
(1) Technion - Israel Institute of Technology, (2) MRC Toxicology Unit, University of Leicester, (3) Hillel Yaffe Medical center, (4) INSERM U976 and Université Paris-Diderot

61 10:15

Stiffening of sclera using bacteriochlorophyll derivative (WST11) and transpupillary near infrared light (NIR) measured by atomic force microscopy

Alexandra Goz (1,2), ,Jurriaan Brekelmans (3), Alexander Brandis (4), ,Sidney R. Cohen (5), Avigdor Scherz (1) ,Arie Marcovich (1,2)
(1) Departments of Plant Sciences, Weizmann Institute of Science, (2) Department of Ophthalmology, Kaplan Medical Center, Rehovot.(3) University Eye Clinic Maastricht, Maastricht, The Netherlands (4) Department of Biological Services, Weizmann Institute of Science, Rehovot, (5) Department of Materials and Interfaces, Weizmann Institute of Science, Rehovot,

62 10:22

Nevus of Ota: Clinical Presentation, Imaging, Complication and Ocular Clinical Classification

Vicktoria Vishnevskia-Dai, Iris Moroz, Keren Zloto,, Ido Didi Fabian, Ayelet Priel, ,Ofira Zloto
Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, Sackler Faculty of Medicine, Tel Aviv University.

10:29 **Discussion**

Coffee and Exhibition 10:35 -11:10

Awards and ISVER update 11:10 -11:30

Retina III 11:30 – 12:35

Moderators:

Tami Livnat and Radgonde Amer

63 11:30 AC

The effect of intravitreal injection timing in eyes with new CNV

Rabeea H.Daood , Maria Tsesler , Rita Ehrlich
(1) Department of Ophthalmology , Rabin medical center , Beilinson Campus ,Petah Tikva , (2) Sackler Medical School , Tel Aviv

64 11:37

A 12-month Prospective Study to Evaluate the Efficacy of Treat and Extend Regimen (T&E) of Intravitreal Aflibercept as a Second-Line Treatment for Diabetic Macular Edema (TADI Study)

Tareq Jaouni (1), Rita Ehrlich (2),(10), Yoreh Barak (3) , Haia katz (4), Russell Pokroy (5,10), Jaime Levi (1), Joel Hanhart (6), Ori Segal (7, 10), Shiri Shulman (8), Michaella Goldstein (9,10), Liran Tiossano (1), Itay Chowers (1)
Ophthalmology Department: (1) Hadassah-Hebrew University Medical Center (2) Rabin Medical Center, (3) Rambam Medical Center, (4) Kaplan Medical Center, (5) Assaf Harofeh Medical Center (6) Shaare Zedek Medical Center, (7) Meir Medical Center, (8) Assuta Medical Center, (9) Tel Aviv Medical Center, (10) Sackler Faculty of Medicine, Tel Aviv University

65 11:44 AC

The Correlation of Response to Treatment with anti-VEGF compounds between the First and Second Treated Eyes in Diabetic Macular Edema

Nadav Levinger, Elishai Assayag, Liran Tiosano, Tomer Batash, Jaime Levy, Itay Chowers
Department of Ophthalmology, Hadassah-Hebrew University Medical Center

66 11:51 AC

Activated protein C reduces leakage from newly formed and pre-existing choroidal neovascularization (CNV) in a murine model

Yehonatan Weinberger (1), Yael Nisgav (2), Dov Weinberger (1,2,3) and Tami Livnat (2,3,4)
(1) Ophthalmology department, Rabin Medical Center, (2) Laboratory of eye research, Felsenstein's Medical Research Center, Petah-Tikva, (3) Sackler faculty of medicine, Tel Aviv University, (4) The Israeli national hemophilia center, Sheba Medical Center

67 11:58 AC

The role of vascular endothelial growth factor (VEGF) in activated protein C (APC)-induced inhibition of choroidal neovascularization (CNV)- a murine model

Alaa Bashir (1), Yael Nisgav (2), Dov Weinberger (1, 2, 3) and Tami Livnat (2,3, 4)
(1) Division of Ophthalmology, Rabin Medical Center- Beilinson campus, (2) Laboratory of Eye research Felsenstein Medical Research Center (FMRC), (3) Sackler School of Medicine, Tel-Aviv University, 4. The Israeli National Hemophilia Center, Sheba Medical Center, Tel Hashomer

68 12:05 AC

Subretinal survival of retinal progenitors (RPs) derived from human embryonic stem cells (hESCs) in different animal models

Hamzah Aweidah (1), Alex Obolensky (1), Ayala Ejzenberg (1), Chen Matsevich (1), Masha Idelson (2), Hanita Khaner (2), Benjamin Reubinoff (2) and Eyal Banin (1)
CRMD, Department of Ophthalmology (1) and Gene Therapy Institute (2), Hadassah-Hebrew University Medical Center

69 12:12

Microglia activation exacerbates retinal degeneration in RPE65/rd12 mouse model for Leber congenital amaurosis

Ettel Bubis (1,2)Ifat sher (1), Hadas Katz(1),Ygal Rotenstreich (1,2)
(1) Goldschleger Eye Institute, Sheba Medical Center, Tel-Hashomer, (2) Sackler Faculty of Medicine, Tel Aviv University

70 12:19

Clinical, Electrophysiological and Immunological Features in Autoimmune Retinopathy

Khaled Safadi, Itay Chowers, Eyal Banin, Boris Rosin, Radgonde Amer
Hadassah Medical Center

12:26 **Discussion**

12:35 – 13:35

Lunch

Start-up and Innovation

13:35 – 15:10

Moderators:

Michael Belkin and Ygal Rotenstreich

#1 13:35 **Update on Visidome: add-on accommodative intraocular lens**

Ehud Assia, Asaf Frihmann, Yokrat Ton

Center for Applied Eye Research, Department of Ophthalmology, Meir Medical Center, Kfar-Saba

#2 13:40 **Eye-tracking based device for measurement of both manifest and latent eye deviation in adults and children**

Tamara Wygnanski–Jaffe (1,2), Michael Belkin (3), Ran Yam (4), Dan Oz (4) and Oren Yehezkel (4)

(1) Goldschleger Eye Institute, Tel-Hashomer,. (2) Sackler Faculty of Medicine, Tel- Aviv University, Tel-Aviv, Soroka Hospital, Beer-Sheva, (3) Goldschleger Eye Research Institute,Sheba Medical Center, Tel Hashomer, (4) . Novasight Ltd., Airport City,

#3 13:45 AC **A Novel Technique Using Ab-Interno Er:YAG Laser Trabeculectomy : A Rabbit Model - Safety And Feasibility Results**

Ari Leshno, Reut Zinger, Yair Rubinstein and Alon Skaat

Goldschleger Eye Institute, Sheba Medical Center, Tel-Hashomer, Israel; Sackler Faculty of Medicine, Tel-Aviv University, Tel-Hashomer,

#4 13:50 **Delivery of therapeutics to the back of the eye using a minimally invasive adjustable-depth blunt injector**

Ygal Rotenstreich(1,2), Ettel Bubis(1,2), Zehavit Goldberg(1,2), Adi Tzameret (1,2), Hana Ziv(2), Sara Pri-Chen(1), Ifat Sher(1).

(1) The Maurice and Gabriela Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, (2) The Sackler School of Medicine, Tel Aviv University

#5 13:55 **Chromatic pupilloperimetry for objective perimetry in retinal and optic nerve neurodegeneration**

Ifat Sher (1), Amit Hamburg (1,2), Yisroel Tucker (1,3), Maya Gurevich (1,2), Alon Skaat (1, 2), Ygal Rotenstreich (1,2)
(1) The Maurice and Gabriela Goldschleger Eye Institute, Sheba Medical Center, Tel Hashomer, (2) The Sackler School of Medicine, Tel Aviv University, (3) St. Georges University of London Medical school, Nicosia, Cyprus

#6 14:00 **Sanoculis**

Yossi Glovinsky

#7 14:05 **Innovative Solutions for Corneal Healing**

EyeYon Medical
Nachum Ferera

#8 14:10 **CorNeat Vision**

Gilad Litvin

#9 14:15 **ViSci**

Yoni Manor

#10 14:20 **Diagnostears**

David Zadok

#11 14:25 **WizePharma**

Or Eisenberg

#12 14:30 **Tactile based imaging for the visually impaired**

Zeev Zalevsky (1,2), Yafim Beiderman (1,2), Sergey Agdarov (1,2) and Michael Belkin (3)
(1) Faculty of Engineering and the Nanotechnology Center, Bar-Ilan University (2) I C Touch team, Bar-Ilan University, (3) Goldshleger Eye Research Institute, Tel-Aviv University, Tel-Hashomer

#14 14:35 **Intraocular Projector for patients with corneal blindness unsuitable for keratoplasty**

Yoav Nahum(1), Ofer Ziv(2), Tomer Exterman(3), Yoni Hadad(3)
(1) Department of Ophthalmlogy, Rabin Medical Center, (2) School of Electrical Engineering, Afeka – Tel Aviv Academic College of Engineering, Tel Aviv, (3) Department of Biomedical Engineering, Technion – Israel Institute of Technology

14:40 **Update on the Light Adjustable Lens**

Dan Schwartz

University of California, San Francisco

The Light Adjustable Lens (LAL) is a photo-sensitive silicone IOL that enables non-invasive, post-operative adjustment of spherocylindrical error. The mechanism of adjustability and results of an FDA pivotal trial will be reviewed. Approaches to addressing presbyopia using LAL technology will also be discussed.

14:55 **Discussion**

Coffee and exhibition 15:05 – 15:40

Rapid fire II 15:40 – 17:00

Moderators:

Arie Marcovich and Eran Pras

71 15:40 **Refractive and ocular findings in individuals with Type-A vs. Type-B behavior patterns**

Devora Kurland (1), Rivkah Lender (1), Ravid Doron (1), Einat Shneor (1) and Hadas Ben-Eli (1,2)

(1) Department of Optometry and Vision Science, Hadassah Academic Collage, (2) Department of Ophthalmology, Hadassah-Hebrew University Medical Center

72 15:43 **High expression of PD-1 and PD-L1 in ocular adnexal sebaceous carcinoma.**

Oded Sagiv, Thomas J. Kandl, Jonathan L. Curry, Jing Ning, Junsheng Ma, Courtney W. Hudgens, John Van Arnam, Jennifer A. Wargo, Bita Esmaeli, Michael T. Tetzlaff

(1) Orbital Oncology and Ophthalmic Plastic Surgery, Department of Plastic Surgery, (2) Department of Pathology, Section of Dermatopathology, (3) Department of Dermatology, (4) Department of Biostatistics, (5) Department of Translational and Molecular Pathology, (6) Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA

73 15:46 **Ocular Injury Seen in Urgent Care Centres**

Einat Shneor (1), Deena R. Zimmerman (2), Michel Millodot (3), Ariela Gordon-Shaag (1)

(1) Dept. of Optometry, Hadassah Academic College (2) TEREM Emergency Medical Centers, Jerusalem, (3) School of Optometry and Vision Sciences, Cardiff University, Cardiff, UK

74 15:49 **Cover Testing: Clinical vs. Infra-Red Eye Tracker- A Comparative Study**

Guy Band (1), Ahmed Kharbat (1), Shimon Mizrahi (2), Avi Caspi (2), Liat Gantz (1)
(1) Department of Optometry and Vision Science, Hadassah Academic College, (2) Department of Electronic Engineering, Jerusalem College of Technology

75 15:52 AC **MicroRNAs as biomarkers for ocular involvement in juvenile idiopathic arthritis**

Shani Pillar (1,2), Nir Pillar (2), Gil Amarilyo (2,3), Liora Harel (2,3), Noam Shomron (2), Michal Kramer (2,4)
(1) Department of Ophthalmology, Meir Medical Center, (2) Sackler Faculty of Medicine, Tel Aviv University, (3) Department of Pediatric Rheumatology, Rabin Medical Center, (4) Department of Ophthalmology, Rabin Medical Center

76 15:55 AC **Balloon Catheter Dilation as the Primary Treatment of Congenital Nasolacrimal Duct Obstruction.**

Inbal Gazit, Eran Pras, Lior Or, Yair Morad, Morris Hartstein
Assaf Harofeh Medical Center, Tel Aviv University

77 15:58 **Novel method for optic nerves and chiasm dissection in mice, for studying optic neuritis.**

Karny Shouchane-Blum (1), Judith Brody (1,2), Katia Pozyuchenko (3), Dan Frenkel (3,4) and Hadas Stiebel-Kalish (1,2,3)
(1) Ophthalmology Department, Rabin Medical Center, (2) Sackler Faculty of Medicine, Tel Aviv University, (3) Department of Neurobiology George S. Wise Faculty of Life Sciences, Tel Aviv University, (4) Sagol School of Neuroscience, Tel Aviv University

78 16:01 AC **Comparison of self-report questionnaire on dry eye with clinical test results: cross sectional study**

Ruth Gamish (1), Sapir Mor-Yossef (1), Gal Shoef (1), Shirel Ruimy Samama (1), Noa Kaufman (1), Einat Shneor (1) and Hadas Ben-Eli (1,2)
(1) Department of Optometry and Vision Science, Hadassah Academic College, (2) Department of Ophthalmology, Hadassah-Hebrew University Medical Center

79 16:03 AC

Characterization of pupil responses to chromatic focal light stimuli in patients with Pseudotumor Cerebri

Amit Hamburg (1,2), Ifat Sher (1), Ruth Huna-Baron (1,2), Ygal Rotenstreich (1,2)
(1) Goldschleger Eye Institute, Sheba Medical Center, Tel-Hashomer (2) Sackler Faculty of Medicine, Tel Aviv University

80 16:06 AC

Effect of light and diurnal variation on macular thickness in X-Linked Retinoschisis: A pilot study

Yair Rubinstein (1,2), Chen Weiner (2,3), Noa Chetrit (1), Hadas Newman (3,4), Idan Hecht (1,3), Nadav Shoshany (1,2), Eran Pras (1,2,3)
(1) .Department of Ophthalmology, Assaf-Harofeh Medical Center, (2)Matlow's Ophthalmogenetic Laboratory, Department of Ophthalmology, Assaf Harofe Medical Center, (3) Sackler faculty of Medicine, Tel Aviv University, (4) Department of Ophthalmology, Tel Aviv Sourasky Medical Center

81 16:09

Effect of circadian rhythm disruptions on the development of type 2 diabetes and cataract in sand rats (*Psamommys obesus*)

Vicktoria Vishnevskia-Dai (1), Carmel Bilu (2,3), and Noga Kronfeld-Schor (2)
(1) Ocular Oncology and Autoimmune service, The Goldschleger Eye Institute, The Chaim Sheba Medical Center, Tel-Hashomer, Sackler Faculty of Medicine,Tel-Aviv University, (2) School of Zoology, Tel-Aviv University, Tel Aviv, (3) Department of Clinical Biochemistry and Pharmacology, Ben-Gurion University of the Negev

82 16:12 AC

Adrenocorticotropic Hormone Gel Treatment for Patients with Refractory Non-Infectious Uveitis

Yael Sharon (1,2), David S. Chu (2,3)
(1) Rabin Medical Center, (2) Metropolitan Eye Research and Surgery Institute, New Jersey, USA, (3) Institute of Ophthalmology and Visual Science, New Jersey Medical School, Rutgers University, New Jersey, USA

83 16:15 AC

Relationship between air pollution and Urgent Care Centers visits for conjunctivitis in Jerusalem

Hadas Shochat (1), Einat Shneor (1), Mieczysław Szyszkowicz (2), Deena Zimmerman (3), Geula Sherf (4), Alexander Foxman (1), and Prof. Ariela Gordon-Shaag (1)
(1) Department of Optometry and Vision Science, Hadassah Academic College, (2) Population Studies Division, Health Canada, Ottawa, Canada, (3) TEREM Emergency Medical Centers, Jerusalem, (4) Department of Environmental Science, Hadassah Academic College

84 16:18

Computed Tomography Induced Cataract – A Population Based Study Of Association Between Radiation Exposure And Cataract Incidence

Jaime Levy (1), Mayyan Yitshak Sade (2,3), Ilan Shelef (4), Victor Novack (2,3), Muhammad Abu Tailakh (2,3), Orly Weinstein (2,5,6)
(1) Department of Ophthalmology, Hadassah Medical Center, (2) Faculty of Health Sciences, Ben-Gurion University of the Negev, (3) Clinical Research Center, Soroka University Medical Center, (4) Radiological Institute, Soroka University Medical Center, (5) Ophthalmology Department, Soroka University Medical Center, (6) Ministry of Health, Israel

85 16:21

Comparison of surgical and outcome parameters of Dacryocystorhinosctomy approaches

Yehonatan Weinberger (1), Inbal Avisar (2)
(1) Ophthalmology department, Rabin Medical Center, (2) Sackler faculty of medicine, Tel Aviv University

86 16:24 AC

Results of Cataract Surgery in Eyes with Adult-Onset Foveomacular-Vitelliform Dystrophy (AFVD)

Tomer Batash, Liran Tiosano, Tareq Jaouni, Jaime Levi, Hadas Ben-Eli, Ori Saban, Michal Ganiel, Itay Chowers
Department of Ophthalmology, Hadassah-Hebrew University Medical-Center

87 16:27 AC

Combined phacoemulcification vitrectomy procedure in proliferative versus non proliferative diabetic retinopathy

Doha Jbaray (1), Amir Hadayer (1,2), Assaf Gershoni (1), Ruth Axer-Siegel , Assaf Dotan (1), Orly Gal-Or (1), Rita Ehrlich(1,2)
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88 16:30 AC

The Cataract Electronic Medical Records Dataset at Hadassah Medical Center

Ori Saban, Hadas Ben-Eli, Michal Ganiel, Tomer Batash, Jaime Levy, Itay Chowers
Department of Ophthalmology, Hadassah Medical Center

89 16:33 AC

Socio-demographic Disparities in Amblyopia Prevalence Among Israeli Adolescents

Itay Nitzan (1,2), Claudia Yahalom (3), Jacob Megreli (1,2), Dana Bez (1,2), Eva Avramovich (2), Adiel Barak (4), Hagai Levine (1)
(1) Hebrew University-Hadassah Braun School of Public Health and Community Medicine, Ein Kerem, (2) Medical Corps, Israel Defense Forces, Israel (3) Department of Ophthalmology, Hebrew University-Hadassah Medical Center, Ein Kerem (4) Department of Ophthalmology, Tel Aviv Sourasky Medical Center and Sackler Faculty of Medicine, Tel Aviv University

91 16:36

The Combination of Whole Exome Sequencing and Clinical Analysis Allows Better Diagnosis of Rare Syndromic Retinal Dystrophies

Samer Khateb (1), Alaa Abu Diab (1), Ala'a AlTalbishi (2), Boris Rosin (1), Moien Kanaan (3), Lara Kamal (3), Anand Swaroop (4), Itay Chowers (1), Eyal Banin (1) and Dror Sharon (1)
(1) Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem (2) St John Eye Hospital, Jerusalem. (3) Hereditary Research Lab, Bethlehem University, Jerusalem. (4) Neurobiology-Neurodegeneration & Repair Laboratory, National Eye Institute, National Institutes of Health, Bethesda, Maryland, USA

16:39 **Discussion**

Concluding remarks 16:45 – 17:00

Itay Chowers

Abstracts
תקצירים

Corneal topography followed pars plana vitrectomy and transscleral 4-point suture fixation of Akreos AO60 intraocular lens (IOL)

Rabeea H.Daood (1,2) , David Barash (1,2) , Yoav Nahum (1,2) , Assaf Dotan (1,2)
(1) Department of Ophthalmology , Rabin medical center , Beilinson Campus ,Petah Tikva , (2) Sackler Medical School , Tel Aviv

Purpose: To describe outcomes and corneal astigmatism after combined pars plana vitrectomy (PPV) and trans scleral 4-point suture fixation of a foldable Akreos AO60 intraocular lens (IOL).

Methods: Retrospective case series of 4 eyes of 4 patients who underwent PPV and transscleral 4 point suture fixation of AKREOS AO60 posterior chamber fixation , all patient have follow up at least for 6 months .
Outcome measures included final best-corrected Snellen visual acuity (BCVA), spherical equivalent (SE) , position of IOL in correlation to other structure of the eye (UBM guided) , Astigmatism of the corneal (Pentacam guided) , intraoperative and postoperative complications.

Results: Mean age at surgery was 77.5 years. Indication for surgery was subluxated or dislocated IOL . The mean preoperative BCVA is 1.13 LogMAR , mean BCVA postoperative 0.51 LogMAR
There were no intraoperative complications . Hypotony was observed in one eye a week post operative .
Post operative UBM have showed good and safe anatomical location no IOL tilt
The mean preoperative total corneal astigmatism was 3.28 D. The mean postoperative residual astigmatism was 4.02 D
PENTACAM topography analysis demonstrated irregular astigmatism in all the cases . Mean follow up was 8 months

Conclusions: Trans-scleral 4-point suture fixation of a foldable Akreos AO60 IOL can be performed safely along with concurrent PPV across varying surgical indications resulting in a substantial improvement in visual acuity with minimal complications.
We noticed that all the patient developed irrigular astigmatism that have been measured by PENTACAM.

Postoperative Position Effect on DSAEK graft Adhesion

Margarita Safir, Biana Dubinsky-Pertzov, Lior Or, Assaf Rozenberg, Eran Pras, Adi Einan-Lifshitz, Yakov Goldich
Assaf Harofeh Medical Center

Purpose: To characterize the association between patient adherence to supine postoperative position after DSAEK and graft detachment and rebubbling rates.

Methods: In this retrospective study medical records of patients who underwent uncomplicated DSAEK surgeries in Assaf Harofeh medical center, between 2010-2018 were reviewed, including nursing documentation of patients positioning compliance during their postoperative hospitalization, which lasts at least 24 hours after surgery. For the purpose of the study- a patient was considered compliant if he was documented as cooperative with supine position throughout the whole hospitalization period.

Results: 170 cases were found allegeable. Main indications for surgery were pseudophakic bullous keratopathy (PBK) (48.9%), previous graft failure (28.8%) and Fuch's endothelial dystrophy (19.4%). Postoperative graft detachment was found in 31 (18.2%) eyes after an average of 3.48±4.04 days. Twenty-six eyes (15.29%) required rebubbling, and 2 eyes (1.18%) were reoperated on due to postoperative graft detachment. Compliance with supine position was documented in 84.1% (143 patients). The rates for non-compliance during the first 24 hours in the detached and non-detached groups were 25.81% (n=8) and 14.39% (n=20) patients respectively, after adjustment for possible confounders OR was 1.44 (95% CI: 0.53-3.87, P=0.457). Comparison of the rates of compliant and non-compliant patients without documented detachment was also statistically insignificant (OR=0.697, 95%, CI:0.26-1.88, P=0.457).

Conclusions: In our retrospective study we did not find a statistically significant influence of prolonged postoperative supine positioning on graft detachment and rebubble rates after DSAEK.

Punching DMEK graft on a contact lens versus punching the graft on the donor stroma: preserving more endothelial cells at the graft margin

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Purpose: To evaluate whether punching a Descemet membrane endothelial keratoplasty (DMEK) corneal grafts on a scaffold contact lens reduces endothelial cells loss at the graft margin, compared to punching the graft on the donor stroma.

Methods: DMEK grafts were prepared using 2 different conditions: punching the DMEK graft on contact lens and punching the graft on the donor stroma following its peeling from the corneal stroma. The tissues samples were evaluated for size of Descemet's membrane denuded areas at 4 points at the graft margin. Grafts preparation time was also compared between methods.

Results: We included 6 pairs of corneas from 3 donors (mean age 66.3±5.1). Grafts that were prepared using contact lens as a scaffold had less Descemet's membrane area denuded of endothelial cells than grafts that were punched directly on the donor stroma (total area of Descemet denuded area: 0.06±0.08 mm^2 vs 1.17±0.02 mm^2, p=0.018; maximal height of denuded area: 59.6±28.4 µ vs. 100.2±59.7µ, p=0.07 ;) This was calculated to represents 2% more endothelial cells available for transplantation in the grafts punched on a contact lens compared to grafts that were punched on the donor stroma. Estimating a normal 0.6% reduction in endothelial cell count a year, punching a graft on a scaffold contact lens might yield a 3-year difference in graft survival. Graft preparation time did not significantly differ between the methods (6.4±0.49 vs 9.8±3.7 minutes, p=0.46).

Conclusions: punching a DMEK grafts on a contact lens preserves more endothelial cells available for transplantation than punching the graft on the donor stroma, which may lead to longer graft survival.

Evaluation of the neuroprotective effect of Azithromycin in a mouse glaucoma model

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Purpose: To compare glaucoma mouse models induced by Healon-5 viscoelastic device versus microspheres injection to the anterior chamber. Also, to measure a possible neuroprotective effect of Azithromycin (AZ) on RGCs survival.

Methods: Two glaucoma models were examined, using wild type (WT) and transgenic (NGS and TLR4 knock-out) mice.
1. Healon-5 injected to the right eye (RE) of NGS mice (n=21), divided to 3 groups: Healon-5-glaucoma model as compared to Healon-5 treated with AZ, and control group treated with AZ (n=7 each).
2. Microspheres injected to the RE of WT mice (n=21) or TLR4KO mice (n=21), with AZ injected to half of the cohort.
IOP was measured. Following euthanization, histological analysis was performed. Analysis of mRNA expression levels of stress-, apoptosis- and inflammatory- related genes were performed to retinas and optic nerves.

Results: In the NGS glaucoma model with and without AZ, average RE IOP peaked on day 14.
In the WT microsphere glaucoma model, RE IOP measurements peaked at 1 week, while in the AZ treated group on 2 weeks.
In the TLR4KO microsphere glaucoma model, RE measurements were 15, 10, and 15. In the AZ treated group, RE values were 18, 17, and 11.
Histological, immunohistochemistry, and molecular analysis is under investigation.

Conclusions: We present a mouse model of glaucoma induced by Healon-5 or microspheres, in two transgenic mice as compared to WT. The measurement of IOP showed the most sensitive were the NGS to Healon-5, with max IOP 2 weeks post injection. In the microsphere injected mice, WT mice showed mild increased IOP one week after injection, and the TLR4KO with the same background showed significantly higher pressure on day 21 ($p=0.01$). All mice and models showed decline of pressure on 21 days. RGC loss was measured and the effect of AZ will be shown.

Laser peripheral iridotomy with and without anti-inflammatory drops after

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Purpose: To evaluate whether the administration of topical steroids is required after elective laser peripheral iridotomy (LI)

Methods: This is a prospective, randomized, double-blind, placebo-controlled clinical trial. Patients with anatomical narrow angles and no other ocular disease that requires LI in both eyes were recruited from the Glaucoma Service, Goldschleger Eye Institute, Sheba Medical Center, Tel-Hashomer. After the LI in the first eye patients were randomly given either topical steroid or placebo (Lyteers) eye drops and were instructed to take four drops per day for four days in the treated eye alone. The second eye had LI within a week and it was treated with the alternate treatment. Patients, treating physicians, investigators and coordinators were all blinded as to which drug was assigned after each treatment.
Intraocular pressure, potency of iridotomy and signs of anterior segment inflammation were evaluated at 1 hour and 1 week after LI treatment in each eye. Symptoms were evaluated during each visit, using the Ocular surface index (OSI) questionnaire.
Non-paramentric paired-comparison tests were applied to compare between the two groups.

Results: Fifteen patients (30 eyes) aged 67.2±6.6 years participated in the study. No significant differences in OSI score, baseline characteristics or LI treatment (e.g. power and location) were observed. No signs of inflammation were detected at the one-week follow-up visit in all eyes. The mean OSI score was 1.2±1.5 and 1.2±1.4 in the treatment and placebo respectively (P=1.00). One eye in each group required retreatment due to iridotomy closure. None of the patients indicated any difference between the two treatments.

Conclusions: Our study suggest that topical steroids are not required after high-powered pulsed laser peripheral iridotomy

Marked Variability in Visual Field Interpretation Among Israel Neuro-Ophthalmologists

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Purpose: The correct interpretation of automated visual fields is essential in a neuro-ophthalmology practice. The various nomenclature used to describe defects has important implications for the localization of abnormalities.

Methods: An anonymous, internet-based survey was performed in which participants were asked to describe 10 visual field abnormalities with free text. In a follow-up study, 6 months later, the participants were asked to evaluate the various descriptions that were initially submitted, and select those that were deemed acceptable and sufficient to describe the abnormality.

Results: Twenty-six neuro-ophthalmologists participated in the study. The respondents collectively provided on average 7.6 unique descriptions for each visual field (SD 3.47, range 3-16). In the follow-up study, on average, only 51% of the respondents indicated that the predominant answer in the first phase was acceptable and sufficient to describe the abnormality (SD 15.9, range 24-76%).

Conclusions: The results demonstrate that there is a great deal of variability in the terminology that neuro-ophthalmologists use describe visual field abnormalities. Collaborative efforts can lead to more consistent terminology, improved communication between clinicians, and better patient care.

Patients with progressive NAION have no distinguishing clinical characteristics

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Purpose: to describe the demographics, clinical characteristics and visual outcome of patients with progressive nonarteritic anterior ischemic optic neuropathy (NAION) and to test the hypothesis that progression in NAION occurs in those presenting soon after symptom onset.

Methods: a retrospective chart review of all patients with NAION seen during the acute stage at a tertiary medical center from 1.2012 to 1.2018. We included patients with documented disc edema at the acute stage and follow-up of at least 3 months. Patients with progressive NAION were identified if they worsened in 2 out of 3 parameters: 1. visual acuity ≥ 3 Snellen lines, 2. Color vision ≥4 Ishihara plates, 3. The visual field defect involved a new quadrant (superior / inferior / nasal / temporal). The clinical characteristics, time from symptom onset to presentation, systemic risk factors and visual outcome were compared to patients with stable NAION. U Mann Whitney and Fisher's exact test were used for numerical and categorical variables respectively. R software for statistical computing was used for statistical analysis.

Results: 98 patients met the inclusion criteria. Seventeen (17.3%) patients had progressive NAION. Their mean age was 56.7 (range 22-74) and 76.5% were men. The most common risk factors were hypertension (in 47%) dyslipidemia (52.9%) and diabetes mellitus (29.4%). Patients with progressive NAION did not differ from stable NAION in their demographics, systemic risk factors or in time from symptom onset to presentation. They also did not differ in their initial visual acuity, color vision or visual field. At last follow-up, median visual acuity was 1.0 LogMAR (IQR 0.48-2) in patients with progressive NAION, vs 0.15 (IQR 0.04-0.6) in stable NAION ($p=9.083e^{-5}$). Median color vision testing was 0% plates correct (IQR 0-30%) vs 100% plates correct (IQR 50-100%) in the stable NAION group ($p=8.44e^{-5}$).

Conclusions: NAION with progression is not associated with the timing of presentation. We found no identifiable risk factors associated with progressive NAION. Since the mainstay of therapeutic research in NAION involves neuroprotection, future neuro-protective medications cannot be targeted to patients prone for worse visual outcome.

Technically Reliable, but Falsely Positive Automated Visual Fields – A Report of 7 Cases from a Neuro-Ophthalmology Practice

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Purpose: Automated visual field testing is challenging for patients to perform accurately. The test provides various indices of reliability, and these indices must be carefully considered when interpreting results. While results with normal reliability indices suggest that detected abnormalities are real, exceptions can occur.

Methods: Retrospective case series

Results: We present 7 cases of patients who presented with concerning visual field defects in tests that were performed with normal technical reliability indices, yet the results were subsequently determined to be falsely positive.

Conclusions: We suggest that when there is a lack of associated symptoms or other findings, that clinicians attempt to immediately repeat the visual field test to assess for reproducibility before initiating an urgent workup.

Osseous Metaplasia (Cataracta Ossea) of Lens Remnants in Chronic Uveitis

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Purpose: To describe clinically and pathologically the rare occurrence of calcification and osseous metaplasia in lens remnants in both eyes of a pseudophakic chronic uveitis patient, and the surgical treatment of this condition.

Methods: 25 gauge pars plana vitrectomy, removal of dislocated intraocular lens (IOL) and secondary IOL fixation in the left eye. Similar procedure was performed in the right eye with 27 gauge pars plana vitrectomy, using the Akreos 4-point scleral fixation technique with Gore-Tex sutures

Results: Hematoxylin and eosin stain demonstrate abundance of calcified tissue and rare osteoclasts in lacunae, compatible with osseous metaplasia (cataracta ossea)

Conclusions: To our knowledge this is the first clinico-pathological report demonstrating cellular metaplasia that resulted in osseous transformation of the cortical lens remnants into bone in both eyes of a psuedophakic patient with chronic granulomatous pan uveitis of unknown etiology. The surgical technique described in the videos demonstrates an effective way of managing this complication.

Mutations in two different genes cause a complex phenotype of high myopia and corneal dystrophy in the same family

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Purpose: To investigate the clinical presentation and the molecular basis of corneal dystrophy and high myopia in consanguineous Bedouin kindred.

Methods: Affected individuals underwent thorough ophthalmologic examination. Molecular analysis included whole-exome sequencing (WES) for the proband, and homozygosity mapping using 750k SNP arrays for the nuclear family. WES variants which passed a filtering cascade were screened using our in-house database of 250 ethnically-matched controls. Restriction length polymorphism (RFLP) and Sanger sequencing were used to validate segregation. cDNA, derived from patients and control leukocytes' RNA, was studied using Sanger sequencing and real-time quantitative PCR.

Results: Eight members of the studied kindred were found to have Reis–Bucklers corneal dystrophy. Two of them also exhibited very high infantile myopia. A novel intronic splicing mutation in *LRPAP1* (NM_002337.3: c.593-3C>G), was found in homozygous state only in the two individuals with myopia. The mutation segregated as a recessive trait, resulting in frame-shift and an early stop codon (p.I199Kfs*12) in the aberrantly spliced transcript. This novel (cryptic) acceptor-site was demonstrated using real time PCR to result in NMD (nonsense-mediated decay), as ~25% and ~50% of the normal LRPAP1 mRNA level were found in affected and carrier individuals, respectively.
A known mutation in *TGFBI* (NM_000358.2: c.1664G>A, p.R555Q (rs121909209) was found using WES analysis and was validated through Sanger sequencing, as a cause for the autosomal dominant corneal dystrophy in this family.

Conclusions: A complex phenotype in the studied kindred is caused by unrelated mutations in two genes: a mutation in ***TGFBI*** causing autosomal dominant Reis–Bucklers corneal dystrophy, and a novel mutation in *LRPAP1* causing autosomal recessive high myopia. This novel intronic splicing mutation in *LRPAP1* causes frame-shift and NMD of the transcript. This is a first report of a splicing *LRPAP1* mutation associated with autosomal recessive high myopia.

Case Series of Bilateral Idiopathic Multiple Pigment Epithelial Detachments

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Purpose: Pigment Epithelial Detachments (PEDs), elevations of the Retinal Pigment Epithelium (RPE) above the Bruch's membrane, are a common finding in retinal disease. They appear in Age-Related Macular Degeneration (AMD) and its variants (e.g., Polypoidal Choroidal Vasculopathy – PCV), several disorders of the RPE and other conditions. Here we describe the findings in three patients (2 males, 1 female) with presumed Idiopathic Multifocal Pigment Epithelium Detachments (IMPED), a condition first identified by Gass and colleagues and thus far described in only five patients in the literature.

Methods: A retrospective case series of three patients with the presumed rare diagnosis of IMPED.

Results: The three patients, in their forties, presented to the Hadassah Retinal Degenerations clinic between the years 2015-2018. All exhibited multiple bilateral PEDs on clinical examination and on wide-field fundus imaging, in the absence of drusen. We confirmed the classification of the lesions as PEDs by OCT. Notably, the patients demonstrated preserved visual acuity and an otherwise normal ophthalmic examination. Electrophysiological testing demonstrated normal retinal and RPE function by full-field electroretinography and electrooculography, respectively. Angiographic studies excluded the diagnoses of NVAMD and PCV. The patients remained stable during the course of follow-up, which was 7, 3.5 and 0.9 years for the study group (including revision of previous imaging studies), during which time we did not note any dynamic changes, either clinically or by ancillary testing.

Conclusion: While in themselves PEDs usually do not necessitate treatment, dynamic changes of PEDs have been associated with possibility of disease progression in AMD and were shown to herald a significant bleeding episode in PCV patients. Here we demonstrate that IMPED, despite being exceedingly rare, appears to represent a distinct clinical entity, seen in relatively young patients. The long-term implications and prognosis of these lesions are not known and warrant further follow-up.

The Effect of Q Score on Macular Thickness and Volume and Peripapillary RNFL Thickness Measurements Using OCT Spectralis

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Purpose: OCT is a non-invasive imaging test to evaluate macular integrity and peripapillary RNFL thickness. The results must be of high quality, to be reliable, reproducible and comparable to patients' previous scans. The Spectralis OCT image quality is expressed by the Q score. This study assessed the effect of the Q score on macular thickness, volume and the peripapillary thickness measurements.

Methods: In this prospective study, 42 eyes of 42 healthy subjects underwent multiple, consecutive scans using the “fast macular volume” and "Glaucoma RNFL" acquisition protocols to acquire images with varied Q scores by adjusting the focusing knob. The Spectralis Q score values are on a scale of 0-40, with 40 representing the best image quality.

Results: We found that all macular regions thickness and volume were significantly higher and showed high variability when Q measurements was below 15.
Q measurements below 20 consistently showed low intraclass correlation coefficients (ICC) in the thickness map of all regions.
Only volume measurements of Q values above 24 demonstrated high ICC.
As for RNFL thickness, we found no significant difference between different Q values.

ICC was acceptable or high in all Q values, in all regions, except for the superior temporal one in which ICC was low for Q value below 15.

Conclusions: Contrary to what was believed until now, the macular thickness and volume reproducibility are more quality dependet than RNFL reproducibility.

Recombinant Adeno-Associated Virus [rAAV9-7m8] Injected in the Peripheral Subretinal Space Spreads Beyond the Bleb Borders in Sheep.

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(1) Koret School of Veterinary Medicine, Hebrew University of Jerusalem, Rehovot, (2) Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, (3) Institute de la Vision, Paris, France, (4) ARO, The Volcani Center, Rishon LeZion.

Purpose: Subretinal injection of an AAV5 vector carrying the *CNGA3* transgene results in long-term recovery of photopic vision in *CNGA3*-mutant day blind sheep. However, the injection causes retinal detachment due to the formation of a subretinal bleb. This can be a grave complication in achromatopsia patients, as the injection is performed in the cone-rich macular region. Therefore, a vector that can be injected in the peripheral subretinal space and spread beyond the bleb borders, expressing its transgene in central retinal areas, may be highly advantageous. In this study we evaluated the capacity of an engineered AAV9 vector injected peripherally to express the GFP transgene beyond the injection site in sheep.

Methods: A modified AAV9 vector, carrying GFP under the control of a cone-specific promoter (AAV9-7m8-pR1.7-GFP), was injected subretinally in eight eyes of six AAV9 seronegative sheep. Two or three peripheral blebs, with combined volumes of 180-450 µL and combined total viral loads of 3*10e9 vg to 1*10e11 vg. GFP expression was monitored *in-vivo* every four weeks by fluorescent fundus photography.

Results: Severe posterior uveitis and retinal detachment were seen within 24 hours in three eyes injected with 370-450 µL (viral loads of 4-7.4*10e10 vg), making further follow up impossible. No complications were seen in five eyes injected with 180-300 µL (viral loads of 3*10e9 to 1*10e11 vg). In these, GFP expression was mild and restricted to the bleb areas in eyes injected with the lowest viral dose. Expression was more robust, and spread well beyond the original bleb areas in correlation with increased viral dose.

Conclusions: Large volumes ($\geq$370µL) and viral loads of AAV-9-7m8-pR1.7-GFP are immunogenic in the subretinal space. However, smaller volumes may be safely injected peripherally, and at high viral loads. The vector has the potential to spread beyond the bleb to the central retina..

The Effect of Reduced Contrast Sensitivity on Color Vision Testing

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(2) Ophthalmology Department, Tel Aviv Medical Center, Tel Aviv

Purpose: To assess the effect of reduced contrast sensitivity on three commonly used color vision tests, in order to establish key discrepancies that may be relevant for clinical practice.

Methods: A prospective non-interventional clinical study of color vision testing performed on 20 healthy subjects using three commonly used color-vision testing devices: Ishihara and Hardy-Rand-Rittler (H-R-R) pseudoisocochromatic plates tests, and Farnsworth D-15 arrangement test performed under progressively reduced contrast sensitivity conditions achieved with a neutral density filter bar.

Results: The Pelli-Robson contrast sensitivity (PRCS) at which 5% of the population should first experience a 10% reduction in color vision testing from baseline was calculated for each of the three-color vision devices: Farnsworth D15 test - 1.81 log contrast sensitivity (CS), HRR test - 1.69 log CS, and Ishihara test - 1.34 log CS. Single factor repeated measures analyses, conducted separately at each contrast sensitivity level revealed no difference between the color vision testing devices at PRCS ^{3}1.80 log CS (P^{3}0.234). However, in all PRCS ≤1.65 log CS, the differences were statistically significant (all P≤0.008), demonstrating a significantly lower percentage of errors in the Ishihara test compared with both the Farnsworth D15 ($P<0.023$) and H-R-R ($P<0.035$) tests.

Conclusions: At high contrast sensitivities, all color vision tests function almost equally, but at decreased levels of contrast sensitivity, H-R-R and Farnsworth D15 are more greatly affected.

Familial encephalopathy and ophthalmoplegia responsive to thiamine treatment

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(1) Department of Ophthalmology, Soroka Medical Center and Clalit Health Services, Faculty of Health Sciences, Ben-Gurion University, (2) The Morris Kahn Laboratory of Human Genetics at the National Institute of Biotechnology in the Negev and Faculty of Health Sciences, Ben-Gurion University, (3) Genetics Institute, Soroka University Medical Center, (4) Department of Imaging, Soroka University Medical Center, (5) Pediatric Neurology Unit, Soroka Medical Center and Faculty of Health Sciences, Ben-Gurion University, Beer Sheva.

Purpose: To investigate the clinical presentation and etiology of the disease in two brothers from a consanguineous Bedouin kindred who presented with acquired encephalopathy and ophthalmoplegia.

Methods: The patients underwent thorough ophthalmologic and neurological examination, as well as a complete metabolic workup. Visual fields, CT and MRI scans of brain and orbits, full field electroretinogram (FFERG) and flash visual evoked potentials (FVEP) were obtained. Molecular analysis included whole-exome sequencing (WES) of the DNA of one of the siblings.

Results: The two siblings, ages 16 and 13 years, had gradual onset of headache, vomiting, diplopia and strabismus. On examination they had nystagmus, ophthalmoplegia, exotropia, partial optic atrophy and visual field defects. Neuroimaging demonstrated encephalopathy consistent with Wernicke or Leigh syndromes. The results of metabolic work-up and of electrophysiological testing were unremarkable. Treatment with high doses of thiamine resulted in marked improvement of clinical and radiological signs: disappearance of headaches, strabismus and diplopia, increase in eye movement range and partial resolution of the brain lesions on MRI. WES analysis did not reveal any rare or known pathogenic variants in the nuclear-encoded genes associated with Wernicke or Leigh syndromes, or in the genes that have been previously reported in association with thiamine metabolism dysfunction syndromes.

Conclusions: Based on the clinical and radiological features, as well as marked improvement following the treatment with high doses of thiamine, our data suggest that the two siblings suffer from a novel thiamine-responsive dysfunction syndrome, whose molecular basis has yet to be elucidated.

Optic nerve crush causes increased damage to diabetic mice

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Purpose: To characterize the vulnerability of diabetic mice (DM) to ischemic optic neuropathy. Optic nerve crush (ONC) is a common model simulating optic neuropathy and is used in this study to evaluate the effect on DM.

Methods: To compare the effect of ONC induced in 7 NOD (NOD/ShiLtJ) and 8 homozygous db/db mice (C57BLKS/J-leprdb/leprdb) DM, type I and II respectively, to 6 wild type (WT) mice. The right optic nerve was crushed and the left served as control. The retinae were extracted for mRNA on day 3 and the optic nerves were gelatin fixated for histological analysis. The expression levels of HO-1 and SOD, stress related genes, were measured using RTPCR.

Results: Four of the 7 (57%) NOD mice survived the procedure and 6 (84%) of 7 db/db. All the WT survived. HO-1 levels significantly increased (4.5 folds) in the WT, remained baseline in db/db and decreased to 0.5 fold in the NOD. SOD levels did not change from baseline in the WT, mildly increased in NOD and decreased in the db/db. Optic nerve staining with luxol fast blue showed severe axonal loss in the diabetic nerves as compared with the WT.

Conclusions: DM are more sensitive to ONC damage and have more morbidity and mortality, especially type I (NOD). HO-1 is an important regulator of the Muller cells in the retina. Muller cells are affected in diabetes. While the levels of HO-1 were elevated in the WT we detected baseline levels (db/db) or decreased (type I, NOD) in the DM. SOD levels remained at baseline. This model can help to explore the pathophysiology underlying optic neuropathy in diabetic patients, and the differences between type I and II.

Glial fibrillary acidic protein (GFAP) and Aquaporin 4 (AQP4) expression are increased in the optic nerves of experimental autoimmune encephalomyelitis (EAE) induced NOD mice

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Purpose: To study the expression of Glial fibrillary acidic protein (GFAP), used as a **marker to** distinguish astrocytes from other glial cells, and Aquaporin 4(AQP4), a water channel protein associated with neuromyelitis optica spectrum disorder (NMOSD) in the optic nerves of NOD mice following induction of EAE, an animal model of demyelinating disease.

Methods : Experimental Autoimmune Encephalomyelitis (EAE) was induced using a subcutaneous immunization of myelin oligodendrocyte glycoprotein (MOG) 35–55 peptide in NOD mice .Whole length optic nerves to chiasms were dissected and analyzed for structural evidence of demyelination and astrocytic loss. Immunohistochemical and qualitative image analysis of fluorescence were performed using independent (two-tailed) T-test for the following primary antibodies: anti-GFAP, anti-AQP4 and anti-MOG.

Results: Both GFAP and AQP4 expression were increased in NOD EAE mice compared to NOD controls ($p<0.001$, $p< 0.05$, respectively).

Conclusions: In the EAE model in which mice are subcutaneously injected with MOG, optic neuritis is accompanied by an increased expression of astrocytes and AQP4. The increase in astrocyte and AQP4 expression may be part of a vicious cycle in which secondary exposure of the astrocytes occurs after the primary stage of inflammatory demyelination. The significance of these findings may be that increased AQP4 exposure continues a vicious cycle inciting further AQP4-antibody attack on the optic nerve. New complement inhibiting drugs being tested may offer a method to halt such a cascade which leads to axonal loss.

An optimized treatment for ocular organophosphate nerve agent insult

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Purpose: Eye exposure to organophosphate (OP) irreversible acetylcholinesterase inhibitors, results in long-term miosis and impaired visual function. The aim of the present study was to find an anti-cholinergic antidote, which would counteract miosis and visual impairment induced by the nerve agents sarin and VX with minimal untoward side-effects.

Methods: Rat pupil width and light reflex were evaluated from 15 min up to two weeks following topical OP exposure with or without topical ocular treatment of atropine or homatropine or with a combined intramuscular treatment of TMB-4 and atropine (TA). Visual function following insult and treatment was assessed using a cued Morris water maze task.

Results: Topical VX exposure showed a dose-dependent miosis with a significant reduction in visual function similar to the effect seen following sarin exposure. Homatropine (2%; w/v) and atropine (0.1%; w/v) treatment ameliorated both sarin and VX-induced miosis and the resulting visual impairment. TA treatment was sufficient in ameliorating the sarin-induced ocular impairment while an additional ocular treatment with either 0.1% atropine or 2% homatropine was necessary following VX exposure.

Conclusions: The use of 0.1% atropine or 2% homatropine was beneficial in ameliorating the ocular insult following VX or sarin ocular exposure and thus should be considered as universal treatments against this intoxication. The findings also emphasize the necessity of additional ocular treatment to the systemic treatment in visually impaired casualties following VX exposure.

A Novel Method for Automated Visual Field Testing on Eyes with Severe Central Vision

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Purpose: Reliable visual field testing requires the tested eye to be fixated on a target. This poses a major obstacle for eyes with severe central vision loss. This study presents a method that can be used if the fellow eye has sufficient visual acuity to reliably fixate.

Methods: A green filter was placed over the fellow eye. A Fastpac algorithm was used with a red stimulus. The green filter prevented transmission of the red stimuli, but allowed visualization of the white fixation light. Subjects were tested by both the conventional and the novel method, performed in a randomized order. The primary outcome was the degree of eye motion on gaze tracking.

Results: Eight subjects were recruited with visual acuity of hand motion or light perception in one eye and at least 6/60 in the fellow eye. In all cases there was less eye motion. A paired t test had a two-tailed p value of less than 0.0001. The mean reduction in motion was 69% (standard deviation 17%). Comparison between the novel and conventional method also demonstrated improved reproducibility in the mapping of the visual field.

Conclusions: The novel method described provided a dramatic improvement in reliability, and offers a feasible solution for visual field testing in patients with unilateral severe central vision loss.

Sensorimotor information and negative BOLD in the deprived visual cortex of congenitally blind

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Purpose: The human sensorimotor system is organized according to known topographic principles. Previous studies have investigated the cortical reorganization following the loss of a body part, the primary source and target of the sensorimotor cortex. However, the influence that other atypical sensorimotor experiences have on the properties of sensorimotor topography has been largely overlooked. Here we asked how the absence of vision from birth affects the topographic organization of sensorimotor cortices. Furthermore, we asked if body movements can recruit the deprived "blind" brain, and what is the spatial profile of such neural activations. We studied these questions by investigating the properties of cortical responses elicited by active movements in people who are congenitally blind in comparison to a sighted control group.

Methods: Nine sighted control and three congenitally blind participants were scanned in a 3-T MRI scanner, the functional data were gathered with a TR of 2 seconds and a voxel size of 2x2x2 millimeters. Subjects were asked to move 12 separate body parts on cue, with no interstimulus interval.

Results: Preliminary results reveal that congenitally blind subjects show ordinary sensorimotor topography along the Precentral and Postcentral gyri, similar to the sighted control group, which conform to the canonical homunculus. Whole brain analysis in the blind group shows that movements of the hands and face area resulted in neural responses in parietal and occipital cortices. Moreover, blind participants had Negative Blood-oxygen-level Dependent (BOLD) responses in associative visual areas around the Precuneus, Angular Gyrus, and Superior Occipital Gyrus.

Conclusions: The results of our ongoing study suggest that topography of primary sensorimotor cortices is not significantly affected by the absence of vision from birth and the atypical sensory and motor experiences that stem from congenital blindness. Upper body movements in congenitally blind result in positive BOLD activations in visual brain areas, which implies that sensorimotor representations might expand to adjacent cortical areas and all the way to primary visual cortex. Negative BOLD spatial patterns were previously discovered in primary motor cortices, our preliminary findings promote further investigation into similar patterns in the visual cortex of congenitally blind. The loci of deactivation fall on visuomotor integration centers, which could underlie a physiological as well as a functional phenomenon.

The Effect of Irrelevant Environmental Noise on the Performance of Visual-to-Auditory Sensory Substitution Devices Used by Blind Adults

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Purpose: Visual-to-auditory Sensory Substitution Devices (SSDs) are a family of non-invasive devices for visual rehabilitation aiming at conveying whole-scene visual information through the intact auditory modality. Although proven effective in lab environments, the use of SSDs has yet to be systematically tested in real-life situations. To start filling this gap, in the present work we tested the ability of expert SSD users to filter out irrelevant background noise while focusing on the relevant audio information.

Methods: Nine blind expert users of the EyeMusic visual-to-auditory SSD performed a series of identification tasks via SSDs (i.e., shape, color, and conjunction of the two features). Their performance was compared in two separate conditions: silent baseline, and with irrelevant background sounds from real-life situations, using the same stimuli in a pseudo-random balanced design.

Results: Although the participants described the background noise as disturbing, no significant performance differences emerged between the two conditions (i.e., noisy; silent) for any of the tasks. In the conjunction task (shape and color) we found a non-significant trend for a disturbing effect of the background noise on performance.

Conclusions: These findings suggest that visual-to-auditory SSDs can indeed be successfully used in noisy environments and that users can still focus on relevant auditory information while inhibiting irrelevant sounds. Our findings take a step towards the actual use of SSDs in real-life situations while potentially impacting rehabilitation of sensory deprived individuals.

Inter-ocular Changes in Visual Temporal Resolution Alters Binocular Summation

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Purpose: Binocular summation (BS), the process by which the brain combines the information received from both eyes, is widely studied in the spatial domain. Here we raise the hypothesis that, similarly to the spatial domain, the gain-control theory stating that information arriving from one eye exerts gain control over the other is valid in the temporal domain. We validate this hypothesis in amblyopic eyes where visual information is processed differently and slower compared with the fellow eye.

Methods: We explored temporal summation in the visual cortex, using a customized dichoptic system, which generates flickering light at various luminance and inter-ocular phase shift for the measurement of the Critical Frequency Fusion (CFF) using psychophysical tools and by recording visual evoked potentials (VEP).

Results: The CFF was measured in 15 normally sighted and 8 amblyopic subjects at different luminance levels under a binocular viewing condition. When no phase shift was introduced, BS was observed at low-luminance flickers in normally sighted but not in amblyopic subjects. In contrast, for the amblyopic subjects, a small phase shift (of 0.1π) resulted in a BS ratio of up to 1.13 at low luminance stimuli. In addition, BS was also observed in amblyopic subjects with conditions aimed at balancing eye performance by presenting lower luminance levels to the normal compared with the amblyopic eye. Furthermore, measure of VEP responses revealed a similar trend wherein introducing a phase-shift to normally sighted subjects decreased the amplitude in responses to binocular stimuli, whereas in amblyopic subjects the VEP amplitude in response to binocular presentation increased when a phase-shift was introduced.

Conclusions: Maintaining a balance between the eyes in the normally sighted and amblyopic subjects, showed that the gain-control model is also valid for in the temporal domain. Further exploring of the effect of BS enhancement in time or space domain is needed, an avenue which we are currently pursuing**.**

Eye tracking control in visual prostheses

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Purpose: Visual scanning by sighted individuals is done using eye and head movements. In contrast, scanning using the Argus II is solely done by head movement, since eye movements can introduce localization errors. Here, we tested if a scanning mode utilizing eye movements increases visual stability and reduces head movements in Argus II users.

Methods: Eye positions were measured in real-time and were used to shift the region of interest (ROI) that is sent to the implant within the wide field of view (FOV) of the scene camera. Participants were able to use combined eye-head scanning: shifting the camera by moving their head and shifting the ROI within the FOV by eye movement. Ten blind individuals implanted with the Argus II retinal prosthesis participated in the study. A white target appeared on a touchscreen monitor and the participants were instructed to report the location of the target by touching the monitor. We compared the spread of the responses, time to complete the task, and amount of head movements between combined eye-head and head-only scanning.

Results: We demonstrated that by correlating the pupil location at the onset of the stimulation with the head-centered percept location we can calibrate and align the eye tracker on Argus II users. All participants benefited from the combined eye-head scanning mode. Better precision, i.e. narrower spread of the perceived location, was observed in 8 out of 10 participants. Nine of 10 were able to adopt a scanning strategy that enabled them to perform the task with significantly less head movement.

Conclusions: Our experimental results, with implanted blind patients, show that integrating a calibrated eye tracker reduces the amount of head motion and improves visual stability in Argus II users.

Study the roles in eye development of BAF155 and BAF170 - the subunits of the chromatin remodeling Swi/Snf complex

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Purpose: A major challenge in developmental neuroscience is to uncover how specific cell fate is programmed at the epigenetic level and to resolve the interplay between chromatin modifiers and tissue specific transcription factors that control lineage specific developmental programs. The ATP-dependent chromatin-remodeling mSWI/SNF (or Brg/Brm-associated factor, BAF) complex is emerging as non-redundant component required for the coordinate activation or repression of gene expression programs during the acquisition of distinct neural cell fates. The **aim** of this study is to uncover the roles of BAF155 and BAF170, which are two important components of the complex, in the developing retinal pigmented epithelium (RPE), a polarized single layer epithelium located between the photoreceptors and the choroid vascular system and is required for their development and function.

Methods: Cre/loxP mutagenesis in developing mouse RPE is underway. The analysis includes histological analysis to identify changes in cell and tissue morphology, molecular analysis to determine changes in gene expression by antibody labeling of specific genes of the RPE.

Results: We generated conditional mutant mice carrying floxed alleles of BAF155 and BAF170 together with RPE specific Cre line (Dct-Cre). The comprehensive phenotypic analyses is underway and is conducted on allelic series of conditional mutations in the BAF155 and BAF170 genes. The results reveal redundant activity of BAF155 and BAF170 genes in RPE differentiation. However the loss of both subunits results in Anophthalmia due to complete arrest in the differentiation of the pigmented lineages of the eye.

Conclusions: BAF155 and BAF170 genes are critical for differentiation of the pigmented lineages of the eye.

The role of the LIM homeodomain 2 (Lhx2) in differentiation of the Mammalian Retinal-Pigmented Epithelium (RPE)

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Normal vision depends on the retinal pigmented epithelium (RPE), a metabolic cell layer vital for development and function of the adjacent retinal photoreceptors. However, the transcriptional regulatory program in the course of RPE differentiation and maintenance is still unclear. Lhx2 is a LIM homeodomain (LIM-HD) member required for the early morphogenesis and patterning of the vertebrate eye.

Purpose: Our current objective is to uncover the roles of Lhx2 complex in the differentiation of the mammalian RPE.

Methods: We have established Lhx2 conditional mutant (cKO) in the mouse RPE. Moreover, to study the role of Lhx2 in human RPE and to further identify direct targets of Lhx2 we utilize RPE generated from human embryonic stem cells (hES-RPE) for chromatin immunoprecipitation followed by sequencing (ChIP-Seq) and for functional studies using lentiviral knockdown approach.

Results: Initial morphological and immunofluorescence analyses of Lhx2 cKO RPE mutants show altered morphology and reduced expression of early RPE key transcription factors. Further investigation of Lhx2 binding sites followed by their annotation, mapped the regulatory elements associated with specific key transcriptional regulators of the RPE.
Considering the importance of RPE for retinal physiology and the recent advance in using hES-RPE for cell-replacement therapy this study will contribute to uncover gene regulatory networks (GRNs) down stream of Lhx2, involved in RPE fate and function.

Carbon nano tubes as a scaffold for hESC differentiation into photoreceptor precursor cells

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Purpose: Carbon Nanotubes (CNTs) have been introduced as an efficient scaffold and interface in various biological applications due to their physical (mechanical and thermal) and electrical properties. Their physical properties are known to influence stem cell proliferation and differentiation, and are therefore used as a scaffold for in vitro differentiation studies and as scaffold for implantation in vivo. Here we introduce our approach of utilizing CNTs as a scaffold for the differentiation of human embryonic stem cells (hESCs) into photoreceptor precursor cells (PRPs) and report preliminary results of the investigation of cell morphology and cell-surface interface and the effect of the CNTs on the differentiation process.

Methods: Three different CNTs types were produced :multiwalled- either vertically or horizontally aligned, and Carbon Nano Fibers (CNFs) 'spaghetti'. CNTs were characterized using SEM imaging. PRPs were obtained from GFP-expressing hESC, following a 24 day differentiation protocol, recently optimized by our group. hESC spheres were seeded on the various CNTs type at day 7 and differentiated until day 24. Biocompatibility of CNTs was assed using 7AAD staining for viability examination. Morphological analysis was achieved through SEM and confocal microscopy and focal adhesion of cells was characterized using actin staining (Phalloidin) and vinucilin..

Results: When comparing hESC differentiation on standard coverslips to differentiation on the various CNTs types, we observed that cells differentiated on CNTs demonstrated comparable viability to those differentiated on coverslips. Interestingly, morphological analysis revealed these cells preferentially grew from the spheres in the directionality of the CNT surface. Cells differentiated on the horizontally aligned fibers assumed the directionality of the fibers whereas on others no significant directionality was observed. Interestingly, cell differentiated on CNF had more protrusions than on the other surfaces.

Conclusions: These results highlight the feasibility of using CNTs as an efficient scaffold for cell differentiation and could form the basis of an innovative approach for vision restoration in patients suffering from outer retinal degeneration in which a directionality in the transplanted cells is desired.

A Putative Missense Mutation in *TUB* in Druze and Arab Patients with Autosomal Recessive Retinitis Pigmentosa

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Purpose: To identify the genetic basis for autosomal recessive retinitis pigmentosa (arRP) among Israeli Druze and Arab patients.

Methods: Genetic analysis was performed by a combination of Whole Exome Sequencing and Sanger sequencing. Western blot and immunostaining of transfected cells were used for analysis of expression level and cellular localization of the mutant protein.

Results: A putative missense mutation in the *TUB* gene, p.E424K, was found homozygously in four RP patients from two consanguineous Druze families and in one Muslim Arab patient from the Jerusalem area. This mutation is rare, affects a highly conserved amino acid, and predicted pathogenic by several prediction tools. The carrier frequency of the p.E424K allele among Druze from Northern Israel is high (7%). However, the frequency of this allele was significantly higher in the patient group versus the control group. Western blot and immunostaining of COS-7 cells transfected with wt and p.E424K TUB revealed no difference in expression level or in cellular localization.

Conclusions: *TUB* mutations cause photoreceptor degeneration in mice, and in a single human family from the UK. Here we report a putative novel *TUB* mutation in several RP patients. The pathogenicity of this mutation is still to be confirmed.

The Complex Expression Pattern of FAM161A which is the most Common Cause of Retinitis Pigmentosa in Israel

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Purpose: *FAM161A* mutations are the most common cause of retinitis pigmentosa (RP) in the Jewish Israeli population. *FAM161A* was reported to produce two major transcripts by alternative splicing of exon 4, which is highly conserved. Our major purpose was to better define the expression pattern of the human and mouse *FAM161A* orthologs. This is likely to result in better understanding of the active isoform/s and therefore is crucial for planning vectors for gene therapy.

Methods: RNA-Sequencing (RNA-seq) data from various tissues in humans and mice were collected from previous publications and mainly from the National Eye Institute (NEI) Commons Database. Aligned BAM files were analyzed using Integrative Genomics Viewer (IGV). Primers for suspected *FAM161A* exons were designed using Primer3 and were used for RT-PCR reactions.

Results: We analyzed a total of 12 RNA-seq experiments (4 human and 8 mouse datasets) of various tissues, and mainly WT and NRL-KO mouse retinal samples. We identified a total of 10 different exons, 7 of which are coding. A detailed analysis of RNA-seq reads across exons, revealed that 63% include exon 4, while only 37% lack this exon, which is not in-line with current knowledge. Interestingly, about 20% of the exon 4- containing transcripts, are not spliced to exon 5, but rather include the whole intron 4 or in some cases use a nechenwly identified donor splice-site within intron 4. Using RT-PCR we verified the inclusion of most newly suspected exonic regions, and additional experiments are currently being performed.

Conclusions: Our data show that the expression pattern of *FAM161A* is much more complicated than others and we previously predicted. In addition, since RP-causing mutations were identified in exon 4, we predict that exon-4 containing transcripts might encode for the most important functional isoforms of FAM161A in the retina. Additional experiments are being done to elaborate on this aiming to correctly design the transcripts for AAV-based FAM161A gene therapy.

A *Drosophila* model for a Dehydrodolichyl Diphosphate Synthase (DHDDS) mutation causing Retinitis Pigmentosa in humans

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Purpose: A founder mutation in the Dehydrodolichyl Diphosphate Synthase gene (*DHDDS*) was reported in 2011. This mutation induced non-syndromic retinitis pigmentosa (RP) in Ashkenazi Jews. The DHDDS enzyme is known to be involved in dolichol synthesize, a lipid molecule that is important for various biological functions, including N-glycosylation. The fact that patients with a DHDDS mutation do not suffer from other clinical problems is surprising because genetic defects in related enzymes cause a systemic phenotype with involvement of multiple organs. The mechanism by which DHDDS variants cause non-syndromic RP is still unknown. We hypothesize that the genetic defect in *DHDDS* partially affects N-glycosylation, causing stress in the metabolically active photoreceptor cells, resulting in their gradual degeneration. Aiming to shed light on DHDDS activity and its function in retinal cells, we propose to analyze a *Drosophila* transgene with knockdown of DHDDS.

Methods: We generated a stable *Drosophila* line in which the *CG10778* gene, the *Drosophila* ortholog of human *DHDDS*, is knocked down by RNAi in the retina (DHDDS-RNAi).

Results: Analysis of these transgenic flies using electron microscopy and functional analysis by electroretinography revealed a unique pattern of retinal degeneration. Genetic analysis showed that knockdown of the *CG10778* gene in total body, or whole wings or in the whole eye caused damage to fly development resulting in lethality, or wing absence or large reduction in eye size, respectively. Electrophysiological assay of the fly rhodopsin level using the Prolonged Depolarizing Afterpotential (PDA) pointed to a drastic reduction of rhodopsin level in the DHDDS-RNAi flies when the RNAi driver was specifically directed to the retina of transgenic flies. This conclusion was strongly supported by Western blot analysis showing directly a pronounced reduction in rhodopsin expression in these specific DHDDS RNAi flies.

Conclusions: This study is expected to allow a better understanding of DHDDS function in the retina and in the future, this information might allow development of a supplemental diet for the patients, aiming to slow-down or even halt the retinal degeneration process.

SCAPER localizes to primary cilia and its mutation causes human ciliopathy syndrome.

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Purpose: To investigate the clinical presentation and the molecular basis of Bardet-Biedl syndrome (BBS) in a consanguineous Bedouin kindred.

Methods: Eight affected individuals underwent clinical phenotyping. Whole-exome sequencing (WES), 750k SNP array, Sanger sequencing and restriction length polymorphism analysis were done. WES variants which passed a filtering cascade were screened through our in-house database of 325 ethnically-matched controls. Wildtype and mutant SCAPER cDNAs, tagged with FLAG or fluorescent proteins, were transfected into several cell lines, analyzed through western-blotting, immuno-fluorescence and live cell imaging. Patients primary fibroblasts were studied (immuno-fluorescence, SEM).

Results: Phenotyping delineated clinical criteria of BBS, with intellectual-disability, RP, obesity and brachydactyly. A novel disease-causing mutation in *SCAPER* (c.2806delC, p.(L936*), NM_020843.2) was found (LOD score 3.88; verified through segregation analysis and no homozygosity in 325 ethnically-matched controls). The translated protein was observed ~50kDa smaller than WT-SCAPER. In transfected cells, the aberrant protein remained sequestered to the primary cilia- mostly at their tip, while the WT was rarely localized along the ciliary axoneme and basal-body. High expression of both WT and mutant SCAPER resulted in formation of microtubule-bundles. Live cell imaging recapitulated SCAPER localization to primary cilia, affecting microtubules during mitosis. SEM studies did not demonstrate structural differences in primary cilia of patient-derived fibroblasts vs controls. However, longer cilia were demonstrated in cells transfected with mutant-SCAPER vs WT, as well as in human affected fibroblasts vs controls.

Conclusions: SCAPER mutations were previously shown to cause RP. We now show that SCAPER plays a role in ciliary dynamics, affecting microtubule-related mitotic progression and cilia length, in line with its peak expression at late G1 and S phase, during ciliary resorption. Thus, SCAPER mutation causes a ciliopathy syndrome– BBS**.**

Infectious knockdown of CREB and HIF-1 for the treatment of metastatic uveal melanoma

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Purpose: To date, there are no effective treatments for metastatic uveal melanoma. We have previously shown that knockdown of the hypoxia regulator gene CREB is effective against uveal melanoma in vitro. The purpose of this study is to test the effect of infectious knockdown of CREB and HIF-1 in vivo.

Methods: Uveal melanoma cells (Mel270) expressing luciferase and infected with a MuLV-based replication competent retroviral (RCR) vector expressing either vACE-CREB, vACE-HIF-1 or vACE-NT (non-target) as a control, were injected subcutaneously over the front shoulder of SCID mice (5 mice per treatment). Tumors were followed weekly via bioluminescence (IVIS, Life Science). After 5 weeks, tumors were excised and measured. Use of animals had been approved by the IACUC of the Hebrew University of Jerusalem, Israel and complied with the ARVO Statement for the Use of Animals in Ophthalmic and Visual Research.

Results: Tumors infected with the armed viruses that knock either CREB or HIF-1 show a flat growth curve as opposed to the steady fast growth of the control tumors. At the end of the experiment, the mean weight of the tumors infected with an armed virus knocking down HIF-1 is only 42% of the mean tumor weight of the control tumors, and the mean weight of the tumors infected with an armed virus knocking down CREB is only 16% of the mean control tumor.

Conclusions: Infectious knockdown via armed viruses targeting the hypoxia regulators CREB and HIF-1 is effective against metastatic uveal melanoma in vivo.

Distinct biological types of ocular adnexal sebaceous carcinoma: HPV-driven and virus-negative tumors arise through non-overlapping molecular-genetic alterations

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.**Purpose:** Ocular adnexal (OA) sebaceous carcinoma is an aggressive malignancy of the eyelid and ocular adnexa that frequently recurs and metastasizes, and effective therapies beyond surgical excision are lacking. There remains a critical need to define the molecular-genetic drivers of the disease to understand carcinomagenesis and progression and to devise novel treatment strategies.

Methods: We present next generation sequencing of a targeted panel of cancer-associated genes in 42 and whole transcriptome RNA sequencing from 8 OA sebaceous carcinomas from 29 patients.

Results: We delineate two potentially distinct molecular-genetic subtypes of OA sebaceous carcinoma. The first is defined by somatic mutations impacting TP53 and/or RB1 (20/29 [70%] patients, including 10 patients whose primary tumors contained co-existing TP53 and RB1 mutations) with frequent concomitant mutations affecting NOTCH genes. These tumors arise in older patients and show frequent local recurrence. The second subtype (9/29 [31%] patients) lacks mutations affecting TP53, RB1, or NOTCH family members, but in 44% (4/9) of these tumors, RNA sequencing and in situ hybridization studies confirm transcriptionally active high-risk human papillomavirus (HPV). These tumors arise in younger patients and have not shown local recurrence.

Conclusions: Together, our findings establish a potential molecular-genetic framework by which to understand the development and progression of OA sebaceous carcinoma and provide key molecular-genetic insights to direct the design of novel therapeutic interventions.

In vivo keratometric changes in rabbit eye induced by topical 17β-estradiol

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Purpose: In vitro, 17β-estradiol (E2) has been shown to modulate the bio-mechanical properties of the cornea, causing a reduced stiffness of the tissue. In light of these reports we hypothesized that topical E2 might affect the refractive properties of the cornea inducing a myopic shift in-vivo.

Methods: A dozen of New Zealand white rabbits aged 16 weeks were used.. The rabbits were randomly divided equally to either the treatment group receiving 1.5% (w/v) E2 eye drops or control group receiving vehicle only. Both groups were given drops (50 µL) to the right eye twice daily 12 hrs apart for 35 days. Keratometry and refraction were evaluated at baseline and on a weekly basis using Righton Retinomax K-plus 3. Pachymetry and intraocular pressure (IOP) were evaluated as well.

Results: No significant differences were observed between the two groups at baseline. As expected from previous studies (Riau et al. 2012), both groups displayed corneal flattening and hyperopic shift in keratometry, however the change-rate was slower in the treatment group (Figure 1). Repeated measure analysis adjusted for baseline weight and pachymetry revealed a significant difference in keratometry between groups ($P = 0.034$) with mean higher keratometry values in the treatment group by up to 0.6 diopters. The difference between the two groups diminished and became statistically insignificant after stopping treatment. No significant changes were observed in terms of IOP and pachymetry throughout the study period. None of the rabbits showed signs of inflammation or any other side-effect in either group.

Conclusions: 1.5 % (w/v) E2 eye drops applied BID induced a myopic shift by affecting keratometry in the rabbit eye. Further investigation to the physiology of this change is needed.

Ocular Magnetic Neurostimulation Promotes Healing of the Corneal Epithelium in Dry Eye Patients

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Purpose: To investigate the effects of a novel treatment with ocular magnetic neurostimulation on corneal epithelial defects and subjective symptoms scores in patients with moderate to severe dry eye disease.

Methods: One eye of each of 9 patients with moderate to severe dry eyes (Sjogren's syndrome, meibomian glands disease) was exposed to 11 minutes of ocular magnetic neurostimulation at 45% intensity, 20 Hz (EpiTech Mag Ltd. protocol). The eye with the more severe corneal staining was treated, while the other eye served as a control. Two microliters of 10% sodium fluorescein solution were instilled in the inferior fornix of each eye, and fluorescein staining of the corneal epithelium was assessed by slit lamp photography and subjective scoring according to the NEI grid scheme. Assessment was performed before treatment, and at 1 hour, 1 day, 1 week (w), and at 1, 2 and 3 months after treatment, respectively. Schirmer's test and fluorescein break up time were also recorded at these time periods. Subjective symptoms scores were evaluated using a dedicated questionnaire, and lubricants consumption was documented. Enrollment of additional patients is ongoing.

Results: Significant reduction of the corneal epithelial staining in treated vs. untreated eyes, relative to baseline, was recorded at 1w (2.2 ± 0.7 vs. -0.5 ± 0.9, $p=0.014$), 4w (3.3 ± 1 vs. 0.4 ± 0.9, $p<0.01$) and 8w (6.1 ± 1.7 vs. 1.8 ± 1.5, $p=0.024$) after magnetic neurostimulation treatment. Significant improvement in symptoms scores was recorded in both eyes at 8w vs. baseline (29.8 ± 4.2 vs. 45.1 ± 2.4, $p<0.01$). Patients reported substantial reduction in overall lubricants consumption. No treatment or device related adverse events were reported.

Conclusions: Ocular magnetic neurostimulation promotes significant healing of the corneal epithelium and substantial reduction of symptoms in moderate to severe dry eye disease.

MicroRNA-184 controls corneal stromal thickness, epithelial cell proliferation, adhesion and response to injury

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Purpose: Our goal was to investigate the involvement of miR-184 in eye development, stem cell differentiation and disease. MicroRNAs (miRNAs) play a role in various physiological processes including embryogenesis, tissue regeneration and diseases. MiR-184 is a highly evolutionally conserved miRNA and the most abundant miRNA in the cornea and lens. In addition, loss-of-function point mutations in miR-184 were linked with familial severe keratoconus, cataract, combined with corneal endothelium defect. Interestingly, while the structure mostly affected in these patients is the corneal stroma, this miRNA is expressed by corneal epithelial cells.
Methods: we have generated a new *MIR184*- knock out (KO) mice and analyzed eye phenotypes including corneal thickness, lens size, shape, and transparency under the binocular, by ultrasound (US), optical coherence tomography (OCT), histology, electron microscopy, immunofluorescet staining and in situ hybridization. To define the molecular network downstream miR-184 and identify cellular processes controlled by miR-184, we performed comparative transcriptome analysis of the corneal epithelium of each genotype by RNA Sequencing (RNAseq).
Results: Histology, US and OCT revealed 15-20% thinning of the corneal stroma of miR-184-null mice. No gross phenotype was found in the lens of miR-184-KO animals. The corneal epithelium of KO mice showed enhanced expression of the proliferation (Ki67) and stem cell (K15) markers, in line with reduced clonogenic potential of limbal epithelial stem/progenitor cells following miR-184 knock down. RNAseq revealed changes in genes that control cell-cell adhesion, adhesion to the basement membrane and response to injury in KO mice. In line, isolated sheets of miR-184 transfected cells showed higher resistance to vortex in vitro while occasional detachment of the corneal epithelium from its underlying stroma and thickening of the basement membrane in the KO mice. Finally, abnormal response to injury was evident in KO mice as compared to wild type counterparts.

Conclusions: Loss-of-function mutation in miR-184 lead to keratoconus and cataract. In line, miR-184-KO showed reduced corneal stromal thickness but no lens phenotype, suggesting of species differences. Notably, this study suggests that miR-184 controls corneal epithelial cell-cell adhesion, cell adhesion to the basement membrane and epithelial healing after injury. We are currently investigating the mechanisms by which miR-184 acts to control these processes.

Loss of the entire limbal stem cell compartment can be repaired by dedifferentiation of corneal committed cells if the niche is intact

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Purpose: To explore tissue cell plasticity and ability of dedifferentiation of committed cells into bona fide limbal stem cells (LSCs)

Methods: We used K15-GFP transgene that labels the limbus with green fluorescent protein and R26R-Confetti;K14-CreERT2 that allows multi-color cell lineage tracing of LSCs with 4 different fluorescent genes. Surgical removal of K15-GFP+ limbus was followed by monitoring potential SC recovery (K15-GFP) and cell origin (Confetti label) in real time under anesthesia.

Results: We discovered that K15-GFP transgene labels LSCs that were located at the margin site of corneal regeneration, as evident by lineage tracing. Remarkably, surgical deletion of the entire LSC pool was restored by Confetti+ corneal committed cells which underwent dedifferentiation into bona fide LSCs. The recovered corneas displayed normal marker expression and appropriate dynaic of LSC regeneration. Interestingly, however, damage to the limbal stromal niche abolished K15-GFP recovery and led to loss of corneal transparency. The underlying mechanism was also investigated.

Conclusions: Altogether, this study indicates that committed corneal cells have large plasticity to dedifferentiate, repopulate the SC pool and correctly reform tissue boundary. By contrast, loss of SC and boundary of the cornea lead to impaired tissue functionality and pathology. We provide mechanistic insights and direct evidence that pathological wound healing by conjunctival cells that was accompanied by neovascularization, loss of transparency and blindness.

P63 plays a key role in corneal development, homeostasis and disease

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Purpose: To investigate the role of P63 in limbal stem cell regulation and deficiency

Methods: We have generated a new knockin mouse model of $P63^{L514F}$ allele that causes ectodermal dysplasia and limbal stem cell deficiency (LSCD) in human. The corneal phenotype of $P63^{+/L514F}$ mutant and P63-null was explored in embryos by immunofluorescent staining and histology. To avoid premature lethality, we have generated a conditional $P63^{L514F}$ knockin mouse model that is controlled by PAX6 regulatory region and is activated at early eye development. We characterized the gross eye phenotypes by histological and immunostaining analyses in homeostasis and following corneal epithelial injury using Algerbrush. To unravel the abnormal pathways in mutant, we performed RNA sequencing (RNAseq) of the corneal epithelium of mutants and control littermates. Further analysis was performed to identify key genes that are differentially expressed in health and disease conditions.

Results: P63-null mice abnormally expressed the ectodermal markers K8/18 and significantly lower levels of the corneal epithelial progenitor and differentiation markers (e.g. K12, K5, K15) suggesting for a developmental failure. In line, the constitutive $P63^{L514F/+}$ mice displayed defects in corneal epithelial commitment and stromal thinning. Interestingly, the conditional $P63^{L514F/+}$ mice displayed multiple eye abnormalities that are reminiscent of defects found in patient that are carriers of the same mutation. These phenotypes include mild corneal opacification and neovascularization, eyelid and eyelash defects. Furthermore, the conditional mutated mice showed impaired repair following surgical wound compared to control. Finally, RNAseq analysis revealed that P63 controls diverse pathways related to regulation of cell localization, adhesion and migration, while P63-mutation leads to enrichment of pathways related to mucus secretion, immune response and chemotaxis.

Conclusions: Altogether, we propose that P63 plays a key role in regulating corneal morphogenesis and that P63-related pathology involves a developmental failure. In addition, this study demonstrates that limbal stem/progenitor cell state is controlled by P63 while mutations in P63 disrupt epithelial homeostasis, leading to loss of corneal transparency and

blindness. A better understanding of the molecular circuitry that is controlled by P63 will pave the way to novel therapeutic approaches for corneal pathologies.

A comprehensive analyses of corneal mRNA level, during sulfur mustard induced ocular late pathology in the rabbit model, using RNA-sequencing

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Purpose: Exposure to sulfur mustard (SM) may result in a severe ocular injury. While some of the eyes show a clinical injury resolution (defined as clinically non-impaired), part of the eyes develop irreversible late ocular pathologies (defined as clinically impaired) that may lead to corneal blindness. Understanding the pathological mechanisms underlying the development of the late pathology may lead to improved treatment options. Therefore, this study aimed to investigate the mRNA expression profile of corneas from clinically impaired eyes, clinically non-impaired eyes and naive eyes.

Methods: Rabbit eyes were exposed to SM vapor and a clinical follow-up was carried out up to 4 weeks using slit lamp microscope. At this time point, corneal samples from clinically impaired, clinically non-impaired and naïve eyes were processed for mRNA differential expression analyses using RNA-sequencing (RNA-seq) application. The differential expression profiles were further processed for pathway enrichment analysis using Ingenuity Pathway Analysis (IPA). Real-time PCR was used for RNA-seq validation.

Results: The late pathology developed in 54%-80% of the eyes following SM ocular exposure, clinically manifested by inflammation, corneal opacity and neovascularization. RNA-seq results showed significant differences in mRNA levels of hundreds of genes between clinically impaired, clinically non-impaired and naïve corneas. Pathway enrichment analysis showed common pathways that were activated in all of the exposed eyes, such as Th1 and Th2 activation pathway, in addition to pathways that were activated only in the clinically impaired corneas, such as IL-6 and ERK5 signaling.

Conclusions: Corneal mRNA expression profiles for the clinically impaired, clinical non-impaired and naïve corneas generated a comprehensive whole transcriptomic database that revealed new factors and pathways that for the first time were shown to be involved in SM-induced late pathology. This data may contribute to the research on both the pathological mechanisms that are involved in the late pathology and the protective pathways that are activated in the clinically non-impaired eyes and may point out towards novel therapeutic strategies.

The Outcomes of Descemet Membrane Endothelial Keratoplasty for Secondary Penetrating Keratoplasty Graft Failure

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Purpose: To present the clinical outcomes of Descemet Membrane Endothelial Keratoplasty (DMEK) performed for Secondary Penetrating Keratoplasty (PKP) graft failure.

Methods: A retrospective review of medical records of patients that underwent DMEK for failed PKP at Hadassah Medical Centre in 2018. Visual acuity was measured according to Snellen chart. Pachymetry was assessed pre and post operatively by anterior OCT (Casia II). Endothelial cell count was measured by specular microscopy. Descemet membrane (DM) was stripped from the posterior stroma so that a 7.5- to 9.5-mm diameter flap of posterior DM with its endothelial monolayer was obtained. The graft size was assessed pre operatively according to the original PK graft size and posterior morphological features such as graft-host interphase scarring and anterior synechiae, examined by anterior OCT (Casia II).

Results: Included were 15 patients (8 males) and 15 eyes. Mean age at performing DMEK was 63 years. Before performing DMEK for failed PKP, 9 eyes underwent one PKP, 5 eyes underwent two PKP's and 1 eye underwent three PKP's. Mean visual acuity before DMEK was 0.04, one month after DMEK was 0.16 and at last follow-up (between 3-6 months after DMEK) increased to 0.3 (**P=0.001). Mean Central Pachymetry before DMEK was 685 (μm), one month after DMEK decreased to 574 (*P=0.04) and at last follow-up (between 3-6 months after DMEK) decreased to 542 (μm) (**P=0.008). Of the 15 eyes, 11 eyes had clear corneas at last follow-up, only three eyes required re-bubbling in the early postoperative phase, one eye needed secondary DMEK because of primary failure and no graft rejection episodes were seen.

Conclusions: DMEK may be a viable option to manage secondary PKP graft failure. It has successful outcomes in many cases and high opportunity to improve visual acuity. Even though the outcomes of DMEK after PKP are not as successful as those after primary PKP, still DMEK after PKP is a promising procedure that provides many advantages like minimally invasive procedure, avoidance of "open sky" surgery and sutures, ocular surface and wound healing complication and lower risk of allograft rejection.

Mechanical analysis of Epiretinal membranes studied by A 3D geometrical computer-aided design model

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Purpose: Epiretinal membranes (ERM) are transparent membranes located on the surface of the neurosensory retina, and constitute the most common type of fibrocellular proliferation. The principal clinical importance of ERMs lies in their tendency to contract. Although they may be asymptomatic in some patients, their progression and thickening may result in macular traction, thus distorting and inducing loss of central visual function and metamorphopsia. There is currently no known data regarding the predictability of ERM behavior, that is to say, which ERM will remain stable and asymptomatic and which will evolve to severely impact the patients' quality of life. In order to further our knowledge and understanding of this condition, we aim to study the mechanical phenomena and properties of ERMs on a 3D geometrical model computer-aided design (CAD), applying numerical model and simulation of the mechanical loads using finite elements (FE) and analyzing the strains and stresses in the model.

Methods: The 3D geometrical model was constructed with Solidworks 3D CAD software (Dassault Systemes Solidworks corp., USA). Static Structural simulations were conducted utilizing Ansys FE software (Ansys, USA).

Results: The model was constructed of a thick layer simulating the human retina in the macular region, on top of which lays a thin sheet simulating the ERM. We have also devised small bumps on the retina mimicking grasping points between the retina and the ERM. During the simulation, we performed a 1 mm pull of the edges of the membrane, in 4 different directions, after which the edges were released. In order to simulate real membrane behavior closely as possible, during each stage of the simulation we defined different types of contact between the retina and the membrane, except for the 4 grasping points, which remained stable throughout the simulation. The same simulations were carried out on different models that differed from each other in the number of grasping points.

Conclusions: We Present our 3D geometrical model of an ERM attached to a retina, and our preliminary results utilizing it to assess the mechanical loads these membranes produce and their properties.

Retinal thinning in Gaucher patients as a predictive test for developing Parkinson's disease

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Purpose: Gaucher disease (GD) is a rare autosomal-recessive lysosomal disorder. Type-1 GD (GD1) is the most common form in the western hemisphere. Ocular involvement in GD1 is uncommon and includes both anterior and posterior segment manifestation. Parkinson disease (PD) and GD have been known to be linked by mutations in the glucocerebrosidase gene, which are considered most common genetic risk factor for PD. Several studies have described correlation between retinal thinning and PD severity. Retinal thinning may serve as a predictor as to which GD patients will develop PD.
The aim of this study was to evaluate the retinal thickness of patients with GD1 compared with healthy control group.

Methods: Macular and optic nerve OCT scans of 30 GD1 patients and 30 healthy volunteers between the ages of 40 and 75 years were evaluated prospectively using swept-source optical coherence tomography (OCT) (DRI OCT-1 Atlantis; Topcon, Tokyo, Japan). Measurements of the RNFL, GCC (from the internal limiting membrane (ILM) to the inner nuclear layer) total retina thickness (from the ILM until retinal pigment epithelium) and macular volume were assessed using automatic segmentation. Each area of the ETDRS grid was compared between the two groups. We also performed autorefraction test to all patients. Patients with a known neurodegenerative disease, PD, high myopia (-6.0 D>) or glaucoma were excluded. For independent samples the Mann-Whitney U test was performed. The Wilcoxson Signed Rank test was used to compare related samples.

Results: Both groups were similar in terms of age, gender and refraction. The average RNFL thickness of patients with GD1 measured 97.66± 8.84 μM. This was significantly thinner than the control group which measured 105.9± 9.05μM ($P<0.05$). The GCC complex was significantly thinner in two distinct areas- the outer nasal and inferior sections of the ETDRS grid. The average GCC, total retinal thickness and macular volume did not differ between the two groups.

Conclusions: Patients with GD1 have significantly thinner RNLF than the healthy population. Further investigation is needed since this finding can be a result of pathological processes of the disease or alternatively, can suggest that RNFL thickness test may be used to identify GD1 patients with high risk of developing PD. GD1 patients with RNFL thinning may be candidates for PD preventive intervention.

Imaging of the retinal and choroidal vasculature in rodents using swept source OCT angiography and fluorescein angiography

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Purpose: To evaluate retinal and choroidal vasculature in rodents under normal and pathologic conditions using swept source optical coherence tomography angiography (OCTA) and fluorescein angiography (FA).

Methods: For OCTA imaging, a Zeiss Plex Elite 9000 (ZPE) swept source OCT system with OCTA capabilities was modified for use in rodent eyes by construction of a simple stage to stabilize the anesthetized animal in proximity to the lens of the instrument and by introducing the proper additional optical correction, which is dependent on the size of the eye imaged. For FA imaging, approximately 0.05-0.1 ml of 10% fluorescein solution was injected intraperitoneally and a Micron III system equipped with the proper filters was used to perform serial photographs of the fundus to follow flow/leakage of the dye. Royal college of surgeons (RCS) rats aged 3 weeks as well as normal adult C57BL6 mice were imaged using both systems to document retinal and choroidal vasculature. In a subset of C57BL6 mice, choroidal neovascularization (CNV) was induced in one eye by laser photocoagulation (Quantel 532 nm laser) according to the Ryan model. Laser parameters included a 100 µm spot, 100 ms pulse duration and 120 mW incident power to rupture Bruch's membrane. Laser-treated eyes were imaged at set times post laser using both OCTA and FA.

Results: In control animals, both OCTA and FA allowed good imaging of the retinal vasculature, while OCTA provided better imaging of choroidal vasculature. Following induction of CNV, both modalities revealed the formation of abnormal vessels at the sites of laser disruption of Bruch's membrane. Leakage from these vessels could only be demonstrated using FA.

Conclusions: Many retinal diseases involve the retinal and choroidal vasculature. To date, in both humans and rodent models, FA and ICG angiography were the main imaging modalities used to assess retinal vasculature and flow. OCTA now provides a non-invasive means to perform this assessment, and by applying relatively simple modifications can be used to examine the vasculature not only in humans but also in rodent eyes.

In vivo imaging of the fibrillar architecture of the posterior vitreous and its relationship to the premacular bursa, Cloquet's canal, prevascular vitreous fissures and cisterns

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Purpose: To describe the fibrillar architecture of the posterior cortical vitreous and identify variations across eyes of different axial lengths *in vivo*.

Methods: Sixty-four eyes of 32 subjects were examined with swept-source optical coherence tomography (SS-OCT). Grading of vitreous degeneration, presence of vitreous cisterns/lacunae, posterior hyaloid status, directionality of vitreous fibers and their relations to vitreous spaces, and lamellar reflectivity of the posterior vitreous were assessed.

Results: A consistent pattern of fibrillar organization was discovered. Eye-wall parallel fibers formed a dense meshwork over the retinal surface and fibers oriented in a perpendicular fashion to this meshwork were found to envelop the various vitreous spaces, intersecting at variable angles of insertion to the eye-wall parallel fibers. Lamellar reflectivity suggestive of splitting of the cortical fibrillar meshwork was detected in 27 eyes (42%) with 56% of these eyes demonstrating perpendicularly oriented intersecting fibers. Fifty-six percent of eyes with lamellar reflectivity had an axial length > 25 mm.

Conclusions: SS-OCT imaging revealed fibrillar organization of the posterior vitreous. Eye wall parallel hyperreflectivity of cortical vitreous was a universal finding. This pattern is suggestive of a splitting of cortical vitreous tissue and may represent a precursor to vitreoschisis. Perpendicular fibers appear to be important constituents of the walls of the various liquid vitreous spaces.

In vivo MRI assessment of bioactive magnetic iron oxide/human serum albumin nanoparticle delivery into the posterior segment of the eye in a rat model of retinal degeneration

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Purpose: Retinal degeneration diseases affect millions of patients worldwide and lead to vision loss. One of the major challenges in the development of treatments for these diseases is the safe and efficient delivery of therapeutics into the back of the eye. Previous studies demonstrated that narrow size distribution core-shell near infra-red fluorescent iron oxide (IO) nanoparticles (NPs) coated with Human Serum Albumin (HSA, IO/HSA NPs) increase the half-life of conjugated therapeutic factors, suggesting they may be used for sustained release of therapeutics. In this study, the in-vivo tracking by MRI and the long term safety of IO/HSA NPs delivery into the suprachoroid of a rat model of retinal degeneration were assessed.

Methods: Twenty-five RCS rats received suprachoroidal injection of 20-nm IO/HSA NPs into the right eye. The left eye was not injected and used as control. Animals were examined by MRI, electroretinogram and histology up to 30 weeks following injection.

Results: IO/HSA NPs were detected in the back part of the rats' eyes up to 30 weeks following injection by MRI, and up to 6 weeks by histology. No significant differences in retinal structure and function were observed between injected and non-injected eyes. There was no significant difference in the weight of injected rats compared to non-injected rats.

Conclusions: MRI could track the nanoparticles in the posterior segment of the injected eyes demonstrating their long-term persistence, and highlighting the possible use of MRI for translational studies in animals and in future clinical studies. Suprachoroidal injection of IO/HSA NPs showed no sign of adverse effects on retinal structure and function in a rat model of retinal degeneration, suggesting that suprachoroidal delivery of IO/HSA NPs is safe and that these NPs may be used in future translational and clinical studies for extended release drug delivery at the back of the eye.

Optical density ratio – a prognostic marker for chronicity in Central Serous Chorioretinopathy

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Purpose: Central serous chorioretinopathy (CSR) can be classified according to its clinical course as acute or chronic. Acute CSR usually resolves spontaneously within 2-3 months. Knowing the potential chronicity at presentation can improve treatment and management of the disease. We investigated the clinical significance and prognostic value of the sub-retinal fluid (SRF) optical density ratio (ODR) in CSR at presentation.

Methods: Medical charts of patients diagnosed with CSR were retrospectively reviewed for cases with follow-up of at least 3 months for whom optical coherence tomography (OCT) was done at presentation prior to any intervention and showed sufficient SRF for sampling. Optical density (OD) measurements were obtained using ImageJ and ODRs were calculated as SRF OD divided by vitreous OD. Subjects were categorized as acute or chronic based on the presence of SRF at follow-up.

Results: Thirty-nine eyes of 41 men and 9 women (mean age 41.4 ±9.1 years) met the inclusion criteria. Three months from presentation, SRF had absorbed in 19 cases (acute group) and remained in 20 (chronic group). There were no significant differences between the groups at presentation in age, sex, visual acuity, and OCT image acquisition parameters. Baseline ODR was significantly higher in the chronic group (1.032±0.321 versus 0.798+0.267 in the acute group, P=0.018). Visual acuity at follow-up was significantly better in the acute group than the chronic group (0.03±0.05 versus 0.12+0.16, respectively, P=0.035). No significant differences were found in choroidal thickness and the need for treatment. Baseline maximal retinal thickness was significantly higher in the chronic group compared to the acute group (496.8±70.7 versus 586.7±160.5microns, respectively, P=0.040).

Conclusions: ODR can be a useful prognostic marker for chronicity in CSR.

Why FA when you can OCTA proliferative diabetic retinopathy patients?

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Purpose: To determine whether Optical Coherence Tomography Angiography (OCT-A) can identify active neovascularization of the disc (NVD) or elsewhere (NVE) in patients with proliferative diabetic retinopathy (PDR), and compare it to normal controls

Methods: eight eyes of six patients with PDR were included in this prospective study. The presence of NVD or NVE was confirmed with Fluorescein angiography (FA). Complete ophthalmic examination, spectral domain-optical coherence tomography and OCT-A were obtained for all patients. Six-millimeter OCT-A images were obtained in a standardized method including a macular scan, optic nerve centered scan, one scan centered on the superior arcade and one scan centered on the inferior arcade. Analysis of all OCT-A images for the presence of NVD or NVE and single line OCT scans over the area of interest was performed independently by 3 retina specialists who did not have access to color fundus photos, FA images or history. Control OCT-A images were used from 18 eyes of non-diabetic controls. The retina specialists were masked when reading the control and study OCT-A images.

Results: Active neovascularization was identified on OCT-A images of patients with PDR in 62.5% of the eyes. That result was statistically different from control eyes (p=0.005). Inter-rater agreement was 82%.

Conclusions: OCT-A may identify neovascularization as agreed upon by multiple retina specialists in patients with PDR, which can spare them the need for FA.

Studying the biocompatibility and 3D cell-scaffold interface of photoreceptor precursors in a microwells array

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Purpose: Delivering cells to replace degenerate cells in degenerative disease of the outer retina in the effort to restore vision carries great hope. Many approaches for optimizing the 3D scaffold for improving the spatial orientation, function, viability and potentially the synaptic formation of transplanted cells have been pursued, and are the focus of many studies. Here we investigated, in vitro, the morphological characterization and viability of single human photoreceptors precursors cells (hPRP) cells in microwells array.

Methods: hPRP were differentiated form human embryonic stem cells following a protocol optimized by our group. GFP labeled PRP cells were seeded on an SU8 scaffold array fabricated by lithography containing 17,424 wells 20µm in diameter and 17 µm in height suitable for a single cell dimension. SU8 surfaces were treated with serum, plasma, matrigel, collagen and PEI to enhance cell attachment. Cells morphology and creation of focal adhesions were monitored for several days after seeding by confocal microscopy and staining for actin and vinculin. Viability of the cells was further evaluated by PI staining. High resolution imaging of the membrane scaffold interface was studied by focused ion beam and scanning electron microscopy (FIB/SEM) technique.

Results: Surface functionalization of SU8 with serum and plasma increased the wettability of SU8 surface and improved the cell attachment. PI staining revealed that SU8 polymer is biocompatible for PRP cells. Centrifugation of the microwell (1400 rpm, 4min) yielded high percentage (> 70%) of cells within the wells. Both confocal and FIB/SEM microscopy showed that cells seeded in microwells filled the entire volume of the well with the gap detected between the cell membrane and the well wall being at the nanometric scale.

Conclusions: SU8 polymer is biocompatible for scaffold fabrication for PRP cells. Surface functionalization is needed to improve cell attachment to SU8 surfaces. Single PRP cells seeded in the wells survived in-vitro and occupied the entire well space.

Oligomeric and fibrillar assemblies of Amyloid-B 42 are highly retinotoxic: Implications for the pathophysiology of Age-Related Macular Degeneration

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Purpose: Amyloid-β (Aβ), the major neurotoxic factor in Alzheimer's disease, was reported as a significant constituent of drusen and was implicated in the pathophysiology of age- related macular degeneration (AMD). Accumulating evidence supports an association between retinal Aβ deposition and compromise of the retinal integrity, yet the major pathogenic Aβ species in the retina and the mechanism of Aβ-mediated neuroretinal toxicity remain unknown. Herein, we examined the impact of distinct supramolecular assemblies of Aβ on the retinal integrity.

Methods: Fibrillar (Aβ40, Aβ42) and oligomeric (Aβ42) preparations synthesized showed clear hallmarks of ordered amyloid structures based on transmission electron microscopy, spectroscopy and ThT Fluorescence. Retinal measures of structure and function were studied longitudinally following intravitreal administration of the Aβ preparations in rats.

Results: Electroretinography (ERG) testing demonstrated that well-defined Aβ species possess differential retinal neurotoxicity, exerting varying degrees of compromise on the functional integrity of the retina. Oligomeric Aβ42 inflicted the major toxic effect, manifesting diminished ERG responses through 30 days post injection. A lesser retinal cytotoxic effect was noted following injection of fibrillar Aβ42, whereas no retinal compromise was recorded in response to Aβ40 fibrils. The toxic effect of Aβ42 organizations was further reflected by retinal glial response in treated eyes, evident by positive Glial Fibrillary Acidic Protein (GFAP) labelling. Fluorescence labelling of Aβ species was used to follow their assembly to the retinal tissue, and immunostaining for Aβ characterized the nature of aggregates found in situ.

Conclusions: These results provide conceptual evidence of the toxicity of particular Aβ species in vivo, and promote the mechanistic understanding of their retinal pathogenicity. Stratifying the impact of pathological Aβ aggregation in the retina may enhance the understanding of amyloid-mediated retinal neurodegeneration, and may merit further investigation as a therapeutic avenue Degeneration in AMD.

Photovoltaic Restoration of Sight in Atrophic Age-related Macular

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Purpose: To evaluate feasibility of restoration of central vision in patients with age-related macular degeneration using a wireless photovoltaic subretinal implant. In particular, to assess safety of sub-retinal implantation and quality of prosthetic vision in patients with geographic atrophy.

Methods: A prospective study in 5 patients with visual acuity ≤20/400 due to geographic atrophy of at least 3 optic discs diameters and no foveal perception. The wireless photovoltaic chip (PRIMA, Pixium Vision) is 2x2mm in size, 30µm in thickness, containing 378 pixels of 100µm in width. Each pixel in the implant converts pulsed near-infrared light (880nm) projected from video goggles into electric current to stimulate the nearby neurons in the inner nuclear layer of the retina. Several surgical techniques have been used, varying in methods of anesthesia (local vs. general) and retinal reattachment (gas vs. oil).

Results: In all patients, surgery lasted approximately 2 hours, chip was successfully implanted under the macula and remains stable, with a follow-up extending now to 11 months in the first patient. In 3 patients chip was placed into a desired position - centrally and close to the inner retina. In 2 patients the implant ended up in suboptimal positions – one in the choroid and another off-center. All 5 patients perceive white-yellow patterns with adjustable brightness, in retinotopically correct locations within previous scotomata. No decrease in natural visual acuity was observed in any of the patients. All 4 patients with subretinal placement of the chip correctly identify bar orientation, with 93.5+/-3.8% accuracy. Out of them, all 3 patients with central placement of the implant demonstrated visual acuity with Landolt C test in the range of 20/460 - 20/550, which is just 15-35% below the theoretical resolution limit for this pixel size (20/400). Patients are now being tested in letter recognition, reading, and other visual tasks.

Conclusions: Wireless chip PRIMA can be safely implanted under the atrophic macula in patients with geographic atrophy and restore central visual perception with acuity close to the theoretical limit of the implant. Implantation did not reduce the natural residual visual acuity of the patients. Implants with smaller pixels are being developed.

The relevance of Ccr1 receptor in a model of retinal degeneration.

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Purpose: Involvement of immune cells in the progression of retinal disease, such as Age-related macular degeneration (AMD), has been well established although their precise role is still unclear. We have previously revealed the deleterious effect of M2a human monocytes-derived macrophages (hmdϕ) in model of light-injured mice. Here, we aimed to determine the underlying mechanism of the process of photoreceptor death associated with M2a hmdϕ.

Methods: We compared 120 cytokines of the supernatant from M1 (n=6) and M2a (n=6) hmdϕ. In addition, we evaluated the mRNA level of the receptor CCR1 in the retina and in the choroid of mice exposed to light (n=8). Immunohistochemistry for CCR1 receptor and Cd11b (n=7) were performed on eye section from mice after light injury. Finally, CCR1 inhibitor was administrated via intravitreal injection immediately after light injury (n=4) and visual function and outer nuclear layer thickness were evaluated via electroretinography and histological analysis respectively, 7 days after injury.

Results: Injection of M2a hmdϕ promoted the recruitment of peripheral myeloid cells as compared to M1 hmdϕ (2.34-fold, p=0.02). Also, we found up-regulation of the level of 9 secreted cytokines in M2a hmdϕ compared to M1 hmdϕ. Most of them were found to bind to CCR1 receptor. Increased CCR1 expression was found in the retina of light-injured mice (2-fold, p=0.007) as well as a strong positive correlation (R2=0.86) between the level of CCR1 expression and the level of retinal damage. After light exposure, CCR1 receptor was found localized in the inner plexiform layer. Finally, blockage of CCR1 receptor showed a trend toward protective effect in the light-damaged mice both in ERG recording (1.65-fold, p=0.04) and histological analysis (1.45-fold, p=0.13).

Conclusions: The mechanism by which M2a exacerbated the death of photoreceptors seems to implicate recruitment of immune cells via CCR1 receptor. In addition, a possible activation of müller cells, also mediated by CCR1 receptor, could be involved in the inflammation process.

Retinal stimulation through a DLP based projection system enables the generation of high-resolution VSDI retinotopic maps

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Purpose: High-resolution recording of visual cortex in response to patterned stimuli in rodents is an important tool for studying various cortical processes resulting from retinal diseases and vision restoration techniques. Voltage sensitive dye imaging (VSDI) is a commonly used imaging modality enabling the high spatial resolution imaging of cortical responses and retinotopic mapping. This work presents the development of a unique projection system combined with VSDI enabling the stimulation and retiontopic mapping at a high spatial resolution in a rodent model.

Methods: We constructed a unique projection system for localized retinal stimulation based on a DMD projector (912x1140 pixels). The system uses visible light (LED 532nm) and NIR (910nm) sources, for the study of combined visible and prosthetic vision, respectively, yielding a retinal image size of 1.1mm wide and 0.7mm high, corresponding to 16.5*10 degrees in the visual field of the rat. The system offers great flexibility and facilitates the generation and projection of visual stimuli at different intensities, temporal frequencies, pulse durations and light-wavelength. More importantly, the system has the advantage of direct control of the retinal stimuli location by a camera imaging, with no need to perform back-projection, as is the case in currently available set-ups.

Results: Using this system, we obtained high-resolution retinotopic maps at an unprecedented resolution of retinal stimuli size of 300µm, corresponding to 5 degrees in the field of view. We calculated a cortical amplification factor of about 30 µm/deg, comparable to previous studies. We were further able to show no cortical responses in areas of localized retinal damage induced by laser injuries.

Conclusions: This system is a useful tool for studying the cortical response to localized retinal stimulation and may shed light on cortical plasticity processes occurring during various retinal pathologies and on the cortical integration of prosthetic and natural vision.

MSCs Encapsulation within Thermo-Responsive Hydrogel as Regenerative Therapy for Retinal Degeneration

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Purpose: ECM-based hydrogel scaffold is a biological cell delivery system which is thermo-responsive, non-immunogenic and bio-degradable. Interestingly, its thermo responsive quality allows the scaffold to turn from a liquid solution to gel at 37^0C, making it potentially useful for future subretinal transplantations. This project aims to analyze the effectiveness of ECM-based hydrogel in accommodating adipose-derived mesenchymal stem cells (ASCs) and supporting cell growth *in vitro*.

Methods: ASCs were purified from human adipose tissue, and expanded *in vitro*. Thermo-responsive ECM-based hydrogel was produced from enzymatically digested, de-cellularized porcine omentum tissue. Explants of ASCs encapsulated in hydrogel were allowed to gelate in physiological conditions (37^0C) on a tissue culture plate. Gelated explants were further cultured and analyzed on days 0, 7 and 14. Cell viability was tested using Live/Dead fluorescence assay. Stem cell phenotype was analyzed with immunofluorescence staining for mesenchymal stem cell marker CD105. ECM hydrogel fiber content was analyzed by immunofluorescence staining for collagen. Stem cell morphology after encapsulation was also analyzed using a scanning electron microscope. 2D cultured ASCs served as controls for phenotype and viability studies.

Results: Cell viability, as indicated by Live/Dead fluorescence assay, was high throughout day 14 (explants 85% ±6.49, controls 95% ±1.5). High stain intensity of CD105 was observed in encapsulated ASCs on day 7 (explants 61% ±12.07, controls 76.95% ±6.7). Collagen staining showed gradual fiber degradation and remodeling of hydrogel by ASCs (67.5% ±11.5 explant coverage on day 0; 21.3% ±17.3 on day 7). SEM imaging of encapsulated ASCs demonstrated cells spreading on the surface of the explant, as well as cell-cell direcpprakadeet interactions on day 7.

Conclusions: ASCs encapsulated in ECM based hydrogel remained highly viable for the 14 days tested period, maintained multipotency and morphology, interacted with adjacent cells through direct cell-cell contact, and gradually degraded the ECM-hydrogel by day 7.

These data suggest that ECM-hydrogel serves as an effective accommodating environment for ASCs, and may serve as a successful cell delivery system in future *in vivo* studies for subretinal transplantations.

Metabolite Amyloids in Human Disease: Oxalate Nanofibrils Induce Comparable Retinopathy in Hyperoxaluria Patients and Treated Animals

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Purpose: The pathology of primary hyperoxaluria, a spectrum of genetic disorders characterized by abnormal oxalate accumulation with subsequent multi-organ dysfunction, has been attributed to the formation of calcium oxalate crystals in various tissues and organs, leading to cellular injury. Here, we present the surprising observation of retinal damage among young patients in the absence of retinal crystals, thus challenging the generality of this accepted mechanism of oxalate crystal-related toxicity.

Methods: We explored the possible formation of alternative supramolecular oxalate organizations and their potential pathological role.

Results: We discovered that oxalate could form ordered fibrils possessing properties similar to those of proteinaceous amyloids. Unlike the canonical oxalate crystals, the formed nanofibrils did not contain calcium. The self-assembled fibrils inflicted cytotoxicity in cultured retinal pigment epithelial cells, as well as retinal toxicity in rats. Notably, wild-type rat eyes treated with the assemblies remarkably recaptured the patterns of retinal dysfunction observed in patients, thus establishing an in vivo model for the oxalate fibrils associated toxicity. The fibrils inflicted a glial response in treated rat eyes, reflected by their internalization into activated retinal Müller cells. Moreover, oxalate fibrils were recognized by antibodies from patient sera, providing further evidence for the occurrence of these assemblies in the disease state.

Conclusions: Taken together, these findings provide a new paradigm for oxalate-associated disease, potentially leading to the development of novel therapeutic avenues for these devastating conditions. Furthermore, our findings provide the first direct clinical indication for the pathogenic role of metabolite-amyloids in human error of metabolism disorders.

Allele Frequency Analysis of Variants Reported to cause Autosomal Dominant Retinal Diseases Revealed that 17% of Genes and 9% of Mutations are Unlikely Pathogenic

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Purpose: Next generation sequencing (NGS) techniques generate a large amount of genetic data that can be used to better characterize the set of disease-causing mutations in the human genome. The vast majority of variants identified in NGS analyses are “incidental” or “secondary” findings, previously termed as “incidentalome”. Our aim was to analyze allele frequencies values of sequence variants that were reported to cause autosomal dominant inherited retinal diseases (AD-IRDs) and examine if there are reported mutations and genes that are unlikely to be pathogenic.

Methods: The genetic information was collected from various databases: reported AD-IRD mutations from PubMed publications and the Human Genome Mutation Database (HGMD), a list of AD-IRD genes from RETNET, allele frequencies from gnomAD, mutation nomenclature from Mutalyzer, and data published regarding segregation analysis and biochemical effect of specific variants on protein function.

Results: We generated a database gathering information on 1,229 variants reported to cause AD-IRDs in 58 genes. While the majority of variants (83%) are not represented in gnomAD, 113 (9%) were found in more than one individual and had a carrier frequency of over 1:100,000. Interestingly, in some cases, these unlikely pathogenic variants were the only ones reported to cause disease in AD inheritance pattern for a particular gene, therefore raising doubt regarding the involvement of 10 (17%) of the genes as AD-IRD causing genes. After excluding the reported mutations that are unlikely pathogenic, our analysis revealed 1100 reported mutations in 48 genes as the cause of nonsyndromic AD-IRDs.

Conclusions: We predict that these data are not limited to a specific disease or inheritance pattern since previous reports indicated that nonpathogenic variants were mistakenly reported as pathogenic mutations in various diseases. To the best of our knowledge, the current study represents the first systematic analysis of autosomal dominant sequence variants reported to cause a specific, yet heterogeneous, disease. Our results should serve as a warning sign for geneticists, mutation database curators, and sequencing panels’ developers not to automatically accept reported mutations as pathogenic, but cross-reference the information with large NGS-based databases.

Cortical response to combined prosthetic and visible stimuli exhibits similarities to natural visual processing

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Purpose: Prosthetic restoration of central vision in age-related macular degeneration (AMD) involves a combination of prosthetic vision in the central macula along with natural vision in the periphery. Here we study cortical interaction of visible and prosthetic stimuli, which is of great clinical and scientific importance

Methods: Subretinal implantation of 1mm-diameter photovoltaic arrays in wild-type rats induced a localized degeneration of the photoreceptors above the implant, whereas the surrounding retina was left intact, similar to localized retinal degeneration caused by AMD. Using a customized projection system, we induced prosthetic and natural visual responses with NIR (910nm) and visible light (532nm), respectively. Each presentation was comprised of a central 1mm prosthetic or visible stimuli encircled with a 3mm visible surround. We recorded visually evoked potentials (VEP) in response to either non-patterned (flash or contrast step) stimuli or to complex grating patterns

Results: Responses for both visible and prosthetic flash stimuli were reduced by increasing a continuous visible light background. Combined prosthetic and natural non-patterned stimuli (flashes and contrast steps) exhibited a simple cortical linear summation. In contrast, responses to alternating-grating targets composed of either visible or prosthetic central area surrounded by visible grating flankers revealed significant lateral inhibition phenomenon. For both prosthetic and visible targets, lateral inhibition increased with the target contrast, reaching a maximum inhibitory effect of 40%.

Conclusions: The observed striking similarities between cortical responses to patterned natural illumination and to combined prosthetic-natural stimuli suggest that basic processing interactions are preserved when a combined information is presented to the visual cortex. These results are an important step for understanding the cortical processing of the combined prosthetic and natural vision and can aid in prosthetic restoration of central vision in AMD patients

Microarchitecture of Schlemm's Canal Before and After Cataract Extraction Surgery

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Purpose: This study aims to characterize the structural and volume changes of Schlemm's canal (SC) in patients before and after cataract extraction (CE) by using enhanced-depth imaging optical coherent tomography (EDI OCT).

Methods: Forty-one serial horizontal EDI-OCT B-scans (interval between B-scans, 69 µm) of the nasal corneoscleral limbus were obtained before and 1 week after CE. The structures of aqueous and blood vessels in each scan were used as landmarks to select overlapping scans between the 2 sets of serial scans (before and after CE). The SC cross-sectional area was measured in each of the selected scans. After 3-dimensional reconstruction, SC volume was determined.

Results: Eleven eyes (Six females and five males) were imaged successfully before and after CE. Mean age was 70.54 ± 11.38 years. The mean axial length was 23.10 ± 0.87 mm. After CE, the mean BCVA in logMAR improved from 0.4 ± 0.13 to 0.2 ± 0.13 (P= 0.028) and there were no significant change in mean IOP before and after CE (15.09 ±1.33 to 15.0 ±2.16 mmHg; P=0.39). The mean SC cross-sectional area increased by 25%, from 4744 ± 376 μm^2 to 5941 ± 1048 μm^2 ($p<0.001$). SC volume of the analyzed region increased also by 25% from 6,641,473±585,954 μm^3 to 8,317,909 ± 1,328,809 μm^3 ($p<0.001$).

Conclusions: These data suggest that CE expands SC dimensions in healthy eyes. EDI OCT of SC may prove useful in the evaluation the SC size in vivo before and after CE.

Non-Pigmented ciliary epithelium deliver oxidative stress alert via exosomes

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Purpose: Nano sized double layer exosomes are known to participate in signaling transfer between cells. Our goal was to explore the role of exosomes as oxidative stress signals transfer in the ocular drainage system, a highly vulnerable system to continue oxidative stress. Exosomes from the aqueous producing cells-Non Pigmented Ciliary Epithelium (NPCE) following moderate oxidative stress were used to treat the aqueous humor draining cells-Trabecular meshwork (TM) under oxidative stress. Non-stressed NPCE and TM cells were used as controls.

Methods: NPCE derived exosomes were extracted from the condition media and incubated with TM cells. TM cell selected mRNA expression was done using qRT-PCR, Catalase and SOD activity was measured using spectroscopy and total cell antioxidant response was done using fluorescence analysis.

Results: Exosomes derived from oxidative stressed NPCE cells were able to induce oxidative stress protecting mechanisms in TM cells under oxidative stress. These mechanisms include, NRF2-Keep1 pathway activation, antioxidant gene expression, lower intracellular oxidative stress response and higher SOD and catalase activity.

Conclusions: Exosomes can deliver oxidative stress alert with effective response between ocular drainage cells.

First-in-Human clinical study to establish the safety and efficacy of automatic Direct Laser Trabeculoplasty (DSLT)

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Purpose: To evaluate the safety and efficacy of automatic DSLT applied without a goniolens at various energies to the sclera overlying the trabecular meshwork (TM) in lowering intra ocular pressure in open angle glaucoma & ocular hypertension.

Methods Nine patients were treated by the DSLT device with100 sequential non-contact laser shots applied automatically directly on the scleral limbus using image analysis of the limbus location and an eye tracking monitor of the location of the eye and of the laser beam. Before the laser was fired multiple safety, checks were automatically performed. If any of these safety checks failed, the laser did not fire. Before *each* pulse was delivered, the image of the eye was automatically analyzed; the new point location is calculated on real-time, in order to compensate for any eye motion. 0.8 to 1.4 mJ were used. The duration of the irradiation was 1.2 seconds

Results: Mean IOP before DSLT was 26.81mmHg, one day after DSLT mean IOP was 19.19mmHg, at 1 week, 1month, 3 months & 6 moths post op the IOP was 25.13; 21.14; 21.60& 23.3mmHg respectively. The higher energy gave better sustained results, e.g., The IOP of the two patients treated by 1.0 mJ was reduced by 35% at 6 months. There was one case of transient conjunctival hemorrhages when the beams hit away from the limbus.

Conclusions: Automatic DSLT is a promising new modality in the treatment of OAG & OHT, further studies with more patients are being conducted in order to establish the long-term efficacy & safety in both POAG and PACG.

Rosmarinic Acid Restores Complete Transparency of Human Cataract *Ex Vivo* and Delays Cataract Formation *In Vivo*

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Purpose: To report on the effect of the identified leading compounds on cataract in rats.

Methods: For the *Ex vivo* screening, fragments of human cataractous lenses were collected from patients undergoing routine clear corneal incision phacoemulsification cataract surgery. Total protein concentration of each cataract sample was adjusted to obtain an optimal absorbance value. The cataract samples were incubated with several concentrations of the screened compounds for their cataract modulating effect. Reversal of protein aggregates was monitored over up to 48 h using the turbidity assay. Next, for assessment of the impact of the identified lead compounds on cataract prophylaxis *in vivo*, the selenite induced rat cataract model was employed. Newborn Whistar rats were treated with subcutaneous sodium selenite injection at the age of 13 days. Study rats were then treated with daily administration of rosmarinic acid, while control rats were treated with the vehicle. The rats were examined daily for assessment of lens opacification.

Results: Each small molecule compound selected for screening was tested on cataract samples obtained from 5-10 different patients. The final total protein concentrations ranged between 0.5-3 mg/mL after adjustment for optimal absorbance. The leading compound, rosmarinic acid, resulted in significant reduction in the optical density of the solution, and thus was selected for further assessment *in vivo*. Rosmarinic acid, administered subcutaneously 4 hours prior to selenium injection, and daily thereafter, remarkably delayed the appearance of lenticular opacification and reduced cataract severity in treated rats. The notable treatment effect was evident upon visual inspection as well as by photo grading of cataract stages. Control rat eyes with selenite-induced cataract demonstrated an average lens opacification score of 5, higher by at least 2-grades compared to the study eyes treated with rosmarinic acid.

Conclusions: We applied a human *ex vivo* assay that allowed for screening of small molecule compounds with potential for cataract modulation. The leading compound indeed delayed the formation of cataract and reduced its severity *in vivo*. These results may provide a proof of concept for future development of pharmacological treatment for cataract.

SOX2 regulates P63 and stem/progenitor cell state in the corneal epithelium

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Purpose: To investigate the role of SOX2 in regulation of limbal stem cell differentiation

Methods: The expression of SOX2 and P63 was explored in the adult murine cornea in vivo and in primary human limbal stem/progenitor cells before and after differentiation by immunefluorescent staining and Western blot analysis. SOX2 or P63 were knocked down by silencing RNA and the effect on gene expression, stem cell clonogenic potential, cell proliferation, and differentiation was explored. Micro-RNA 450b that can repress SOX2 was identified in silico, and its expression was tested in vivo while its function was explored by transfections into limbal cells and by co-transfection with cloned SOX2-3'-untranslated region followed by dual luciferase assay.

Results: We show that SOX2 regulates P63 to control corneal epithelial stem/progenitor cell function. SOX2 and P63 were co-expressed in the stem/progenitor cell compartments of the murine cornea in vivo and in undifferentiated human limbal epithelial stem/progenitor cells in vitro. In line, a new consensus site that allows SOX2 mediated regulation of P63 enhancer was identified while repression of SOX2 reduced P63 expression, suggesting that SOX2 is upstream to P63. Importantly, knock down of SOX2 significantly attenuated cell proliferation, long-term colony forming potential of stem/progenitor cells and induced robust cell differentiation. However, this effect was reverted by forced expression of P63, suggesting that SOX2 acts, at least in part, through P63. Finally, miR-450b was identified as a direct repressor of SOX2 that was required for SOX2/P63 down-regulation and cell differentiation.

Conclusions: Altogether, we propose that SOX2/P63 pathway and their regulation by miR-450b is an essential regulator of corneal stem/progenitor cells while mutations in SOX2 or P63 may disrupt epithelial regeneration, leading to loss of corneal transparency and blindness. A better understanding of the molecular network that is controlled by these key transcription factors will shed light on LSC self-renewal pathways and will potentially be harnessed into novel therapeutic approaches for corneal pathologies.

Stiffening of sclera using bacteriochlorophyll derivative (WST11) and transpupillary near infrared light (NIR) measured by atomic force microscopy

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Purpose to demonstrate scleral stiffening in rabbit eyes *ex-vivo* and *in-vivo* induced by impregnation of WST11 and transpupillary near infrared (NIR) illumination by atomic force microscopy (AFM).

Methods: For the *ex-vivo* experiments, four pairs of rabbit eyes were used. One eye of each pair was randomly chosen for treatment. The pupil was dilated with tropicamide 1% drops and the episcleral tissue was removed. The equatorial sclera was impregnated with WST11 in saline for 20 minutes. Afterwards, the sclera was illuminated transpupillary at 755nm (NIR) using a 3 mirror Goldman lens for 10 minutes. The incident light was measured to be 10 mW/cm^2. For the *in-vivo* experiments, three rabbits 12 weeks-old were anesthetized by intramuscular injection of ketamine and xylazine. Then the conjunctiva was incised in one eye and a custom cannula with fenestrations on its internal side was introduced into subtenon's space down to posterior sclera. The treatment area was identified by indentation with the cannula visualized by an indirect ophthalmoscope and 1ml of WST11 solution was injected slowly. After 20 minutes, NIR illumination by laser mounted on indirect ophthalmoscope was delivered transpupillary for 10 minutes using a 20-diopter lens. Immediately after treatment, the rabbits were sacrificed and the eyes were enucleated. Finally, the eyes from *ex-vivo* and *in-vivo* treatments were dissected, the retina and choroid were removed and scleral samples were examined by AFM to evaluate scleral stiffness.

Results: AFM measurements of the equatorial sclera from *ex-vivo* eyes showed that the average Young's modulus after treatment of the internal and external sides of the sclera were 1.7 (p= 0.1726) and 3.82 (p=0.007) times greater respectively than untreated controls. Young's modulus of the posterior sclera from *in-vivo* eyes showed an increase of 4.36 fold (p=0.05), after treatment.

Conclusions: WST11 followed transpupillary NIR illumination significantly increased scleral stiffness in *ex-vivo* and *in-vivo* rabbit eyes. Transpupillary NIR illumination can avoid surgical scleral exposure and associated complications. This treatment may be suitable to halt the progression of degenerative myopia

Nevus of Ota: Clinical Presentation, Imaging, Complication and Ocular Clinical Classification

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Purpose: To summarize the ocular clinical presentation, imaging, treatment and prognosis of patients with nevus of Ota (NO).
Based on our finding to suggest a clinical ocular classification for the condition.

Methods: Retrospective case series. The medical records were retrieved and the following parameters were analyzed: demographics (gender and age at diagnosis), medical history and medications, laterality of the condition, clinical presentation, treatment, and complications.
In addition, Images of patients with NO, were compared to age and gender-matched controls without the condition.

Results: The mean age at nevus of Ota diagnosis of the 20 study patients was 43.14 years. The patients presented with various extents of hyperpigmentation, as well as with iris nodules and iris crypts. Seventeen patients had type I according to the Tanino classification, 2 patients had type II, and 1 patient had type IV (bilateral presentation). We further classified all cases in according to the ocular involvement. One patient underwent malignant transformation to choroidal melanoma and 3 patients developed glaucoma. The mean thickness of the choroid was 0.72 mM in the nevus group and 0.74 mM in the control group (matched pairs, P = 0.550). The mean thickness of the iris was 0.55 mM in the nevus group was and 0.501 mM in the control group (matched pairs, P = 0.297).

Conclusions: Nevus of Ota is a congenital condition that carries the potential for malignant transformation. In search of possible risk factors for malignant transformation, we suggest adding a new clinical classification based on the involved ocular component and extent of that involvement.

The effect of intravitreal injection timing in eyes with new CNV

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Purpose: To study the optimal period of time between new CNV diagnosis and treatment initiation on visual and anatomical outcomes.

Methods: We retrospectively reviewed 159 eyes of patients with naive CNV, treated with anti VEGF intravitreal injections at a tertiary medical center between the years 2012-2017.
Outcome measures included final best-corrected Snellen visual acuity (BCVA), central macular thickness (CMT) according to the correlation with treatment initiation period.
Using SPSS statistics software, correlations were tested for the period of time from OCT to patients' admission to the ophthalmology clinic and for the period of time from their admission to first injection of AVASTIN.

Results: After finding no significance for age, gender and eye variables (p=0.79, p=0.987, p=0.105 respectively), we found that the time a patient wait from clinical diagnosis to start treatment with AVASTIN, has a statistically significant effect on visual acuity improvement (p=0.011). using Mann Whitny U test, we found the optimal time frame to treatment lasts up to 8 days. No significance was found for improvement in CMT (p=0.560) in immediate treatment. When comparing clinical and anatomical results of patients treated immediately on their first visit with those treated 1-7 days later or 7-14 days no statistical significance was found.
In contrary, time from OCT to first clinical examination, had statistically significant effect on improvement in CMT (p=0.039).

Conclusions: Treatment with anti-VEGF injections should be initiated up to 8 days from admission in order to achieve greater improvement in visual acuity. However, prompt treatment seems to have no significant effect on anatomical outcomes.

A 12-month Prospective Study to Evaluate the Efficacy of Treat and Extend Regimen (T&E) of Intravitreal Aflibercept as a Second-Line Treatment for Diabetic Macular Edema (TADI Study)

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Purpose: To evaluate the efficacy of intravitreal aflibercept as a second-line therapy in eyes with persistent diabetic macular edema (DME) despite initial bevacizumab treatment.

Methods: A prospective multicenter study was conducted in Israeli retina clinics. Inclusion criteria included DME treated with at least 6 bevacizumab injections. Central subfield thickness according to SD-OCT was >300 microns with presence of subretinal and/or intraretinal fluid and best corrected ETDRS visual acuity between 20/30 to 20/200. Exclusion criteria included other ophthalmic pathology causing macular edema and recent ophthalmic surgery. Eyes were treated with intravitreal aflibercept injections. Starting from the first follow-up (1 month after the first aflibercept injection), a treat-and-extend regimen was applied. Treatment intervals were extended by 2 weeks when the macula appeared dry per SD-OCT. Primary outcome was CST thickness at week 52.

Results: Forty-eight eyes (n=43 patients) from 9 centers were recruited to the study, and 44 eyes completed 52 weeks of follow-up. Mean age±SD was 62.3±9 years, and the patients received a mean of 7.9±3.5 bevacizumab injections before enrolment. There was no improvement of CST under bevacizumab therapy. HbA1c levels at baseline and at week 52 were 8.2±1.9% and 8.2±1.7%, respectively ($p>0.05$). The mean (±SD) CST under intravitreal aflibercept therapy reduced from a baseline of 468±130.9 micron to 305.5±67.4 micron at 52 weeks ($p<0.05$). BCVA improved from 64.1±15.6 ETDRS letters at baseline to 75.2±8.4 letters at week 52 ($p<0.05$). Twenty of the eyes (41%) were extended beyond 4-weeks interval, and have received a mean of 10.94±2 injections of the maximal possible 13 injections during the study.

Conclusions: Eyes with persistent DME under initial bevacizumab therapy show marked reduction in macular thickness and improvement of visual acuity following one-year treatment with intravitreal aflibercept using T&E algorithm without a loading dosage.

The Correlation of Response to Treatment with anti-VEGF compounds between the First and Second Treated Eyes in Diabetic Macular Edema

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Purpose: Bevacizumab serves as a first-line therapy for diabetic macular edema (DME) in Israel. We aim to assess the correlation of treatment outcomes between the first and second treated eyes in patients with DME.

Methods: Data was collected retrospectively on consecutive group of patients that initiated bevacizumab therapy for DME in both eyes. Data collection included visual acuity (VA), results of eye exams, and quantitative and qualitative optical coherence tomography (OCT) parameters.

Results: 64 eyes of 32 patients were included. Baseline VA (mean±SD) was similar in the both eyes treated (RE=0.43±0.303, LE=0.5±0.236, P=0.324; r=0.268 P=0.161), and after 6 injections (RE=0.51±0.266, LE=0.54±0.193, P=0.7; with correlation of r=0.318 P=0.199). There was no difference in the mean baseline (±SD) central foveal thickness (CFT) before treatment (RE 453±179, LE 403±160; P>0.05). After the first intravitreal injection there was a strong correlation between CFT of the RE (411±154) and the LE (427±170, P<0.001; with correlation of r = 0.635, P<0.001) which persisted after the 2nd injection (RE = 449±169, LE 425±173; P=0.5; with correlation of r =0.529; P=0.008), and the 3rd injection (RE CFT 445±160, LE CFT 401±163 P=0.176; with correlation of r=0.388; P=0.025). After the 6th injection there was similar CFT in the RE =401±92 and the LE =405±131 (P=0.91; with correlation of r = -0.96, P = 0.695). In total, none of the patient had a VA improvement or worsening in one eye of more than 3 line that was not accompanied by similar VA change in the other eye at 6 injections.

Conclusions: Strong correlation in treatment outcome exist between fellow eyes of the same patient. The VA have similar correlations between unrelated patients
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Activated protein C reduces leakage from newly formed and pre-existing choroidal neovascularization (CNV) in a murine model

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Purpose: To study the ability of activated protein C (APC) to reduce leakage from newly formed and pre-existing choroidal neovascularization (CNV) in a murine model.

Methods: CNV was induced in C57BL/6J mice using indirect ophthalmoscope guided laser. APC (1µg/1µl saline/eye) or 1µl saline were injected intravitreally Immediately following injury or 7 days post CNV induction. Leakage from CNV was evaluated 7 days post treatment based on fluorescein angiography (FA) sequence monitoring using Optos© fundus camera. Laser spots appearance were interpreted by 2 masked retinal specialists, and were classified as "leakage", hyperfluorescent lesion with blurred margins increasing in size; or "staining", hyperfluorescent lesion with distinct margins lacking a progressive increase in size with increased intensity only. One day post FA evaluation, FITC-dextran (500k) was injected to the mice hearts, eyes were enucleated and choroidal-retinal pigment epithelium (RPE) flat-mounts were prepared. CNV area, volume and vascular penetration were evaluated using 3D confocal imaging of FITC-dextran.

Results: APC treatment significantly reduced leakage from newly formed CNV as well as pre-existing CNV as reflected by FA. Quantitative assessment of leaking lesions revealed that in newly formed CNV, significant leakage was revealed in 74% (20 out of 27) of the laser applications in the saline-injected mice, but only in 23% (7 out of 30) of APC-treated mice ($P < 0.001$). In pre-existing CNV, 100% of the leakage was reduced by 31% (8 out of 26) in saline-injected mice whereas in the in APC-treated mice, significantly reduction in pathological leakage was measured, 85% (23 out of 27) of the laser applications ($P < 0.001$).
With correlation to the clinical findings, APC treatment induced statistically significant reduction in CNV volume, area and vascular penetration in comparison to saline treated mice.
Histologic examination showed no evidence of retinal toxicity in eyes that were injected with APC.

Conclusions: APC reduced leakage from Pre-existing CNV and from newly formed CNV. APC ability to decrease CNV growth and leakage should be further investigated as a possible effective treatment for CNV.

The role of vascular endothelial growth factor (VEGF) in activated protein C (APC)-induced inhibition of choroidal neovascularization (CNV)- a murine model

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Purpose: to study the role of vascular endothelial growth factor (VEGF) in activated protein C (APC)-induced inhibition of choroidal neovascularization (CNV) using laser induced CNV murine model

Methods: CNV was induced in C57BL/6J mice using indirect laser ophthalmoscope. Immediately following laser injury, the right eyes of the mice were injected intravitreally with 1µg APC diluted in 1µl saline/eye or 1µl saline/eye. Left eye served as untreated Naïve control. Three ,14 and 30 days after CNV induction, mice were euthanized, eyes were enucleated and cryo- preserved. Serial 10µm cryosections, parallel to the optic nerve axis, were obtained. Immunofluorescence staining using anti-VEGF antibodies was applied on 2-3 mice/ each time point. At least 5 sections of each eye which pass through the lesions were scanned and images were captured using a fluorescence microscope. Two masked reviewers graded the staining of the lesion area in a semi quantification scale of 0-4, to assess the levels of VEGF.

Results: Laser applications resulted in statistically significant elevation in VEGF levels as compared to the naïve untreated control (1.75± 0.47 vs. 0.50 ± 1.00 respectively, p=0.04). Three days after APC treatment, VEGF levels were decreased from 2.79±0.29 to 1.0± 0.70 as compared to saline treated eyes (p=0.08). Statistically significant reduction in VEGF levels was noted 14 days after APC treatment (0.24± 0.21 for APC treated mice vs. 1.75± 0.47 for saline treated mice; p=0.05). After 30 days from APC treatment, no difference in VEGF levels was noted between APC treated and untreated mice. (0.78 ± 0.11 vs. 0.72 ±0.27, respectively; p=0.82) .

Conclusions: APC treatment induced reduction in VEGF levels in CNV lesion sites. Further studies should clarify the contribution of VEGF to the protective effect of APC on the retina.

Subretinal survival of retinal progenitors (RPs) derived from human embryonic stem cells (hESCs) in different animal models

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Purpose: To examine the survival of RPs derived from hESCs following subretinal (SR) transplantation in immunodeficient rodent models.

Methods: hESCs (HAD102 line) engineered to express GFP were differentiated *in-vitro* towards a retinal fate using 2 protocols: To obtain RPs, hESCs were grown with bFGF, nicotinamide and CHIR while Retinal Pigmented Epithelium (RPE) cells were derived using our previously published protocol (Idelson et al., Cell Stem Cells, 2009).
Between 75-150K cells were transplanted as a suspension to the SR space of 3 animal models: Royal College of Surgeons (RCS) rats (n=66 eyes), Nude-RCS rats (n=18 eyes) and NSG mice (n=53 eyes). RCS rats were treated with Cyclosporine in the drinking water to reduce rejection. Nude-RCS rats are athymic and lack T cells, while NSG mice lack mature T, B and NK cells.
Success of engraftment was determined at 4 weeks (4w) post-transplant by *in-vivo* visualization of GFP expression using a Micron-III Retinal Microscope. Further survival, graft rejection or tumor formation was examined at set time points using the Micron-III and in select cases by Spectralis-OCT imaging *in-vivo* as well as by retinal histology.

Results: In RCS rats receiving hESC-derived RPs (n=42), cell rejection (often manifest as development of retinal detachment) was observed in 25% of eyes at 6w, rising to 70% rejection at 8w. In order to try and reduce cells rejection, RPs were then transplanted in Nude-RCS eyes (n=18). However, in this model rejection was also noted at 6w in 62% of eyes.
Interestingly, hESC-derived RPE cells survived in RCS rats for 8w or more with no signs of acute rejection (n=24).
Survival of RPs in NSG mice (n=27) was much improved, with 100% survival at 6w, 90% at 10w and 80% survival at 16w. However, in 2/4 eyes further followed for 22w, marked proliferation of the cells occurred with tumor development. In similarity to transplants in RCS rats, no signs of acute rejection were noted when hESC-derived RPE cells were transplanted in NSG mice (n=26).

Conclusions: Immune status of recipient animals influences transplant survival. NSG, a highly immunodeficient mouse, provides a better model for studying long term survival, differentiation and possible integration of RPs. hESC-derived RPs invoke much higher levels of rejection than RPE cells

derived from the same hESC line even when transplanted in immune-deficient animals.

Microglia activation exacerbates retinal degeneration in RPE65/rd12 mouse model for Leber congenital amaurosis

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Purpose: To assess the effect of treatment with minocycline on microglia activation and retinal degeneration in RPE65/rd12 mouse model of Leber congenital amaurosis.

Methods: Six RPE65/rd12 mice were treated with Minocycline (50mg/kg,) by intraperitoneal injection once a day for a period of two months. Seven mice were injected with PBS as control. Retinal function was evaluated using electroretinogram at baseline, 2, 4 and 8 weeks of treatment. The presence, distribution and activation status of microglial cells in the sub-retinal layer was assessed in flat mounts at the end of the treatment. The sub-retinal flat mounts were stained with microglial marker (Iba-1) and counterstained with DAPI. Images were analyzed using ImageJ.

Results: Mice treated with minocycline presented a twofold higher dark and light adapted b-wave and 2.5 fold higher light adapted a-wave compared with control mice after 8 weeks of treatment commencement ($p=0.04$, $p=0.03$, $p=0.03$, respectively). Moreover, retinas of minocyclin-treated mice presented with lower microglial cell number in the subretinal space compared to controls (mean± SE: 33.28 ± 2.8 vs 46.63± 2.13, $p=0.007$).

Conclusions: Minocycline treatment inhibited microglial cell activation and migration to the outer retina and improved both scotopic and photopic ERG responses in RPE65/rd12 mouse model of retinal degeneration due to retinoid cycle defect. These results provide a rationale for using minocycline as a therapeutic agent for treating LCA and possibly other RP forms associated with retinoid cycle defects.

Clinical, Electrophysiological and Immunological Features in Autoimmune Retinopathy

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Purpose: To present our experience in diagnosing and managing patients with AIR.

Methods: A retrospective review of medical records of patients diagnosed with AIR at Hadassah Medical Center between the years 2009-2017.

Results: Included were nine patients (6 males) with a mean age at presentation of 64.67 years. Five patients had previous cancer, of whom three had prostate cancer. The median period between onset of ocular symptoms and diagnosis was 36 months. Average visual acuity at presentation was 0.5 and was 0.3 at last follow-up. ERG demonstrated markedly reduced cone and rod amplitudes in all patients. Treatment included immunosuppression and plasmapheresis. After treatment, the ERG amplitudes stabilized in the majority but worsened in patients who stopped the treatment.

Conclusions: AIR is a diagnostic and therapeutic challenge to ophthalmologists. Diagnosis is based on a combination of clinically progressive disease with electrophysiological compromise and presence of circulating anti-retinal autoantibodies. Long-term immunosuppression is the mainstay of treatment, however, it is a condition associated with poor prognosis.

Update on Visidome: add-on accommodative intraocular lens

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Purpose: To present recent studies on a new accommodative intraocular lens in animal models

Methods: animal studies were done on living animal eyes in animal models: short (4 weeks) and long (6 month) follow up in rabbit eyes and a 3 month study in mini-pig eyes. The add-on lens was implanted in the ciliary sulcus following in-the-bag implantation of a conventional intraocular lens. IOL positioning, sizing and tissue reaction were investigated by gross inspection during follow up and histological examination after the animals were sacrificed. Intraocular pressure was monitored.

Results: All surgeries were performed successfully through a small incision. The add-on element was placed correctly with direct contact with the ciliary muscle. There was no or mild inflammatory tissue response and IOP was maintained.

Conclusion: Positioning of the add-on optical element is tolerated well and it has the potential for clinical use as an accommodative intraocular lens.

Eye-tracking based device for measurement of both manifest and latent eye deviation in adults and children

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Purpose: The current gold standard test for eye deviation measurement is the manual prism cover test. This test is at times challenging and limited by the level of cooperation and the examiner's skill. Cover tests are time-consuming and cumbersome and studies have shown high inter-examiner variabilityMoreover, the angle of strabismus itself may vary and the current tests do not allow for quick multiple testing of the same patient.

Methods: We conducted a clinical trial to evaluate the accuracy and repeatability of the Eyeswift, a novel eye deviation angle measurement method using an automatic system based on eye tracking, and compared it to the prism cover tests. A group of 24 adult subjects with eye deviations, were tested by multiple examiners using \both the automatic and cover tests in a masked fashion.

Results: A correlation of 89% was found between the automatic test and the golden standard of prism cover tests. The repeatability of the automated test was twice as high as that of the manual test (mean STD 1.35 vs. 0.71 respectively ($P<0.005$ paired t-test)). The average deviation measured by the automatic test was 13.5±1.5 (SD) and comparable to the cover test results of 14.2±1.3 (SD). The duration of the automatic test was….

Conclusions: The automated measurement is an accurate reproducible system. The system also reduces chair time significantly and has the potential of becoming a standard of care.
The system performs accurate automated orthoptic measurements. This can increase the work efficiency of ophthalmologists, in addition it may aid in prescription of prisms, monitor orthoptic therapy and provide pre and post surgerrt measurements

A Novel Technique Using Ab-Interno Er:YAG Laser Trabeculectomy : A Rabbit Model - Safety And Feasibility Results

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Purpose: To evaluate the safety and feasibility of a novel technique using Ab-Interno Er:YAG laser trabeculectomy.

Methods: A prospective, non-randomized clinical trial using an animal model of New-Zealand White rabbits. MMC was injected to the subconjunctival space prior the procedure. The laser was guided through an optical fiber probe and inserted into the anterior chamber through a 1mm clear corneal incision. The probe was placed juxtaposed to the trabecular meshwork. A pulsed wave was generated (wave length: 100-400 μsec; frequency: 10-500Hz; power 0.1-1.2 W) creating a new drainage sclerostomy connecting the anterior chamber to the subconjunctival space. Clinical evaluation (including slit-lamp examination of the anterior and posterior segments and tonometry) was performed prior the procedure, and at day 1,7,14 and 23 post procedure. Three animals were randomly sacrificed at day 1, 14 and 23 for histopathological processing and evaluation of the operated eye.

Results: Nine eyes of nine rabbits (three left and six right) were included.
No significant complications were noted during the procedure, except for a mild contact of the laser probe with the iris, due to the anatomic structure of the rabbit iris. Medium to large blebs formed in all animals in the end of the procedure.
Functional bleb were observed during follow-up in all but one eye (in which the bleb flattened at day 7). Maximal reduction of IOP was observed at day 7 (6.8±1.4 mmHg versus 12.9±2.2 mmHg at baseline, P=0.028).
None of the eyes exhibited clinical signs of inflammation or infection during the follow-up period. Except for one eye, all had non-reactive pupils.
Only minor degree of coagulation necrosis, lateral to the tunnel formation, was noted at all time-points.

Conclusions: Ab-Interno Er:YAG laser trabeculectomy seems to be a safe and feasible procedure , causing only minor coagulation necrosis without damaging nearby structures. It might be considered as a new surgical glauocoma treatment for lowering intraocular pressure. Further prospective clinical studies are needed to assess the effectiveness of this novel method.

Delivery of therapeutics to the back of the eye using a minimally invasive adjustable-depth blunt injector

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Purpose: Retinal degeneration diseases affect millions of patients worldwide and lead to vision loss. One of the major challenges in the development of treatments for these diseases is the safe and efficient delivery of therapeutics into the back of the eye. We developed a novel system and method for delivery of therapeutics into the extravascular spaces of the choroid (EVSC).

Methods: RCS rats, New Zealand rabbits and domestic pigs were injected with therapeutics including Indocyanine Green, Bevacizumab, narrow size iron oxide nanoparticles (IONP), Triamicolone Acetonide, and human mesenchymal stromal cells. Animals were examined by fundus imaging, spectral domain OCT, MRI, Intra ocular pressure, electroretinogram and histology up to 30 weeks following injection to assess safety and efficacy of the delivery.

Results: Injected therapeutics were distributed throughout the choroid covering >80% of the posterior segment surface immediately following injection. Mild (15-30mmHg) increase in IOP was recorded 2 minutes after injection. IOP returned to baseline values within 20 minutes. No change in IOP was recorded in the contralateral, non-injected control eyes. No retinal detachment, choroidal hemorrhage, inflammation or epiretinal membrane formation were detected in any of the injected eyes or contralateral control eyes. Transplantation of human mesenchymal stromal cells ameliorated retinal function in RCS rats for 5 months. Cells and IONPs were identified in rabbit and rat eyes for 10 and 30 weeks post injection, respectively.

Conclusions: The minimally invasive delivery system may be used to safely inject large volumes of therapeutics into the EVSC from the same location used for intravitreal injections. Injected therapeutics are spread in close proximity to the target tissues – choroid and retinal pigment. This injection system may present an innovative treatment delivery strategy and may lead to development of novel and advanced treatments as well as sustained treatments for blinding diseases without visual axis obscuration.

Chromatic pupilloperimetry for objective perimetry in retinal and optic nerve neurodegeneration

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Purpose: Static automated perimetry is the gold standard for measuring visual field (VF) defects. However, it is limited by its subjective nature and variability and cannot be performed with uncooperative subjects. We developed a novel chromatic pupilloperimeter (CP) that records rod- cone- and melanopsin-mediated pupil responses (PR) for very small (0.43°) red and blue light stimuli presented at 54 targets in a 24-2 degree VF.

Methods: 47 patients with retinitis pigmentosa (RP), glaucoma, age related macular degeneration (AMD), diabetic macular edema (DME) and Best vitelliform macular degeneration (BVMD), and 70 age similar controls were tested with the CP. Fifteen parameters of the PR were evaluated including maximal percentage of pupil contraction (PPC), maximal velocity of pupil contraction (MCV) and relaxation (MRV) and their latencies (LMCV and LMRV, respectively). Patient's PR were compared to their subjective VF testing (Humphrey 24-2) and spectral domain optical coherence tomography (SD-OCT) findings.

Results: Retinitis pigmentosa patients presented significantly diminished PR for blue and red light in areas that were abnormal by subjective perimetry. In these areas, PCP and MCV were lower than 3 standard errors away from the mean of controls. The average deviation in the LMCV for red light was significantly higher in RP patients compared with controls and correlated with Humphrey mean deviation (MD) score and OCT Ellipsoid Zone area. AMD patients presented with lower than normal MCV and MRV. The mean and median MCV recorded in BVMD patients in response to red light correlated with their Humphrey MD score and best corrected visual acuity. Glaucoma patients demonstrated normal latency of pupil contraction but significantly reduced PPC compared with controls in all VF defect locations in response to blue light ($p<0.0001$), correlating with RNFL thickness.

Conclusions: Chromatic pupilloperimetry may potentially be used for objective non-invasive assessment of rod-, cone- and melanopsin cell function in different locations of the retina associated with VF defects due to retinal and optic nerve degeneration. Different parameters of PR for focal chromatic stimuli may clarify the pathophysiology of different neurodegeneration diseases.

Tactile based imaging for the visually impaired

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Purpose: We aim to build a device for the blind and the visually impaired that translates camera or internet images into point tactile mechanical-acoustic pressure that can stimulate the cornea and the sclera.

Methods: The proposed vision device comprises a spectacles frame incorporating a miniature camera as well as a communication channel and a cornea non-touching AudioPixel chip acting as an array of mini speakers. The electrical output of the camera or the data received via the communication channel (e.g. images from the internet), after proper image processing, are transmitted to the chip, and its mini speakers provide tactile stimulation to the cornea. After some training, the wearer can correlate corneal spatial-tactile stimulation with real images.
The specially designed AudioPixel chip contains 32×32 mini speakers. The array generates spatially distributed pressure waves that stimulate the highly innervated corneal surface in many points simultaneously. This stimulation can simulate vision through the corneal sensory nerves instead of the malfunctional retina. Applying proper time-multiplexing super resolving concepts and a symbolic imaging can yield image resolutions that will be sufficient to allow visually impaired to function in a society.

Results: In general, we tested about 10 subjects (9 males and one female) in ages of 20-60. All were not visually impaired. We were able to transmit simple shapes via spatial tactile stimulation of the cornea/sclera. Shapes such as upper horizontal line, mid vertical line, lower horizontal line, X shape etc. It was found that successful identification depends on the shape of the stimulation pattern and it was around 70% of success rate.
We were able to quantify the two-points discrimination capability of the cornea which is somewhere between 1-1.5mm. We also performed clinical trials to measure the reaction time of 2 subjects to tactile pressure stimulation applied to the cornea. The average time was 1.25 and 1.28 sec respectively.
We also transmitted arrow via spatial tactile stimulation of the cornea and navigated people via maze without them seeing the maze.

Conclusions: We propose novel concept of solving some of the vision problems of blind and visually impaired people via non-retinal stimulation of the cornea. Preliminary quantified mapping of the spatial responsivity of the human cornea was clinically demonstrated and used for transmission of visual spatial information. We have constructed a prototype, demonstrated our unique operation principle in preliminary clinical trials in the lab as well as in real-life operational environment involving Audiopixel matrix.

Intraocular Projector for patients with corneal blindness unsuitable for keratoplasty

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Purpose: Corneal opacification is a primary cause of treatable blindness. Annually, approximately 100,000 keratoplasties are performed worldwide, though it is estimated that the number of patients is orders of magnitude greater. Patients with severe ocular surface disease such as Stevens Johnson Syndrome or Ocular Cicatricial Pemphigoid are not good candidates for conventional keratoplasty. The gold standard treatment for these patients is Osteo-Odonto-Keratoprosthesis , a demanding multistage high-risk procedure. For these patients, an intraocular projector can possibly provide the retina an image of good quality, bypassing the opaque cornea.

Methods: The presented project is a preliminary study of the concept of an intraocular projector. This device will receive data and energy wirelessly from an external device, and will project an image onto the retina. A thorough study of the relevant physical and biological constraints was performed, and two proof-of-concept experiments were made. In the first one, a eyeglasses-mounted camera was connected to a cellphone via wifi. In the second one, a 5X5mm image was projected from the cellphone through a pinhole onto a screen 12mm away.

Results: In the first experiment, data from the eyeglasses-mounted camera could be transferred online to the cellphone. In the second experiment, blurry images could be readily identified on the screen, simulating a possible projection solution that is independent of axial length.

Conclusions: An image generated by an external device can be transferred to a projecting device, and projected 1.2mm away with reasonable quality. Further research and development of this concept should focus of the miniaturization and encapsulation of the projector itself, energy transfer and improvement of image quality.

Refractive and ocular findings in individuals with Type-A vs. Type-B behavior patterns

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Purpose: The Type-A personality theory was developed in the 1950s as a chronic heart disease risk factor, and has been associated with heightened muscle tension (Chen and Coorough, 1986), increased sympathetic nervous system activity (Lee and Watanuke, 2007) and different ocular findings (e.g. Bubella et al., 2014). This study compares accommodative lag and pupil size among individuals displaying Type-A vs. Type-B behavior patterns (TABP/TBBP).

Methods: Healthy subjects with 6/6 DVA (Snellen), J1+ NVA (Jaeger), 40 SOA (PH Randot Test) and 8 CPM (BAF) participated in the study. Subjects answered the Bortner Type-A questionnaire (Cooper, 2013) in order to be classified by behavior pattern. Accommodative lag was measured with FCC and MEM. Pupil size was measured on an enlarged photograph of the eye with a ruler held underneath, taken in consistent lighting conditions (10 lux.). Multiple unpaired t-tests were performed on the results of the right eye to compare the mean results of the two behavior pattern groups.

Results: 60 female subjects (36 TABP, 24 TBBP), ages 18 to 35 (mean age 22.88±3.92 years), participated in this study. TABP individuals displayed a significantly higher accommodative lag in FCC ($p>0.04$). However, no statistically significant difference between TABP and TBBP subjects was found in pupil size ($p=0.90$) or MEM ($p=0.36$).

Conclusions: TABP individuals have a higher accommodative lag in FCC relative to TBBP. Previous studies show that FCC and MEM are not interchangeable tests (Locke & Somers, 1989), and this study indicates that the difference may be attributed to the subjective component in FCC which allows it to be influenced by behavior pattern, and may influence the subjective refraction test.

High expression of PD-1 and PD-L1 in ocular adnexal sebaceous carcinoma.

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Purpose: Ocular adnexal sebaceous carcinoma (OASC) is an aggressive malignancy that frequently recurs locally and metastasizes. Surgical extirpation may produce significant aesthetic morbidity, and effective systemic therapies for locally advanced or metastatic disease are largely ineffective. Immune checkpoint inhibitors have shown efficacy in the management of several solid tumors where tumor cell PD-L1 expression correlates with improved response. In this paper we aim to determine whether OASC might be amenable to immune checkpoint blockade.

Methods: We performed comprehensive immune profiling for CD3, CD8, PD-1, FOXP3, and PD-L1 in 24 patients with primary OASC. The composition, distribution and density of the tumor associated immune infiltrate were quantified by automated image analysis and correlated with measures of clinical outcome.

Results: Tumor cells in 12 OASCs (50%) expressed PD-L1. Higher densities of CD3+ ($p = 0.01$), CD8+ ($p = 0.006$), and PD-1+ ($p = 0.024$) tumor-associated T cells were associated with higher T category (≥T3a per the 7th edition of the American Joint Committee on Cancer staging manual). Higher tumor cell expression of PD-L1 correlated with higher density of PD-1+ tumor-associated T cells ($p = 0.021$).

Conclusions: Since a CD3+ CD8+ PD-1 + T-cell infiltrate represents a "suppressed T-cell phenotype" apparently permissive toward OASC progression, our findings provide a mechanistic rationale for the effective application of immune checkpoint blockade in OASC to abrogate PD-1/PD-L1 interaction and effectively unleash the immune infiltrate to treat higher-stage tumors.

Ocular Injury Seen in Urgent Care Centres

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Purpose: Cornea and conjunctiva injuries (CCI) comprise a large portion of patients presenting to hospital-based emergency departments (ED) with ocular involvement. Urgent Care Centres)UCC) are offer community based emergency care at lower cost than hospital-based emergency departments (ED) and with greater temporal convenience than primary care office settings. While there are many studies regarding the use of hospital-based ED by patients with CCI, this is the first study that describes the demographics and etiology of CCI presenting to UCC and risk factors for subsequent ED referral.

Methods: This retrospective study was approved by the institutional ethics committee. The setting is a UCC system, modelled on USA urgent care facilities, which had 17 branches at the time of the study. Electronic Medical Record data (between Nov 1, 2015 and Oct 31, 2016) of patients diagnosed corneal disorder, foreign body and eye disorder were retrieved and reviewed for inclusion/ exclusion criteria. Data collected included gender, age, chief complaint, diagnosis, treatment, discharge status (sent home or referred to ED) and temporal occurrence (time of year, and day of the week). ICD-9 codes were assigned to each record. Data were analysed by descriptive statistics and logistic regression analysis.

Results: Of study patients, 4797 presented with CCI (0.8%) with an average age of 32.6 ±18.2 years (71.3% men). Of these, 26.4% were referred to the ED compared to 6.8% from UCC. ICD-9 code Foreign body of the eye was the most common cause of CCI (56.5%) followed by the following ICD-9 codes: trauma (18.1%), chemical in the eye (11.1%) and contact lens related injury (5.1). Different logistic regression analyses showed the following risk factors for ED referral: age (22-64), male gender, ICD-9 Code FB, work related injury and the presence of a clinical abrasion in the eye.

Conclusions: Most CCI can be treated at UCC emphasizing the importance of this mode of health care delivery in the overall health system. The frequency of work related injuries and FB stresses the need for greater awareness of the need for eye protection.

Cover Testing: Clinical vs. Infra-Red Eye Tracker- A Comparative Study

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Purpose: This study examined the agreement between the clinical cover test (CT) and the CT performed with an eye tracker (ET). The right and left eye (RE, LE) position under the cover, typically assumed to be consistent in the CT, was compared. Additionally, the effect of cover duration on the measurements was assessed.

Methods: The SMI Red250 Infra Red (IR) eye tracker was used to record eye movements. An IR filter, synchronized with the eye position recording to indicate the precise cover and uncover times, was placed in front of a given eye for either three or 10 seconds to simulate the CT examination. The order of testing was pseudorandom and included three measurements of alternating near penlight CT, followed by near ET CT, or vice versa.
The study was approved by the institutional ethics committee. College students (N=30, 11 male) between the ages of 21-28 (mean age: 24.5± 2.22) with a mean VA of -0.03 ± 0.04 (logMAR) and with 20" stereopsis were enrolled. The CT and the ET CT results were compared using a paired t-test, as well as correlation and Bland and Altman (B-A) analysis.

Results: Clinical CT results were significantly correlated (R=0.9, R=0.89) but significantly different (p=0.001, p=0.002) from the RE and LE ET measurements, respectively. B-A analysis demonstrated that the ET tends to measure less XP than the CT with a mean difference of 1.20^{Δ} and 1.17^{Δ}, and limits of agreement (LOA) of $\pm 6.96^{\Delta}$ and $\pm 7.45^{\Delta}$ for the RE and LE, respectively. Mean CT results were $4.27 \pm 3.96^{\Delta}$ exophoria (XP), and mean ET three and 10 second results were $3.07 \pm 3.30^{\Delta}$ XP (RE), $3.10 \pm 3.05^{\Delta}$ XP (LE), and $2.80 \pm 3.39^{\Delta}$ XP (RE) and $4.18 \pm 3.80^{\Delta}$ XP (LE). RE and LE ET measurements were significantly correlated (R=0.98) and not significantly different (p=0.80). Three second and 10 second ET RE measurements were significantly correlated (R=0.97) but significantly different (p=0.00). B-A analysis demonstrated a mean difference of 0.96^{Δ} with three seconds yielding lower absolute values than 10 seconds, and LOA of $\pm 4.08^{\Delta}$.

Conclusions: Clinical CT and ET measurements were not interchangeable, with CT measurements indicating greater heterophoria than ET measurements. RE and LE ET measurements were confirmed to be interchangeable, however 10 sec cover durations result in larger absolute heterophoria measurements compared to three second cover. Clinicians should be aware of the effect of testing conditions on their CT findings.

MicroRNAs as biomarkers for ocular involvement in juvenile idiopathic arthritis

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Purpose: Juvenile idiopathic arthritis-associated uveitis (JIA-U) is a silent vision-robing disease. Favorable visual outcome depends largely upon early diagnosis and aggressive treatment to eradicate inflammation. This study was aimed to investigate microRNA's (miRNA) expression in JIA-U and explore a possible role as predictive biomarkers of the disease.

Methods: NanoString miRNA expression assay was performed on peripheral blood mononuclear cells (PBMCs) of 12 JIA patients: four patients with active uveitis (active group), four patients with uveitis in remission (non-active group) and four patients without uveitis (control group). Expression analysis was performed.

Results: Differential expression was found for several miRNAs in JIA with and without uveitis (all following adjusted p values<0.05). miR-432 and miR-337 were increased in the JIA-U groups (active and non-active) vs. control. Conversely, miR-582, miR-199b, miR-450a and miR-1537 were decreased for JIA-U patients vs. controls. Also noteworthy, miR-423 and miR-320e were increased in active vs. non-active uveitis and in active vs. control, thus indicating presence of active uveitis.

Conclusions: This study is the first to demonstrate different expression profiles of miRNAs in JIA patients with and without uveitis. If verified in larger studies, these findings may enable to identify JIA patients prone to develop uveitis.

Balloon Catheter Dilation as the Primary Treatment of Congenital Nasolacrimal Duct Obstruction.

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Purpose: To report the outcome of balloon catheter dilation as the primary treatment of congenital nasolacrimal duct obstruction (NLDO) in children of all ages.

Methods: A 10 years retrospective study of 148 children (270 eyes) ages 9 to 159 months (mean 29.6 ±17.7 months) who previously had not undergone a nasolacrimal surgical procedure and who presented with clinical signs of NLDO. All children underwent balloon catheter dilation of the nasolacrimal duct.

Results: Treatment success defined as complete resolution of NLDO symptoms present at the follow up visit at 1 week - 6 months after surgery was 87% (234 of 270 eyes). Partial success defined as occasional tearing which was acceptable to parents was in 3% (9 eyes). Only 10% of the children underwent a second procedure due to complete failure.
In a sub analysis by age groups: under 18 months, between 18-36 months and above 36 months - complete resolution rates were 85%, 93% and 77% and partial success rates were 3%, 3% and 4% respectively. There was statistically significant difference between the age groups (p-value= 0.007).

Conclusions: In children under 36 months of age, balloon catheter dilation as a primary treatment of NLDO resulted in complete resolution or substantial improvement of symptoms in 93% of children. Children older than 36 months have a less favorable outcome of 81% .
In this large cohort of patients with NLDO, balloon catheter dilation seems as an excellent procedure for primary treatment of congenital NLDO, particularly under the age of 36 months .

Novel method for optic nerves and chiasm dissection in mice, for studying optic neuritis.

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Purpose: Optic neuritis (ON) is an inflammatory disease of the optic nerves which may also involve the optic chiasm. ON is often studied in the animal model of mouse experimental autoimmune encephalomyelitis (EAE). The small size of the optic nerves and chiasm, as well as their location in the cranial vault makes their dissection in the mouse a challenging task. Present techniques do not enable the dissection of the optic nerve or chiasm in their entirety. One technique, commonly used for studying the retina, involves detaching the eye globe and pulling it out with a portion of the retrobulbar optic nerve. This technique may cause traction artifacts on the nerve. We present a dissection method better suited for examining the whole length of the optic nerves and chiasm in the mouse EAE.

Methods: We developed a technique for dissecting the optic nerves and chiasm through a craniotomy incision.

Results: We describe the stages necessary for exposing the optic nerves, the chiasm and the optic tracts and detaching them with minimal traction damage to the collected specimens.

Conclusions: We present a novel method for dissection of optic nerves and chiasm. This new protocol can provide researchers with adequate specimens for the study of optic neuritis and other disease models affecting the proximal optic nerves and chiasm.

Comparison of self-report questionnaire on dry eye with clinical test results: cross sectional study

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Purpose: Dry Eye Syndrome (DES) is a common complaint in ophthalmology and is defined as a chronic and progressive multifactorial disorder of the ocular surface, which results in symptoms of discomfort and visual disturbance and potential damage to the ocular surface (McDonald et al.,2015). In this cross-sectional study, we examined the correlation between self-report dry eye symptoms to the objective tests results in DES cases vs. controls, in contact lens (CL) wearers vs. non-CL wearers (N-CL), and in post refractive surgery (P-RS) vs. non-refractive surgery (N-RS) subjects.

Methods: 138 healthy subjects (96 females; 69 DES cases and 69 age-and-sex matched controls) with age range of 18-35, (mean age of 24.22±3.29 y.) were included in this study. One eye of each participant was tested, using TBUT and Ocular Surface Disease Index (OSDI) questionnaire. Dry eye cases were diagnosed by positive TBUT test of less than 5 sec and\or OSDI score>25 points. Analysis was done with Pearson's correlations and Independent Samples T-test.

Results: Mean TBUT result was higher in controls than DES cases (5.91±2.62 vs.4.00±2.06 respectively**;** $p<0.001$), and OSDI score was higher on DES cases vs. controls (16.95±10.**33** vs.11.18±**9.48** respectively**;** $p<0.001$). A slight and negative correlation between TBUT and OSDI among DES cases and controls was found ($r=-0.339$, $p<0.001$). There was no statistically significant difference in TBUT between CL and N-CL wearers ($p<0.001$). No correlation was found between signs and symptoms for patients after refractive surgery (N=4) and CL wearers (N=35), due to the small cohort of these groups.

Conclusions: OSDI questionnaire is not interchangeable to TBUT test on DES and NON-DES patients, implying there is not linear correlation between signs of dry eyes and the reported symptoms measured by these two tests.

Characterization of pupil responses to chromatic focal light stimuli in patients with Pseudotumor Cerebri

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Purpose: To assess the pupil reflex in response to focal chromatic light stimuli in patients with Pseudotumor cerebri (PTC).

Methods: Four Pseudotumor cerebri (PTC) patients (all females, age: 26.2± 4.3, mean± SD) and eight healthy age-matched controls (5 females, 3 males age 29.2± 6.3) were enrolled.

Ophthalmic assessments included complete ophthalmic examination, color vision, optic coherence tomography (SD-OCT), Pupil responses (PR) to focal blue (485nm, 170 cd/m^2) and red (624 nm, 1000 cd/m^2) -light stimuli presented at 54 targets in a 24-2 VF were recorded by chromatic pupilloperimeter. The percentage change of pupil size (PPC) and the maximal relaxation velocity (MRV) of the patients was compared to the PR of controls. Patients were tested within 48h of diagnosis, then at 1 week and 2 months following acetazolamide intervention.

Results: In three of the patients, substantially lower PPC and MRV (≥ 4 SD lower than mean of controls) were recorded in the first visit. Pupil responses to blue but not red stimuli improved with acetazolamide treatment, suggesting a residual effect on the cone-mediated PLR. The pupil responses improved mostly in the center of the visual fields.

Conclusions: Multifactorial analysis of the PLR for focal blue and red light stimuli may enable objective noninvasive sensitive assessment of the function of visual pathways mediating the PLR in PTC patients as well as response to treatment.

Effect of light and diurnal variation on macular thickness in X-Linked Retinoschisis: A pilot study

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Background: Diurnal variations in foveal thickness have been reported in several ocular pathologies including X-linked retinoschisis (XLRS), but its underlying mechanism is poorly understood. Rods are active under scotopic conditions with high metabolic demand. Avoidance of dark conditions lowers the overall metabolic demands of the retina and may have positive effect on metabolic activity and macular thickness.

Purpose: To evaluate whether exposure to light and diurnal variation influence macular thickness in XLRS patients.

Methods: Five non-related patients with clinical suspicion of XLRS underwent RS1 gene sequencing and Optical Coherence Tomography measurements at three consecutive times: morning following sleep in a dark room, morning following sleep in an illuminated room and late afternoon following sleep in an illuminated room. Central macular thickness was compared between measurements and molecular analysis was performed.

Results: Five RS1 mutations were identified: p.Gly140Arg, p.Arg141Cys, p.Gly109Glu and p.Pro193Leu and p.Arg200His in patients 1-5, respectively. Two patients (4-5) had atrophied macula and were excluded from macular thickness variation analysis. A significant decrease in central macular thickness (CMT) between morning and late afternoon measurements was observed in all patients (1-3: mean: 455.0±32 µm to 342.17±39 µm, 25%). Morning measurements following sleep in an illuminated room show a CMT reduction in all eyes of all patients with a mean reduction of 113 µm (mean: 547.17±105 µm to 455.0±32 µm, 17%).

Conclusions: Among patients with genetically confirmed XLRS, retinal thickness significantly reduced following sleep in an illuminated room and further decreased at the afternoon compared to the morning of the same day. These results could help shed light on the pathophysiologic process underlying intraretinal fluid accumulation involved with the disease.

Effect of circadian rhythm disruptions on the development of type 2 diabetes and cataract in sand rats (*Psamommys obesus*)

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Purpose: To Study the effect of short photoperiod acclimation on the development of diabetes and metabolic cataract, utilizing a non-traditional diurnal animal model, the fat sand rat (*Psamommys obesus*).

Methods: 56 sand rats were exposed in groups of 14 to 2x2 experiments: 1. Day length (short photoperiod vs. neutral photoperiod) 2.Diet (standard rodent diet vs. low energy diet) as variables. After 20 weeks under these conditions, we performed an oral glucose tolerance test and examined the lens opacity.

Results: Short photoperiod acclimation, which dampens the behavioral and molecular daily rhythms amplitude, accelerated the development of T2DM and cataract, compared to neutral photoperiod. 42.8% (6/14) of the sand rats kept under short photoperiod with standard rodent diet developed mature cataract vs. none in those kept under neutral photoperiod.

Conclusions: Short photoperiod acclimatization accelerated the onset of diabetes and resulted in the development of metabolic mature cataract. We suggest that reduced robustness of the circadian system of diurnal species increases their susceptibility to diabetes, and consequently to cataract development. We believe that using diurnal animal models to study circadian rhythms related diseases will produce new insights that may eventually lead to the development of more effective treatments, and recommendations for better artificial lighting usage, which will enhance daily rhythms. A large-scale patient research is needed to test the applicability of our results to the human lens.

Adrenocorticotropic Hormone Gel Treatment for Patients with Refractory Non-Infectious Uveitis

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Purpose: To describe the potential role of adrenocorticotropic hormone (ACTH) gel treatment in patients with chronic and refractory non-infectious uveitis.

Methods: The medical records of patients with non-infectious uveitis, treated with 80 units ACTH gel, administered subcutaneously twice-weekly (H.P. Acthar® Gel; repository corticotropin injection; Mallinckrodt Pharmaceuticals, St. Louis, MO) were reviewed. Complete clinical evaluation including visual acuity, intraocular pressure, presence of intraocular inflammation, as well as ocular complications and potential side effects was recorded and analyzed in all patients. Refractory disease was defined as uveitis that remained uncontrolled on therapy and/or was dependent on systemic and local corticosteroids. Therapy failure was defined as an absent of clinical improvement of inflammation with treatment.

Results: We report the clinical course of five patients with bilateral, non-infectious uveitis, treated with ACTH gel for a mean of 14 months. Types of uveitis included anterior, intermediate and pan-uveitis. All patients had chronic, refractory and steroid-dependent ocular inflammation with subsequent development of ocular complications, including band keratopathy, cataract, synechiae formation, glaucoma, macular edema and epiretinal membrane. Treatment with ACTH gel was administered, and clinical outcome measures were observed. All patients demonstrated significant improvement in disease activity, stable visual acuity, and an absence of side effects to therapy. Systemic steroids dosage was successfully reduced from a mean dose of 14 mg/day upon the initiation of ACTH gel treatment to 5 mg/day at last follow up.

Conclusions: Subcutaneous ACTH gel has shown to be a safe and effective therapy in the management of non-infectious uveitis. Specifically, ACTH gel plays a role in refractory and steroid-dependent cases and in those who do not respond to or are unable to tolerate other immunomodulatory therapies.

Relationship between air pollution and Urgent Care Centers visits for conjunctivitis in Jerusalem

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Purpose: Several studies have shown associations between air pollution and emergency department (ED) visits for conjunctivitis. They found that exposure to pollutants such as O_3, particular matter ($PM_{2.5}$, PM_{10}) and SO_2, increases the risk of conjunctivitis visits at ED. However, most cases of conjunctivitis are likely to be treated in the community at regular clinics or at Urgent Care Centers (UCC). This study examine the associations between UCC visits for conjunctivitis and ambient air pollution levels Jerusalem, Israel.

Methods: This anonymous retrospective study included UCC visits with the diagnosis of conjunctivitis in Jerusalem, for the period 1/01/2008-31/01/2018. Daily average levels of wind speed and direction, temperature, relative humidity, CO, SO_2, NO_x, NO_2, PM_{10} and $PM_{2.5}$ and of O_3, were obtained from continuous monitoring stations. A time-stratified case-crossover method was used to estimate the associations between visits for conjunctivitis and exposure to air pollutants. Modeling was performed feeding into the models the pollution variables and meteorological factors lagged by the same number of days, from 0 to 10 days. In addition, the model considers holidays and weekends, and the number of days from the time of exposure to arrival to UCC. Descriptive statistics and correlation coefficients were obtained.

Results: During the study period, 15,599 subjects were diagnosed with conjunctivitis, of which 8,002 (51%) were men. One third (29.0%) of the subjects were younger than five. The model showed the following pollutants are risk factors for conjunctivitis ($p<0.05$): NO_2 lagged 8-9 days, NO_X lagged 5, 7-9 days, NO lagged 5 and 9 days and $PM_{2.5}$ lagged at 8 days. In contrast, the following factors were protective ($p<0.05$): NO_X, O_3 and CO lagged, 3, 5 and 7 days, respectively.

Conclusions: The findings of this study suggest that there are associations between levels of air pollution and UCC visits for conjunctivitis, with different temporal trends for each ambient air pollutant. On certain days exposure to pollution is a risk factor and on others it is protective.

Computed Tomography Induced Cataract – A Population Based Study Of Association Between Radiation Exposure And Cataract Incidence

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Purpose: To examine the association between radiation exposure from computed tomography (CT) studies and cataract incidence and to explore dose dependency between CT associated radiation exposure and cataract formation.

Methods: A population based retrospective cohort study including Southern Israel residents who underwent CT scans in Soroka University Medical Center (SUMC) between the years 1996-2014 was performed. As a reference group, we included residents who underwent ultrasonic (US) tests but not CT during the same study period.

Results: A total of 61,885 subjects were included, of whom 66.7% (n=41,256) underwent at least one CT scan between the years 1996-2014. In a multivariate analysis we found no association between cataract and head and neck CT (HR 0.99, 95% CI 0.82; 1.20) or other CT (HR 0.97, 95% CI 0.76; 1.24). In stratification by age, a significant increased risk for cataract associated with head and neck CT (HR 2.25, 95% CI 1.41; 3.59) but not with other CT (HR 1.32, 95% CI 0.67; 2.58) was observed among subjects younger than 60 years. No association between CT and cataract was observed among subjects older than 60 years.

Conclusions: In our study population, we found a significant increased risk for cataract associated with head and neck CT among subjects younger than 60 years.

Comparison of surgical and outcome parameters of Dacryocystorhinosctomy approaches

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Purpose: To compare outcomes of patients with nasolacrimal duct obstruction treated with simultaneous bilateral or unilateral dacryocystorhinostomy (DCR) in external or endoscopic-endonasal approach.

Methods: Retrospective charts review in Rabin medical center between 2012-2017 of patients adults and children. Data was collected on patient age and sex, surgery and anesthesia type and duration, and complications (intra and post-operative hemorrhage, nasal synechia, reoperation rates and others).

Results: 96 adults and 27 children underwent 111 and 41 surgical procedures, respectively. In the adults, durations of anesthesia and surgery were significantly longer in the external bilateral DCR group (130 and 90 min respectively) than in the bilateral endoscopic-endonasal approach. In the children, no significant between-group difference in surgery duration was found. In neither age population was bilateral endoscopic surgery associated with excessive intraoperative or postoperative complications of hemorrhage, infection, and epiphora.

Conclusions: Shorter anesthesia and surgery, together with similar and low rate of complications, suggests that in cases of bilateral nasolacrimal duct obstruction in adults and children, simultaneous bilateral endoscopic-endonasal dacryocystorhinostomy may yield excellent therapeutic results.

Results of Cataract Surgery in Eyes with Adult-Onset Foveomacular-Vitelliform Dystrophy (AFVD)

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Purpose: Retinal disease process poses a question on the safety and outcomes of imminent cataract-surgery. For instance, cataract-surgery in the presence of intra-retinal fluid can worsen diabetic macular edema and on the other hand has no adverse effect on age related macular degeneration (AMD). However, the outcomes and safety of cataract-surgery in AFVD eyes is unknown.

Methods: Data was collected retrospectively on AFVD eyes that underwent cataract-surgery. Eyes with NVAMD that had cataract-surgery served as controls. We compared the outcome of surgery to a dataset of 1304 cataract -surgeries conducted in Hadassah and to a dataset of total 83 AFVD eyes presented in our clinic at the time of diagnosis. Data collection included demographics, visual-acuity (LogMAR), results of eye exams and optical coherence tomography.

Results: The study included 29 consecutive eyes (17 NVAMD, 12 AFVD). Mean-age (years) 82±4.7 (NVAND) and 81.3±5.7 (AFVD); 18 females, 11 males.
VA of AFVD before surgery (0.5±0.6) was not statistically different 1 week (0.29±0.59) or over 1 month post-surgery (0.25±0.61); p=0.075 and P=0.18 respectively. 3 months post-surgery, no CNV occurred.
Significant difference was found when comparing VA of AFVD before surgery (0.5±0.6) to total 83 AFVD eyes (0.22±0.57) P=0.04. 1 month post-surgery no difference was found comparing the groups (0.25±0.61 post-surgery) P=0.188.
Borderline difference was found comparing VA of NVAMD and AFVD before surgery (NVAMD=0.8±0.85, AFVD=0.5±0.6, P=0.058). 1 month post-surgery, no difference was found comparing VA (NVAMD=0.5±0.55, AFVD=0.25±0.61, P=0.078). Mean VA of cataract surgeries conducted in Hadassah at a similar period improved from 1.2 to 0.76 post-surgery, compared to improvement to 0.5 NVAMD and 0.25 AFVD post-surgery.

Conclusions: Following cataract surgery, mean VA improved in eyes with AFVD (0.25) and NVAMD (0.3). There were trends for better-corrected VA of AFVD eyes compared to NVAMD eyes, improvement of VA of AFVD eyes following surgery, and improved VA of AFVD and NVAMD eyes compared to total group of eyes having cataract surgery. The VA of AFVD before surgery was significantly lower than the total AFVD eyes presented at time of diagnosis. Post-surgery, VA of AFVD improved and was not statistically different than AFVD eyes presented at diagnosis.
These findings indicate the safety and efficacy of cataract-surgery in AFVD eyes.

Combined phacoemulcification vitrectomy procedure in proliferative versus non proliferative diabetic retinopathy

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Purpose: To compare intra and post-operative complications in combined phaco vitrectomy surgeries performed in patients with proliferative diabetic retinpathy (PDR) versus non proliferative diabetic retinopathy (NPDR).

Methods: Retrospective, case series of patients with diabetic retinopathy who underwent combined phaco-vitrectomy surgery at Rabin medical center between 2008 – 2017. We compared intra operative complications including posterior capsular tear, retinal tear, macular hole and hemorrhage and post-operative complications including corneal edema, increased intra ocular pressure, neovascular glaucoma, persistent inflammation, posterior synechiae, VH, retinal detachment, epiretinal membrane, cystoid macular edema and posterior capsular opacity. The patients were divided into 2 groups patients with proliferative diabetic retinopathy versus non proliferative diabetic retinopathy

Results: A total of 104 patients were included in this study. The PDR group was comprised of 80 eyes (76.9%), and the NPDR group of 24 eyes (23.1%). The mean follow-up period in both groups was 12 months. The most common indications for surgery in the PDR group were VH (57.5%), ERM (23.9%), and TRD (14.1%) (Table 2), while ERM (34%), RRD (14%) and VMT (10%) were the most common ones in the NPDR group. We report a low rate of complications in both groups, without statistically significant differences between the groups. Iatrogenic retinal tear was the most common intra-operative complication in both groups and was observed in 19% of PDR eyes and in 8% of NPDR eyes (p=0.195), while intra ocular bleeding occurred in 10% and 4%, respectively (p=0.63) and posterior capsular rupture occurred in 5% and 0%, respectively (p= 0.57).
CME was the most common post-operative complication in both the PDR and NPDR groups (26.9% and 28%, respectively, p=0.842) followed by the formation of ERM (18.7% and 16%, respectively, p= 0.764). Complications such as corneal edema, persistent inflammation and neo-vascular glaucoma were observed only among PDR eyes, though this difference was not statistically significant.

Conclusions: There were no statistically significant differences regarding intra and post-operative complications between PDR and NPDR patients undergoing combined phaco-vitrectomy surgery. We are reassured that combined phaco-vitrecomy is a safe procedure in both groups of patients.

The Cataract Electronic Medical Records Dataset at Hadassah Medical Center

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Purpose: To perform a big data Electronic Medical Records (EMR) evaluation for cataract surgery at Hadassah Medical Center during 2013-2018 as a model for EMR mining for quality assurance and research poses.

Methods: A retrospective study was performed to extract routinely collected data from EMR of all consecutive patients undergoing cataract surgery at Hadassah Medical Center from 2013 until 2018. Data included age, gender, uncorrected and pinhole (PH) visual acuity (VA) and intraocular pressure (IOP) before and at different time points after surgery, and the need of reoperations during the first year following cataract extraction. Statistical analysis was based on Wilcoxon, Chi-Square and Mann-Whitney U-tests.

Results: From a database of 11,545 patients, only 2684 (23.2%) surgeries had the complete pre-defined information and were included for statistical analysis. While the surgeries rate increased in the tested period, the missing data was decreased per year (valid data in 2018: 25.3% of cases, and in 2013: 6.7%). VA pre- or post-surgery was the most common missing parameter in the data. Mean age at the time of surgery was 69.8±14.6 years and 52% of the cases were males. Median uncorrected logMAR VA (UCVA) improved from 0.6 before surgery to 0.4 after surgery ($P<0.001$). The median best corrected VA was 0.4 pre- and 0.3 post-surgery ($P<0.001$), with no statistically significant difference between genders for all measured VA's ($P=0.45$). Mean IOP was statistically significant increased after surgery, yet, with no clinical relevance (13.9±3.9 mmHg vs. 14.1±4.3 mmHg respectively, $p=0.005$).

Conclusions: Routinely collected electronic data provide sufficient for VA outcomes of cataract surgery and risk of postoperative retinal detachment in minority of cases on the defined time period. Missing values are in downward trend, implying for improvement in data collection. Inaccuracies in big data from EMR are major challenge in applying this methodology for quality assurance purposes. Further analysis may identify preoperative risk factors for intra- or postoperative complications.

Socio-demographic Disparities in Amblyopia Prevalence Among Israeli Adolescents

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Purpose: Amblyopia is a significant cause of visual deficit in childhood and one of the most common causes of persistent visual impairment among adults. Characterization of diagnosed adolescents may contribute to a broader understanding of the epidemiologic profile of amblyopia. Therefore, we aimed to evaluate whether there are socio-demographic disparities in amblyopia prevalence among Israeli adolescents, in order to identify susceptible groups in population.

Methods: A nationwide, population-based, cross-sectional study. The study population consisted of Israeli candidates for military service examined between 1993 and 2017. All candidates underwent visual acuity examination prior to their recruitment. Socio-demographic data and previous medical record were documented as well. Amblyopia was defined as best corrected visual acuity (BCVA) < 6/9 in either eye or as an interocular difference ≥ 2 lines, without an accompanying ocular disorder. Associations were analyzed using logistic regression models. Results are presented as odds ratio (OR) with 95% confidence interval (CI).

Results: Among 1,219,464 candidates (55.35% males) aged 17.15 ± 0.26 years, who were born in Israel, amblyopia was diagnosed in 1.07%, with unilateral amblyopia comprising 79.43% of diagnosed cases. Females had elevated odds for amblyopia compared with males (OR 1.17, 95%CI 1.12-1.21). Being in the lowest socioeconomic status (SES) increased the odds of having amblyopia in both genders, compared with the highest SES (males: OR 1.64, 95%CI 1.45-1.87; females: OR 1.47, 95%CI 1.20-1.81). Above average cognitive function score (CFS) decreased and below average CFS increased the odds of having amblyopia in both genders, compared with average CFS (males: OR 0.83, 95%CI 0.78-0.88, OR 1.27, 95%CI 1.19-1.35; females: OR 0.87, 95%CI 0.81-0.93, OR 1.27, 95%CI 1.19-1.36). Among males, Orthodox and Ultra-orthodox education were associated with increased odds for amblyopia, compared with secular education (OR 1.16, 95%CI 1.09-1.25, OR 1.90, 95%CI 1.73-2.09).

Conclusions: We found substantial socio-demographic disparities in amblyopia prevalence among Israeli adolescents. Demonstration of inequities at a national level could aid future guidance of health policy and augmentation of current screening programs.

The Combination of Whole Exome Sequencing and Clinical Analysis Allows Better Diagnosis of Rare Syndromic Retinal Dystrophies

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Purpose: To identify the accurate clinical diagnosis of rare syndromic inherited retinal diseases (IRDs) based on the combination of clinical and genetic analyses.

Methods: Four unrelated families with various autosomal recessive syndromic IRDs, were genetically investigated using whole exome sequencing (WES).

Results: Two affected subjects in family MOL0760 presented with a distinctive combination of short stature, developmental delay, congenital mental retardation, microcephaly, facial dysmorphism and retinitis pigmentosa (RP). Subjects were clinically diagnosed with suspected Kabuki syndrome. WES revealed a homozygous nonsense mutation (c. 5492dup, p.Asn1831Lysfs*8) in *VPS13B* that is known to cause Cohen syndrome. The index case of family MOL1514 presented with both RP and liver dysfunction, suspected initially to be related. WES identified a homozygous frameshift mutation (c.1787_1788del, p.His596Argfs*47) in *AGBL5,* associated with nonsyndromic RP. The MOL1592 family included three affected subjects with crystalline retinopathy, skin ichthyosis, short stature and congenital adrenal hypoplasia, and were found to harbor a homozygous nonsense mutation (c.682C>T, p.Arg228Cys) in *ALDH3A2*, reported to cause Sjögren-Larsson syndrome (SLS). In the fourth family, SJ002, two siblings presented with hypotony; psychomotor delay, dysmorphic facial features, pathologic myopia, progressive external ophthalmoplegia and diffuse retinal atrophy. Probands were suspected to have atypical Kearns-Sayre syndrome, but were diagnosed with combined oxidative phosphorylation deficiency-20 due to a novel suspected missense variant (c.1691C>T, p.Ala564Val) in *VARS2*.

Conclusion: Our findings emphasize the important complement of WES and thorough clinical investigation in establishing precise clinical diagnosis. This approach constitutes the basis for personalized medicine in rare IRDs.