The American Ophthalmological Society

ONE HUNDRED AND FIFTY-NINTH ANNUAL MEETING

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MAY 18–20, 2023
THE OMNI GROVE PARK INN
ASHEVILLE, NORTH CAROLINA

The American Ophthalmological Society

Office of the Executive Vice President
Portland, OR
May 2023

THE ONE HUNDRED AND FIFTY-NINTH ANNUAL MEETING
of the Society will be held at The Omni Grove Park Inn in Ashville, NC

Thursday through Saturday
May 18–20, 2023

COMMITTEE ON PROGRAMS

Sean P. Donahue, Chair
Jennifer I. Lim
Carol L. Karp
M. Roy Wilson

The American Ophthalmological Society

THE ONE HUNDRED AND FIFTY-NINTH ANNUAL MEETING

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TARGET AUDIENCE

This activity has been designed to meet the educational needs of ophthalmologists across all subspecialties involved in clinical or surgical eye care, academic, and leadership who are actively involved in or previously cared for patients.

MEETING OBJECTIVES

The objectives of the 2023 Annual Meeting are to:

- Apply new imaging modalities to evaluation of patients with retinal, glaucoma, and other ophthalmic diseases.
- Assess the application of new drug delivery techniques in the clinical practice of ophthalmic patient care.
- Recognize and describe new information about diagnosis and treatment of various categories of ophthalmic diseases, including pediatrics, cornea, glaucoma, and retina.
- Assess the impact of new research in the evaluation and management of ophthalmic disease.
- Recognize the risks and benefits of gene therapy in patients with inherited retinal disease.
- Recognize age-related specifics of visual function.

ACCREDITATION STATMENT

In support of improving patient care, this activity has been planned and implemented by Medical Education Resources (MER) and American Ophthalmological Society. MER is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

PHYSICIAN CREDIT DESIGNATION STATEMENT

Medical Education Resources designates this live activity for a maximum of 13.0 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

FINANCIAL DISCLOSURE / CONFLICTS OF INTEREST

It is the policy of Medical Education Resources to ensure balance, independence, objectivity, and scientific rigor in all its educational activities. In accordance with this policy, MER identifies conflicts of interest with its instructors, content managers, and other individuals who are able to control the content of an activity. Conflicts are resolved by MER to ensure that all scientific research referred to, reported, or used in a continuing education activity conforms to the generally accepted standards of experimental design, data collection, and analysis.

Relevant financial disclosures of all presenting authors, staff, and members of the Committee on Programs are listed on pages 7–8 in this program book. If the presenter has a financial disclosure related to the specific presentation, the disclosure will be stated verbally and presented on the first slide of their presentation. Audience participants are required to state their financial disclosure before they join a discussion of a paper or poster.

FDA STATUS DISCLAIMER

Some material on recent developments may include information on drug or device applications that are not considered community standard, that reflect indications not included in approved FDA labeling, or that are approved for use only in restricted research settings. This information is provided as education only so physicians may be aware of alternative methods of the practice of medicine, and should not be considered endorsement, promotion, or in any way encouragement to use such applications. The FDA has stated that it is the responsibility of the physician to determine the FDA status of each drug or device he or she wishes to use in clinical practice, and to use these products with appropriate patient consent and in compliance with applicable laws.

The Society provides the opportunity for material to be presented for educational purposes only. The material represents the approach, ideas, statement, or opinion of the presenter and/or author(s), not necessarily the only or best methods or procedure in every case, nor the position of the Society. The material is not intended to replace the physician's own judgment or give specific advice for case management. The Society specifically disclaims any and all liability for injury or other damages of any kind for any and all claims that may arise out of the use of any technique demonstrated or described in any material by any presenter and/or author(s), whether such claims are asserted by a physician or any other person.

PARTICIPATION AND CONSENT TO BE RECORDED

The 2023 Annual Meeting will be recorded for subsequent posting on the Society's website, including discussion. Submitting questions to discuss a presentation is considered implicit consent to the participant's discussion being included in this recording. Attendees who do not wish to be recorded should refrain from submitting questions.

BYLAWS

The following Bylaws are published each year in the program as a reminder to the members of the Society:

ARTICLE IX, Section 3 – Any member who shall be absent from meetings for three consecutive years without acceptable excuse shall be dropped from the roll, except for Honorary Members, Emeritus Members, Members of twenty years standing or those then serving in the armed forces. An excuse for absence is acceptable only when a member is ill, or when there is illness of a member of his or her immediate family and may not be considered approved until received in written form and acted upon by the Council. The Council shall have the authority to approve other excuses only upon a finding of exceptional circumstances. This Bylaw shall be printed in every call for the Annual Meeting.

CANDIDATES WHOSE THESES WERE APPROVED AFTER THE 2022 ANNUAL MEETING:

Renato Ambrosio	Rio de Janeiro, Brazil
Francesco Bandello	Milan, Italy
Claude Burgoyne	Portland, OR
Winston Chamberlain	Portland, OR
Ta Chen Peter Chang	Miami, FL
John Chen	Rochester, MN
Karl Csaky	Dallas, TX
Jacque Duncan	San Francisco, CA
K. Thiran Jayasundera	Ann Arbor, MI
Ronald Mancini	Dallas, TX
Jonathan Myers	Swarthmore, PA
Victor Perez	Miami, FL
Ryan Rush	Amarillo, TX
Bhavna Sheth	Milwaukee, WI

IN MEMORIAM

The Executive Vice President has received notice of the deaths of the following members during the past year:

William B. Glew, MD	Chevy Chase, MD	Joined 1979
David L. Knox, MD	Baltimore, MD	Joined 1973

FINANCIAL DISCLOSURES

The following are the relevant healthcare-related financial disclosures of those involved in the preparation or presentation of this AOS event. The AOS Committee on Programs gathered this information to plan the program and has attempted to manage relevant conflicts of interest to present a balanced program. The presenter will indicate on the first slide and verbally at the beginning of the talk, if any of the financial disclosures listed has a relationship to the specific presentation. Participants that might speak from the floor are **required** to state their financial disclosures before they speak.

CATEGORY	CODE	DESCRIPTION
Consultant/ Advisor	C	Consultant fee, paid advisory boards or fees for attending a meeting (for the past 1 year)
Employee	E	Employed by a commercial entity
Lecture Fees	L	Lecture fees (honoraria), travel fees or reimbursements when speaking at the invitation of a commercial entity (for the past 1 year)
Equity Owner	O	Equity ownership/stock options of publicly or privately traded firms (excluding mutual funds) with manufacturers of commercial ophthalmic products or commercial ophthalmic services
Patents/Royalty	P	Patents and/or royalties that might be viewed as creating a potential conflict of interest
Grant Support	S	Grant support for the past 1 year (all sources) and all sources used for this project

ASBELL, Penny
C – Glia LLC

BENNETT, Jean
C – Akouos, Frontera, RegenXBio, Spark Therapeutics
O – Opus Genetics

CHEN, Teresa
S – Alcon Laboratories, Fidelity Charitable Fund, NIH

CORREA, Zelia
C – Castle Biosciences Inc

GROSSNIKLAUS, Hans
C – Aura Biosciences

GUO, Lucie
P – Stanford (patent)

HALLER, Julia
C – Genentech Inc, Regeneron Pharmaceuticals Inc
O – Outlook Therapeutics

HANES, Justin
O – NovusBio LLC, Novus Vision LLC

HUANG, David
P – Visionix/Optovue
S – Visionix/Optovue

JAYASUNDERA, K. Thiran
P – University of Michigan (patent)

JURKUNAS, Ula
P – Harvard (patent)

KARP, Carol
C – Interfeen Biologics
O – Interfeen Biologics

KIM, Judy
C – Allergan, Genentech Inc/ Roche, Novartis, Regeneron Pharmaceuticals Inc
S – Optos

KUPPERMANN, Baruch
C – Allegro Ophthalmics, Allergan, Aviceda Therapeutics, Clearside, EyeBio, Eyedaptic, Genentech Inc, Glaukos Corporation, InflammX Therapeutics, Iveric Bio, jCyte, Novartis Pharmaceuticals, Regeneron Pharmaceuticals Inc, ReVAnna Therapeutics, Ripple Therapeutics, Theravance Biopharma
L – Allergan, Genentech Inc
S – Allegro Ophthalmics, Allergan, Genentech Inc, Ionis, Iveric Bio, Novartis Pharmaceuticals, Regeneron Pharmaceuticals Inc, RegenXBio

LIM, Jennifer
C – Genentech Inc/Roche, Opthea, Regeneron Pharmaceuticals Inc
S – Eyenuk, Regeneron Pharmaceuticals Inc

MEDEIROS, Felipe
C – Alcon, Allergan, Carl-Zeiss Meditec, Heidelberg Engineering, Novartis Pharmaceuticals, Perceive Therapeutics, Stuart Therapeutics

OLSEN, Timothy
O – iMacular Regeneration LLC

PEREZ, Victor
S – NIH/NEI R01EY024485

SARRAF, David
C – Amgen, Bayer, Genentech Inc, Iveric Bio, Novartis Pharmaceuticals, Optovue/Visionix
S – Amgen, Boehringer, Genentech Inc, Heidelberg and Topcon, Optovue/Visionix, Regeneron Pharmaceuticals Inc

SEDDON, Johanna
O – Apellis Pharmaceuticals Inc, Gemini Therapeutics Inc

SINGER, Michael
G – Unity Biotechnology

SMALL, Kent
P – Molecular Insight Research Foundation

TSENG, Victoria
S – Research to Prevent Blindness

WALLACE, David
S – National Eye Institute

WIGGS, Janey
C – Editas

WILSON, M. Edward
S – EyePoint, Ocular Therapeutix, Ophtec

WILSON, Steven
P – Cleveland Clinic and Steven E. Wilson (patent pending)

WLADIS, Edward
O – Praxis Biotechnology

NO RELEVANT FINANCIAL RELATIONSHIPS TO DISCLOSE

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AUGSBURGER, James
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KERR, Natalie
KHANDWALA, Nikhila
KIM, Ivana
KITAYAMA, Ken
LEFFLER, Christopher
LISCH, Walter
MENDEZ, Amber
MIELER, William
PARIKH, Ravi
PARSA, Cameron
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SHERRY, Brooke
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SINGH, Arun
SKUTA, Gregory
SMALL, Kent
SPAETH, George
STEIN, Joshua
TRABOULSI, Elias
TSANG, Stephen
VAN METER, Woodford
WANG, Sophia
WEISENTHAL, Robert
WILSON, David
WILSON, M. Roy
YOUNG, Terri

**Members of the Committee on Programs*

AOS 2023 Program

American Ophthalmological Society
Meeting Schedule

THURSDAY, MAY 18		
11:30 AM – 5:00 PM	Registration Desk Open	*Heritage Foyer*
12:00 PM – 1:00 PM	New Member Luncheon (by invitation)	*Mountain View Terrace*
1:30 PM – 3:00 PM	New Member Spotlight Presentations	*Heritage AB*
3:00 PM – 5:00 PM	Paper Session I	*Heritage AB*
6:30 PM – 8:30 PM	Reception Welcoming New Members (formal)	*Mountain View Terrace*
FRIDAY, MAY 19		
6:30 AM – 1:00 PM	Registration Desk Open	*Heritage Foyer*
7:00 AM – 8:30 AM	Breakfast	*Heritage Foyer*
7:00 AM – 11:00 AM	Spouse / Guest Hospitality Lounge Open	*Skyline Room*
7:30 AM – 8:00 AM	Marilyn T. Miller Lecture	*Heritage AB*
8:00 AM – 9:45 AM	Knapp Symposium	*Heritage AB*
9:45 AM – 10:30 AM	Poster Session I - Coffee Break	*Heritage C*
10:30 AM – 12:50 PM	Paper Session II	*Heritage AB*
1:00 PM – 5:30 PM	Golf Tournament	*Omni Golf Club*
2:00 PM – 3:30 PM	Wild Food Stroll	*Hotel Lobby*
6:30 PM – 8:00 PM	Reception & 9th Annual Artistic Soirée (business casual)	*Seely Pavilion*

American Ophthalmological Society
Meeting Schedule

SATURDAY, MAY 20		
6:00 AM – 12:30 PM	Registration Desk Open	*Heritage Foyer*
6:00 AM – 8:30 AM	Breakfast	*Heritage Foyer*
6:30 AM – 7:15 AM	Executive Session (members only)	*Heritage AB*
7:00 AM – 11:00 AM	Spouse/Guest Hospitality Lounge Open	*Skyline Room*
7:30 AM – 9:15 AM	Saturday Symposium	*Heritage AB*
9:15 AM – 10:00 AM	Poster Session II - Coffee Break	*Heritage C*
10:00 AM – 12:20 PM	Paper Session III	*Heritage AB*
12:30 PM – 2:00 PM	Emeritus Luncheon (by invitation)	*Skyline Room*
1:00 PM – 3:00 PM	Tennis Tournament	*Sports Complex* *Tennis Courts*
4:00 PM – 5:00 PM	Women's Leadership Afternoon Tea (male colleagues welcome!)	*Skyline Room*
6:00 PM – 6:45 PM	Closing Reception	*Heritage C*
7:00 PM – 9:00 PM	Gala Banquet (formal)	*Heritage AB*

**Subject to change*

FRIDAY, MAY 19, 2023

Marilyn T. Miller Lecture

GENE THERAPY FOR RETINAL DEGENERATIONS – WHERE DO WE STAND NOW?

Jean Bennett, MD, PhD
Philadelphia, PA

Herman Knapp Symposium

ENHANCING AND PROLONGING DRUG DELIVERY TO THE EYE

ENHANCING TOPICAL DRUG DELIVERY THROUGH BIOMATERIALS
Justin Hanes, PhD
Baltimore, MD

SUPRACHOROIDAL CANNULATION AND MICRO-NEEDLE DELIVERY
Timothy Olsen, MD
Rochester, MN

GENE THERAPY DELIVERY FOR AGE-RELATED MACULAR DEGENERATION
Jacque Duncan, MD
San Francisco, CA

PORT DELIVERY SYSTEM AND OTHER INTRAOCULAR STORAGE DEVICES
Baruch Kuppermann, MD, PhD
Newport Beach, CA

POLYMERIC NANOPARTICLES, MICROPARTICLES, HYDROGELS, AND NANOPORE FILMS
Jennifer Kang-Mieler, PhD
Chicago, IL

INTRA-ARTERIAL DRUG DELIVERY FOR OCULAR CANCERS
Jasmine Francis, MD
New York, NY

SATURDAY, MAY 20, 2023

Saturday Symposium

IMAGING THE IMPACT OF AGING AND SPECIFIC DISEASE STATES ON THE VISUAL SYSTEM

THE AGING BRAIN AND ITS IMPACT ON VISUAL FUNCTION
Felipe Medeiros, MD, PhD
Durham, NC

AGING FEATURES ON OCT, OCTA, AND FLUORESCENCE LIFETIME IMAGING OPHTHALMOSCOPY (FLIO)
David Sarraf, MD
Los Angeles, CA

IMAGING THE RETINA IN ALZHEIMER'S DISEASE - CURRENT EVIDENCE AND UNMET NEEDS
Amani Fawzi, MD
Chicago, IL

HIGH RESOLUTION IMAGING OF THE ANTERIOR SEGMENT FOR OCULAR SURFACE TUMORS AND AGE-RELATED CONDITIONS
Carol Karp, MD
Miami, FL

NERVE FIBER THICKNESS, OPTIC NERVE THINNING, AND AGING
David Huang, MD, PhD
Portland, OR

AOS 2023

Paper Abstracts

The following abstracts of papers selected to be presented at the meeting are printed in presentation order. The order of presentations has been arranged by the Committee on Programs.

Papers presented at this meeting may be published in other medical journals after this meeting PROVIDED THE AUTHORS ADHERE TO THE STRICT GUIDELINES IN THE AUTHOR INSTRUCTIONS LISTED AT aosonline.org AND CONSULT WITH THE EDITOR OF THE TRANSACTIONS.

Papers are limited to 7 minutes and the first discussant to 3 minutes. General discussion will be limited to 9 minutes.

PLEASE NOTE THE FOLLOWING PROGRAM KEY:

Bold = *AOS Member*
* = *Presenter*
♦ = *Financial Disclosure*

(Presenters will indicate their financial disclosure verbally and in the first slide.)

THURSDAY 3:00–3:20 PM

PHASE I TRIAL OF TOPICAL TRAMETININB FOR THE TREATMENT OF ROSACEA

Edward Wladis♦*, Jacqueline Busingye, Alejandro Adam

Purpose: Rosacea is a significant cause of ocular surface disease. Previous studies have implicated distinct kinases (p38 and ERK) in cutaneous specimens of rosacea, suggesting that suppression of the mitogen-associated protein kinase (MAPK) might be an effective approach to treat this disease, and this strategy appears to be effective in animal models of rosacea. This phase I study was performed to assess the safety and tolerability of a topical MAPK inhibitor in the management of rosacea.

Methods: Over twenty-two days, patients with rosacea that was refractory to conventional therapies (n = 12) were randomized to apply a topical MAPK inhibitor (trametinib) to one cheek and a placebo vehicle cream to the contralateral side. Skin irritation was assessed on days 1, 8, 15, and 22 through a standardized scoring system (ranging from 0-7), and blood samples were drawn to assess systemic absorption.

Results: All patients completed the trial and utilized the creams. No adverse events were detected. Mean skin irritation scores were not statistically significantly different between the two sides at all time points.

Conclusion: Topical trametinib appears to be safe and well-tolerated in the management of rosacea, and no adverse events were detected. In light of the serious deleterious effects of this disease on the ocular surface and the limited efficacy of our current therapeutic armamentarium, this phase I trial represents a significant advancement towards a meaningful treatment for rosacea. Based on these findings, this treatment strategy can be safely expanded to explore efficacy.

Discussant: **Anat Galor**

THURSDAY 3:20–3:40 PM

CULTIVATED AUTOLOGOUS LIMBAL EPITHELIAL CELL (CALEC) TRANSPLANTATION: PRODUCT DEVELOPMENT, MANUFACTURE, AND INITIAL EVALUATION OF FEASIBILITY

Ula V. Jurkunas[♦*]

Purpose: To develop a novel cell therapy, cultivated autologous limbal epithelial cells (CALEC) in serum-free and xeno-free system, in order to treat unilateral limbal stem cell (LSC) deficiency.

Methods: The manufacturing platform employed critical technological innovation of two-step process for LSC isolation and expansion onto human amniotic membrane and rigorous quality control measures using xenobiotic-free, serum-free, and antibiotic-free method.

Results: Small limbal biopsies were used to generate CALEC constructs in an average of 16 days. Cultivated cells maintained epithelial cell phenotype with colony forming and proliferative capacities, with high viability and metabolic activity during manufacture and transportation.
Analysis of LSC biomarkers showed preservation of 'stemness' in CALEC constructs. After pre-clinical development, CALEC grafts were manufactured in a current good manufacturing practices compliant facility. A Phase I clinical trial enrolled five patients with unilateral LSC deficiency. Clinical case histories with 12 months follow-up are reported for the first four patients who received successful CALEC transplants.

Conclusion: This initial clinical trial establishes the feasibility of CALEC technique with no immediate safety concerns.

Discussant: **Woodford S. Van Meter**

THURSDAY 3:40–4:00 PM

AN IRIS REGISTRY-BASED ASSESSMENT OF PRIMARY OPEN-ANGLE GLAUCOMA PRACTICE PATTERNS IN ACADEMIC VERSUS NONACADEMIC SETTINGS

Gregory Skuta*, Kai Ding, Flora Lum, **Anne Coleman**

Purpose: To compare patient demographic data; level of severity; and clinical, diagnostic, and surgical practice patterns in patients with primary open-angle glaucoma (POAG) in an academic setting versus nonacademic setting using the American Academy of Ophthalmology IRIS Registry (Intelligent Research in Sight).

Methods: A retrospective cohort study of IRIS Registry data that included patients with POAG who were seen between January 2016 and December 2019 and had at least 1 year of follow-up.

Results: Of 3,707,084 distinct eyes with POAG, 3% (109,920) were included in the academic subcohort and 97% (3,597,164) were included in the nonacademic subcohort. Among the findings of greatest note ($P < .0001$ for all comparisons) were a higher proportion of eyes of Black patients, a higher proportion of eyes with level 3 severity, and a higher mean cup-to-disc ratio in eyes in the academic setting. The relative frequency of gonioscopy, pachymetry, and visual field testing in conjunction with new patient visits was also notably higher in the academic setting. For glaucoma surgical procedures, the greatest proportional differences in relative frequency were seen for tube shunt procedures (2.55-fold higher in the academic setting), iStent and Hydrus procedures (2.52-fold higher in the nonacademic setting), and endoscopic cyclophotocoagulation (5.80-fold higher in the nonacademic setting).

Conclusion: Based on IRIS Registry data, notable differences appear to exist with regard to ethnoracial groups, glaucoma severity, and diagnostic and surgical practice patterns in academic versus nonacademic settings. By understanding these differences, potential opportunities exist in the development of educational programs related to clinical and surgical glaucoma care.

Discussant: **Carla Siegfried**

THURSDAY 4:00–4:20 PM

PROGRESSIVE MEIBOMIAN GLAND DYSFUNCTION IN OCULAR GRAFT-VERSUS-HOST DISEASE: A VICIOUS CYCLE OF OCULAR SURFACE INFLAMMATORY DAMAGE

Victor L. Perez[♦*], Hazem M. Mousa, Matias Soifer, Cole Beatty, Stephanie Sarantopoulos, Daniel Saban, Robert Levy

Purpose: To investigate the role of aggressive Meibomian gland dysfunction (MGD) in the immune-pathogenesis of ocular graft-versus-host disease (GVHD).

Methods: In mice, an allogeneic GVHD model was established by transferring bone marrow (BM) and purified splenic T-cells from C57BL/6J mice into irradiated C3-SW. H2b mice (BM+T). Control groups received BM-only (BMO). Mice were scored clinically across the post-transplantation period. MGD severity was categorized using degree of atrophy on harvested lids. Immune disease was analyzed using flow cytometry of tissues along with fluorescent tracking of BM cells onto the ocular surface. In humans, parameters from 57 patients with ocular GVHD presenting to the Duke Eye Center were retrospectively reviewed. MGD was categorized using the degree of atrophy on Meibographs. Immune analysis was done using high-parameter flow cytometry on tear samples.

Results: Compared to BMO, BM+T mice had higher systemic disease scores that correlated with tear fluid loss and eyelid edema. BM+T had higher immune cell infiltration in the ocular tissues and higher CD4+-cell cytokine expression in draining lymph nodes. BM+T mice with worse MGD scores had significantly worse corneal staining. In ocular GVHD patients, 96.4% had other organs affected. Ocular GVHD patients had abnormal parameters on dry eye testing, high matrix metalloproteinase-9 positivity (91.7%), and abundance of immune cells in tear samples. Ocular surface disease signs were worse in patients with higher MGD severity scores.

Conclusion: Ocular GVHD is driven by a systemic T-cell driven process that involves the Meibomian glands leading to a robust form of ocular surface disease that correlates with MGD severity.

Discussant: **Penny A. Asbell**[♦]

THURSDAY 4:20–4:40 PM

USE OF NATURAL LANGUAGE PROCESSING TO ACCURATELY IDENTIFY CATARACTS AND OTHER LENS PATHOLOGY IN ELECTRONIC HEALTH RECORD DATA - A STUDY USING THE SIGHT OUTCOMES RESEARCH COLLABORATIVE (SOURCE) REPOSITORY

Joshua Stein*, Yunshu Zhou, Chris Andrews, Victoria Addis, Jill Bixler, **Judy Kim**, Brian McMillian, Saleha Munir, Jeffrey Schultz, Brian Stagg, Sophia Wang, Fasika Woreta

Purpose: Nearly all published Big Data analyses in ophthalmology have been completely reliant upon ICD billing codes to identify the presence of ocular pathology and to assess for disease stability. However, for a variety of reasons, billing codes can be inaccurate. Here we validate an alternative way to identify and characterize ocular pathology using natural language processing (NLP).

Methods: We developed an NLP algorithm capable of searching free text lens exam data inputted by clinicians into the electronic health record. The algorithm identifies the type(s) of cataract present, cataract density, presence of intraocular lenses (IOLs), location of the IOL, status of the capsule, and presence of other lens pathology (e.g., lens dislocation, phimosis). We applied our algorithm to all 17.5 million lens exam records in the SOURCE repository, which captures eye care for more than 3 million eye care recipients receiving care at 11 large US health care systems. We randomly selected 4314 unique lens exam entries and asked 11 clinicians to review the NLP output to validate whether it correctly identified and categorized the lens pathology present.

Results: Among the 4314 lens exam entries, the NLP algorithm correctly identified and properly categorized all lens pathology present in 4104 (95.1%) of the entries as validated by clinicians. There were only 210 entries (4.9%) identified with errors. Among less common lens pathology, the mentions identified by the algorithm were corroborated by a reviewing clinician for 100% of mentions of pseudoexfoliation material; 99.7% for mentions of phimosis, subluxation, and synechiae; and 96.9% for mentions of phacodonesis. Algorithm errors included incorrectly accounting for negation (e.g., "no evidence of pxf") and improper assignment of "pigment on the lens capsule" as evidence of posterior capsule opacification.

Conclusion: We developed an algorithm using NLP that accurately identifies and classifies lens abnormalities routinely documented by eye care professionals. Algorithms such as this will help researchers properly identify and classify ocular pathology to augment the sorts of questions that can be answered using electronic health record data.

Discussant: **George L. Spaeth**

THURSDAY 4:40–5:00 PM

A MODEL TO PREDICT REFRACTIVE SHIFT AFTER OCULAR GROWTH IN CHILDREN UNDERGOING BILATERAL CATARACT SURGERY

M. Edward Wilson♦*, Emily Ye, Rupal Trivedi

Purpose: To develop a model for predicting refractive shift following cataract surgery in children undergoing bilateral cataract surgery between ages 2-18 with the goal of improving intraocular lens (IOL) power selection.

Methods: A retrospective review was conducted for bilateral cataract surgery in children ages 2-18 with primary intraocular lens (IOL) implantation, at least 1 year of follow up and at least 2 post-operative refraction measurements. Patients with traumatic etiology or ectopia lentis were excluded. A multivariable generalized estimating equation (GEE) model was fit that included patient characteristics univariately associated with post-operative refraction at $p<0.02$ as well as two-way interactions between all univariate variables and time-dependent variables.

Results: The study included 142 patients with a median age of 6.3 years at surgery and mean of 7.45 years of follow-up. The mean refractive shift for the patient population was -1.78. Beta values of the final multivariable GEE model to predict post-operative change in refraction include: intercept (0.590, $P= 0.044$), target refraction (-0.093, $P= 0.505$), age at surgery (0.239, $P<0.001$), age at post-operative exam before age 12 (-0.275, $P<0.001$), age at post-operative exam after age 12 (0.135, $P= 0.009$), interaction between age at post-operative exam and target refraction (-0.05, $P= 0.013$), interaction between age at post-operative exam after age 12 and target refraction (0.073, $P=0.023$).

Conclusion: In our study, we use pre-operative factors such as age and target refraction to create a multivariable GEE model that can predict the amount of refractive shift a child may experience as the eye grows. This information is invaluable in the pre-operative planning before cataract surgery to aid in the selection of intraocular lens to be implanted.

Discussant: **Terri L. Young**

FRIDAY 10:30 AM–10:50 AM

FAMILY HISTORY OF AGE-RELATED MACULAR DEGENERATION (AMD) AND GENETIC VARIANTS PREDICT PROGRESSION TO ADVANCED AMD, ADJUSTING FOR BASELINE MACULAR STATUS, DEMOGRAPHIC AND LIFESTYLE PREDICTORS

Johanna Seddon[♦*], Dikha De, Bernard Rosner

Purpose: To determine if family history of age-related macular degeneration (AMD) and genetic variants identify eyes at higher risk for progression to advanced AMD (AAMD).

Methods: Eyes with non-advanced AMD at baseline in the longitudinal Age-Related Eye Disease Study were classified using the severity score. Non-genetic and genetic predictors of progression to AAMD were evaluated. Cox proportional hazards models based on the eye as the unit of analysis were used to calculate hazard ratios (HR), accounting for correlated data. A composite risk score was calculated using beta estimates from demographic and behavioral variables (age, race, BMI, smoking status, treatment group, multivitamin intake), ocular factors (baseline severity group, status of fellow eye), AMD family history, and 12 statistically significant genetic variants (in complement, angiogenesis, lipid, inflammatory, extra-cellular matrix, and DNA repair pathways) were selected from stepwise regression. Discrimination between progressing and non-progressing eyes in various models with different predictors was assessed using C-statistics and Net Reclassification Improvement (NRI).

Results: Among 4910 eyes, 863 progressed to AAMD over 12 years. Baseline AMD severity group and status of the fellow eye were important predictors, and genetic factors provided additional discrimination. Family history of AMD independently predicted progression after accounting for genetic and other covariates: 1 family member vs. none (HR = 1.21, 95% CI: 1.02, 1.43; P = 0.03); ≥ 2 family members vs. none (HR= 1.55, 95% CI: 1.26, 1.90; P < 0.001). The composite risk score predicted progression to AAMD (HR = 5.57, 90th vs. 10th percentile), providing superior fit versus models with only ocular or non-genetic variables (NRI, P < 0.001). It also discriminated between progressing and non-progressing eyes within each AMD severity group. An online risk calculator is available to implement these methods.

Conclusion: Genetic variants and family history provided additional discrimination in AAMD prediction models, after accounting for ocular and other covariates.

Discussant: **Kent Small**[♦]

FRIDAY 10:50 AM–11:10 AM

CRISPR EDITING DEMONSTRATES RS10490924 RAISED OXIDATIVE STRESS IN IPSC-DERIVED RETINAL CELLS FROM PATIENTS WITH ARMS2/HTRA1-RELATED AMD

Stephen Tsang*, Ya-Ju Chang, Laura Jenny, Yong Shi Li, Xuan Cui, Yang Kong, Janet Sparrow

Purpose: Until now, CRISPR has yet to be applied to isolate tightly linked genome-wide association studies (GWAS) alleles in age-related macular degeneration, as Cas9 tends to re-cut the non-coding donor template. Disease modeling tends to utilize conventional cultured cells as the metabolic backdrop. Given that these induced pluripotent stem cell-derived retinal cells more closely resemble fetal than adult cells, conventional cultures are inappropriate for studying the late onset disorders.

Methods: Here, we utilized pharmacologically aged cells, which better recapitulate the conditions in the older adult eye to investigate the causative allele in age-related macular degeneration (AMD).

Results: The sole age-related maculopathy susceptibility ARMS2 rs10490924, encoding a nonsynonymous A69S (G>T) variant in ARMS2 within the 10q26.13 linkage disequilibrium block, decreased the antioxidant functional capacity of retinal pigment epithelium (RPE) in a cell-autonomous manner. Sodium phenylbutyrate preferentially reverses the cell death caused by ARMS2 rs10490924 but not HTRA1 rs11200638.

Conclusion: This study serves as a proof of concept for the use of patient-specific iPSCs for functional annotation of tightly linked GWAS to study the etiology of a late-onset disease phenotype. Our findings resolve a longstanding controversy about the causative allele in AMD. More importantly, we demonstrate that antioxidant NaPB administration may be useful for treating AMD, a prevalent late-onset neurodegenerative disorder.

Discussant: **Janey L. Wiggs♦**

FRIDAY 11:10 AM–11:30 AM

DETECTION OF EARLY DIABETIC RETINOPATHY USING OCTA BLOODFLOW ANALYSIS

Jennifer Lim♦*, Albert Dadzie, David Le, Mansour Abtahi, Behrouz Ebrahimi, Taeyoon Son, Xincheng Yao

Purpose: To determine whether quantitative analysis of bloodflow based on OCTA images can detect early diabetic retinopathy (DR).

Methods: We performed a retrospective, IRB approved, OCTA imaging study to compare the bloodflow parameters of diabetic patients without diabetic retinopathy (NoDR), diabetic patients with mild nonproliferative DR (mild NPDR) and healthy controls. Inclusion criteria included good image quality, 6 mm x 6 mm scans and foveal centration. A thresholding algorithm was used to remove noise from OCTA images. Enface projections of the superficial vascular plexus (SVP) and the deep capillary plexus (DCP) were used to determine blood flow index (BFI) values for SVP and for DCP. Normalized BFI (NBFI) was calculated by dividing BFI by the standard deviation of the noise removed. NBFI thus compensated for noise from variable pigmentation and illumination irradiance that could affect quantification of BFI. BFI and NBFI of the SVP and DCP were compared for all three groups (control, NoDR, mild NPDR). Multiple group comparisons were performed using one-way ANOVA or Kruskal–Wallis one-way ANOVA. Corresponding individual comparisons were performed using Student's t-test or Mann-Whitney's t-test.

Results: A total of 77 eyes, 47 diabetic eyes (21 eyes from 15 diabetic patients with NoDR and 26 eyes from 22 patients with mild NPDR) and 30 control eyes (20 healthy subjects), underwent OCTA BFI and NBFI analyses. BFI of the DCP could differentiate between control vs mild NPDR ($p=0.0002$) and between NoDR vs mild NPDR ($p=0.0140$). NBFI of the SVP could differentiate all three groups from each other (ANOVA, $p<0.0001$) and between control vs mild NPDR ($p<0.0001$), NoDR vs mild NPDR ($p=0.0002$). NBFI of the DCP could differentiate all three groups from each other (ANOVA, $p<0.0001$) and between control versus NoDR ($p=0.0416$), control vs mild NPDR ($p=0.0093$) and NoDR vs mild NPDR ($p<0.0001$).

Conclusion: Quantitative OCTA analysis using NBFI of the SVP and the DCP is a useful OCTA biomarker that can detect early DR. NBFI of the DCP is the most sensitive bloodflow parameter to distinguish NoDR, mild NPDR and control eyes from one another.

Discussant: **Amani Fawzi**

FRIDAY 11:30 AM–11:50 AM

PLANNING AN ARTIFICIAL INTELLIGENCE-BASED DIABETIC RETINOPATHY SCREENING PROGRAM USING HUMAN CENTERED DESIGN

R.V. Paul Chan*, Angelica Scanzera, Cameron Beversluis, Archit Potharazu, Ariel Leifer, Emily Cole, David Du, Jerry Krishnan, Hugh Musick

Purpose: To describe the use of a human-centered design process when planning an artificial intelligence (AI)-based strategy for diabetic retinopathy (DR) screening using EyeScreen (EyeNuk, Inc, Woodland Hills, CA).

Methods: We adapted the UK Design Council's Double Diamond model to include five phases (Frame, Observe, Define, Build, and Evaluate) in the design process. In the first Diamond, the Frame and Observe phases are used to explore the context as broadly as possible to gain understanding of the problem. In the Define phase, the problem is reframed based on an analysis of the information gained from the first two steps to inform the development of solutions. In the second Diamond, a wide array of possible solutions are considered, prioritized, and developed (Build). Evaluation is where those concepts in the Build phase are refined, iterated on, and chosen for implementation, and implementation follows after.

Results: Findings from the pre-implementation phases (Frame, Observe, Define, Build, Evaluate) are presented in this report. Over a 12-month period (July 1, 2021 to June 2022), there were over 1,500 patients with diabetes within a single Family Medicine (FM) practice and an estimated 30-40 patients per month who were overdue for DR screening at UI Health (Chicago, Illinois). Only 11% of referrals from FM to Ophthalmology for DR screening resulted in completed visits. While both FM and Ophthalmology reported a shared goal of preventing vision loss through screening and referral, the two groups viewed the DR screening itself very differently and had different definitions of success. The results suggested the need to build optionality, iterate workflows, and prioritize the referral of patients with a positive DR screen to Ophthalmology.

Conclusion: An adapted Double-Diamond model can be utilized to guide the development of a stakeholder-supported AI-based DR screening program. Future work will discuss implementation, post-implementation program evaluation and modifications.

Discussant: **Judy E. Kim♦**

FRIDAY 11:50 AM–12:10 PM

UBX1325, A NOVEL SENOLYTIC CANDIDATE FOR PATIENTS WITH DME: 24-WEEKS RESULTS FOR BEHOLD PHASE 2 STUDY

Michael Singer♦*, **Quan Nguyen**, Sharon Klier, Jamie Dananberg

Purpose: Senescence is implicated in vascular pathology of DME. This Ph 2 study is evaluating the safety and efficacy of a novel, small molecule, Bcl-xL inhibitor senolytic agent and assesses the evidence of activity of a single IVT injection of UBX1325 in patients with DME.

Methods: This study is prospective, randomized, double-masked of UBX1325 vs. sham. The study enrolled those ≥18 years with DME, BCVA 73 to 20 ETDRS letters and residual retinal fluid plus ≥2 anti-VEGF injections in the last 6 months. 65 patients were randomized 1:1 to receive either one IVT injection of UBX1325 10 μg or sham. Primary endpoint is change from baseline in safety and tolerability at 24 weeks. Secondary endpoints included BCVA, CST, rescue rate, retinal fluid, leakage, and capillary nonperfusion.

Results: Data was assessed through 24 weeks. UBX1325 showed a sustained improvement in BCVA through 24 weeks with a significant increase of 7.6 letters and CST stability in patients without anti-VEGF rescue (~60% of patients on UBX1325 remain rescue-free at 6 months).
There were no events of IOI. AEs occurring at higher rates vs. sham were largely attributable to IVT procedure.

Conclusion: UBX1325 is a novel senolytic agent that is being investigated for the treatment of DME. This data represents the potential proof-of-concept for the safety and tolerability and the effect of a senolytic agent on visual function and on retinal structure, capillary leakage, and ischemia. As this mechanism of action is orthogonal to anti-VEGF therapy, UBX1325 could provide an important benefit as a stand-alone treatment, in combination regimen, or for use in patients who have a suboptimal response to current standard of care treatments for diabetic macular edema.

Discussant: **Baruch Kuppermann♦**

FRIDAY 12:10 PM–12:30 PM

INTERNAL LIMITING MEMBRANE PEELING IN PATIENTS UNDERGOING VITRECTOMY FOR DIABETIC TRACTIONAL RETINAL DETACHMENT: A RANDOMIZED CLINICAL TRIAL

Ryan Rush*

Purpose: To evaluate the merits of internal limiting membrane (ILM) peeling in proliferative diabetic retinopathy (PDR) patients undergoing pars plana vitrectomy (PPV) for the indication of tractional retinal detachment (TRD).

Methods: This study was conducted as a randomized clinical trial at a single university-allied teaching facility in Montemorelos, Mexico. One hundred and ninety one PDR subjects requiring PPV for the indication of TRD were enrolled into the trial. Subjects were prospectively randomized into one of two study groups during PPV: Group A subjects underwent ILM peeling, whereas Group B subjects did not undergo ILM peeling. The primary outcome was the incidence of postoperative epiretinal membrane (ERM) development between cohorts at the end of a 6-month trial period. The secondary outcome was achievement of 20/50 Snellen visual acuity or better at 6 months between cohorts.

Results: One hundred and thirty nine subjects underwent randomization and completed the 6-month trial period. Group A had 3.1% (2/64) of subjects develop a postoperative ERM, while Group B had 26.7% (20/75) of subjects develop a postoperative ERM during the 6-month trial period ($p<0.001$). Group A had 21.9% (14/64) of subjects and Group B had 9.3% (7/75) of subjects achieve Snellen BCVA of 20/50 or better at 6 months ($p=0.039$).

Conclusion: PDR patients undergoing PPV for TRD have a lower incidence of postoperative ERM formation and a greater likelihood of achieving 20/50 or better acuity at 6 months when ILM peeling is undertaken. Specialists may therefore consider ILM peeling to be a beneficial surgical maneuver in this patient population. Limitations of the trial's generalizability include enrolling exclusively indigent patients from a developing country, performance of same-session cataract surgery on all phakic subjects, and permitting the use of anti-vascular endothelial growth factor in the postoperative period whenever certain prespecified conditions were met.

Discussant: **Timothy W. Olsen♦**

FRIDAY 12:30 PM–12:50 PM

MONTH 60 OUTCOMES AFTER TREATMENT INITIATION WITH ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY FOR MACULAR EDEMA DUE TO CENTRAL RETINAL OR HEMIRETINAL VEIN OCCLUSION

Ingrid Scott*, Paul VanVeldhuisen, Neal Oden, Michael Ip, Barbara Blodi

Purpose: To investigate 5-year outcomes in eyes initially treated with aflibercept or bevacizumab for macular edema due to central retinal (CRVO) or hemiretinal vein occlusion (HRVO).

Methods: Long-term follow-up (LTF) after a randomized clinical trial from sixty-four centers in the United States. Participants were followed up to 60 months and treated at investigator discretion after completing the 12-month treatment protocol. Main outcomes are visual acuity letter score (VALS) and central subfield thickness (CST) on optical coherence tomography.

Results: Seventy-five percent (248/330) of eligible participants completed at least one visit between Months 24 and 60, and 45% completed the Month 60 visit. Among participants completing Month 60, overall mean VALS improvement over baseline was 13.5 (95% CI: 9.6, 17.5), less than the mean improvement of 20.6 (95% CI: 18.7, 22.4) observed at Month 12, with no significant differences between originally assigned study groups. Further, 66% (99/150) had at least one treatment between Months 48 and 60 with a mean (SD) of 3.41 (3.69) treatments over this period. Mean CST was 671 microns at baseline and 261 microns (95% CI: 241.2, 280.9) at Month 60.

Conclusion: While VALS improved substantially when patients were treated per protocol through Month 12, improvement lessened when treatment was at investigator discretion and fewer treatments were received although VALS remained markedly improved over baseline through Year 5. Most patients continued to receive treatment in Year 5. This suggests that continued monitoring and, if warranted, treatment with anti-VEGF therapy, benefits patients with macular edema associated with CRVO or HRVO.

Discussant: **Julia A. Haller♦**

SATURDAY 10:00–10:20 AM

FIVE-YEAR OUTCOMES OF RANIBIZUMAB VS. LASER THERAPY FOR THE TREATMENT OF VERY LOW BIRTHWEIGHT INFANTS WITH RETINOPATHY OF PREMATURITY RAINBOW EXTENSION STUDY

James Reynolds*, Brian Fleck, Neil Marlow, Alistair Fielder, Domenico Lepore, Andreas Stahl, Han Hao, Mia Weisberger

Purpose: Intravitreal injection of VEGF inhibitors is increasingly used to treat retinopathy of prematurity (ROP). The purpose of this study is to compare the long-term efficacy of ranibizumab vs. laser and assess the long-term safety of intravitreal ranibizumab injections.

Methods: RAINBOW was an open label, randomized trial comparing intravitreal ranibizumab (0.1mg and 0.2mg) with laser therapy for the treatment of ROP in 201 very low birthweight infants (<1500g). 180 infants entered the RAINBOW extension study which evaluated treatment outcomes to 5 years. Participants had local ophthalmic, development, and health assessments. The primary outcome was visual acuity. Secondary outcomes included structural ocular abnormalities; development, motor function, health status, and additional ocular data.

Results: 156 (87%) children completed the extension study (ranibizumab 0.2mg: 54, ranibizumab 0.1mg: 55, Laser: 47).

124/156 (79.5%) of children provided ETDRS acuities. The difference in mean ETDRS letter score between ranibizumab 0.2 mg compared to laser was 4.7 (95% CI: -1.1, 10.5). Difference between the ranibizumab 0.1 mg and laser arms was 2.5 (95%CI: -3.4, 8.3). The proportion of patients with ETDRS score of ≥71 letters was 32.8% in the ranibizumab 0.2 mg arm, 23.1% the ranibizumab 0.1 mg arm and 20.4%in the laser arm.

Structural retinal abnormalities were present in 11 children (ranibizumab 0.2mg: 1, ranibizumab 0.1mg: 4, Laser: 6).

No differences between the three trial arms in developmental scores, growth attainment or vision-related quality of life were observed.

Conclusion: The RAINBOW extension study confirms the outcomes of the original RAINBOW report and demonstrated no significant effect of ranibizumab on systemic development of the child.

Discussant: **David K. Wallace♦**

SATURDAY 10:20–10:40 AM

USE OF IMMUNOSUPPRESSION AND SUBSEQUENT CANCER INCIDENCE: COHORT STUDY

John H. Kempen*

Purpose: To evaluate the incidence of any cancer and of putatively immunosuppression-related cancers after immunosuppressive treatment compared to persons unexposed to immunosuppression.

Methods: Retrospective cohort study of patients with non-infectious ocular inflammatory disease seen at United States ocular inflammatory disease subspecialty practices, excluding persons with HIV and prior cancer diagnosis. We obtained data regarding immunosuppressive drug use and other characteristics by protocol-driven chart review. Immunosuppressive drugs studied included antimetabolites (primarily methotrexate, azathioprine, and mycophenolate mofetil), calcineurin inhibitors (cyclosporine and tacrolimus), alkylating agents (primarily cyclophosphamide and chlorambucil), and Tumor Necrosis Factor (TNF) inhibitors (primarily infliximab, adalimumab, and etanercept) were examined. Cancer incidence was ascertained by linkage to twelve state cancer registries from 1996-2015. Cancer incidence was analyzed using Cox regression survival analysis, using 0-, 3- and 5-year lags after immunosuppression began.

Results: We studied 10,872 individuals at risk of incident cancer who resided in one of the 12 states covered; 812 primary cancers were identified through cancer incidence tracing. Neither TNF inhibitor, antimetabolite, calcineurin inhibitor nor alkylating agent classes were associated with statistically significant increases in any-cancer incidence. We found statistically significant reduced hazards in all subject cohort (including those with systemic inflammatory disease [SID]) for adalimumab and chlorambucil but not in the non-SID cohort; and increased hazards for tacrolimus and etanercept in the non-SID cohort but not the cohort.

Conclusion: We did not find significantly increased risk of overall or site-specific cancer incidence associated with the most commonly used immunosuppressive drug classes and with many specific drugs. Further research may clarify potentially protective or harmful effects of specific agents that tended to be associated with reduced or increased cancer incidence.

Discussant: **J. Fernando Arevalo**

SATURDAY 10:40–11:00 AM

TEN-YEAR OUTCOMES OF UVEAL MELANOMA BASED ON THE CANCER GENOME ATLAS (TCGA) CLASSIFICATION IN 1001 CASES

Carol Shields*, Eileen Mayro, Zeynep Bas, Philip Dockery, Antonio Yaghy, Sara Lally, Arupa Gaguly, **Jerry Shields**

Purpose: To understand the prognostic value of The Cancer Genome Atlas (TCGA) for uveal melanoma metastasis, using a simplified 4-category classification, based on tumor DNA.

Methods: A retrospective cohort study of 1001 eyes with uveal melanoma at a single center, categorized according to TCGA as Group A, B, C, or D (by fine-needle aspiration biopsy for DNA analysis), and treated with standard methods, was studied for melanoma-related metastasis at 5 and 10 years.

Results: Of 1001 eyes with uveal melanoma, the TCGA categories included Group A (n=486, 49%), B (n=141, 14%), C (n=260, 26%), and D (n=114, 11%). By comparison, increasing category (A vs. B vs. C vs. D) was associated with entering features of older age (56.8 vs. 52.8 vs. 61.1 vs. 63.5 years, $p<0.001$), less often visual acuity of 20/20-20/50 (80% vs. 67% vs. 70% vs. 65%, $p=0.001$), tumor location further from the optic disc ($p<0.001$) and foveola ($p<0.001$), and greater median tumor basal diameter (10.0 vs. 13.0 vs. 14.0 vs. 16.0 mm, $p<0.001$) and tumor thickness (3.5 vs. 5.2 vs. 6.0 vs. 7.1 mm, $p<0.001$). Kaplan-Meier (5-year/10-year) rate of metastasis was 4%/6% for Group A, 12%/20% for Group B, 33%/49% for Group C, and 60%/not available for Group D.

Conclusion: A simplified 4-category classification of uveal melanoma using TCGA, based on tumor DNA, is highly predictive of risk for metastatic disease.

Discussant: **Ivana K. Kim**

SATURDAY 11:00–11:20 AM

COMPARATIVE SURVIVAL OF PATIENTS WITH UVEAL MELANOMA ACCORDING TO GENE EXPRESSION PROFILE AND PRAME EXPRESSION: INTERIM 36-MONTH ANALYSIS OF THE COLLABORATIVE OCULAR ONCOLOGY GROUP STUDY NUMBER 2

Zelia Correa♦*, Amy Schefler, Prithvi Mruthyunjaya, Tom Aaberg Jr., Cristina Decatur, Alison Skalet, **J. William Harbour**

Purpose: Gene expression profiling (GEP) discriminates uveal melanoma (UM) patients by metastatic risk into Class 1 (low) and Class 2 (high). GEP was validated prospectively the first Collaborative Ocular Oncology Group (COOG) Study. Preferentially expressed antigen in melanoma (PRAME) was recently found to impact metastatic risk in UM. The purpose of this study is to evaluate the role PRAME status and GEP on the survival prognosis of patients enrolled in the COOG Study Number 2 (COOG2) study.

Methods: COOG2 is an NCI-sponsored 25-center prospective study to evaluate the role of new prognostic biomarkers for patients with UM. The study evaluated the prognostic value of PRAME expression with GEP, and deep targeted sequencing for UM mutations. Patient baseline and follow-up data are recorded in a REDCap database. Incidence of metastasis was calculated, and impact of clinical and molecular features were assessed by multivariate analysis. Hazard ratios (95% CI) were calculated.

Results: 1586 patients with posterior UM met inclusion criteria; the mean age was 61 years and49% were women. Mean follow up was 34.3 months (95%CI 32.7-35.8). Median UM thickness was 5.4mm (range 0.5-18mm) and basal diameter was 12mm (1.9-32mm). Plaque brachytherapy was the most common treatment (80%) and tumor tissue was obtained via fine needle aspiration in 85% of patients. GEP was designated as Class 1 in1077 patients (68%) and Class 2 in 496 (32%), and PRAME was negative (-) in 1103patients (70%) and positive (+) in 470 (30%). Incidence of metastasis for Class 1 PRAME– patients was 3.1% (1.9-4.9%) compared to Class 2 PRAME + 45.3% (37.7-52.7%) ($p<0.001$). Metastatic risk was significantly higher in tumors with ciliary body involvement ($p=0.009$). Multivariate analysis identified a 21.49 (12.67-36.43) fold increase in risk of metastasis among Class2 PRAME + patients.

Conclusion: This is the first prospective multicenter study evaluating the role of PRAME expression in further refining GEP's prognostic ability to estimate metastatic risk in UM. Longer follow up of these patients will likely allow new strategies for metastatic surveillance, enrollment in adjuvant trials, and targeted therapy. The inclusion of patients from a diverse multi-center population enhances the applicability of these results.

Discussant: **James J. Augsburger**

SATURDAY 11:20–11:40 PM

SMALL CHOROIDAL MELANOMA: EVIDENCE FOR OVER TREATMENT

Arun Singh*

Purpose: To quantify potential loss (loss of vision) and gain (freedom from metastasis) in patients with small choroidal melanoma treated after period of surveillance to document growth.

Methods: A total of 167 patients with small choroidal melanoma (size 5.0-16.0 mm in largest basal diameter and 1.0 mm to 2.5 mm in height): 42 treated after surveillance (documented growth) and 125 treated immediately. A prediction model was applied to each patient in the immediate treatment group to obtain the predicted risk of melanoma (high risk versus low risk). Potential loss (loss of vision) and gain (freedom from metastasis) was compared between the low-risk immediate treatment group and those treated after surveillance.

Results: By using optimal cut point (0.60; 95% CI 0.37-0.61) of predicted risk for small choroidal melanoma (sensitivity 0.74, specificity 0.95), we identified 94 (75%) patients as high risk (score >=0.6) and the remaining 31 (25%) as having low risk melanoma (score <0.6). Over a median follow-up of 34.6 months, 5 developed metastasis (high risk=4, low risk=1) compared with 1 patient in the surveillance group. Initial visual acuity and loss of <15 letters visual acuity was not significantly different at 36 months between the low risk immediately treated and those treated after surveillance (81% vs 83%), respectively.

Conclusion: Low risk choroidal melanoma identified by prediction model can be labelled as an indeterminate melanocytic tumor. Such patients can be managed by surveillance to document growth prior to receiving vision threatening treatment without increased risk of metastatic death.

Discussant: **Hans E. Grossniklaus♦**

SATURDAY 11:40 PM–12:00 PM

LONG TERM OUTCOMES OF THE INTRAOPERATIVE RELAXED MUSCLE POSITIONING TECHNIQUE OF STRABISMUS SURGERY IN THYROID EYE DISEASE

Elias Traboulsi*, Justin Muste, Kevin Wang, Catherine Hwang, Julian Perry

Purpose: Strabismus and diplopia are common in patients with thyroid eye disease (TED). The intraoperative relaxed muscle positioning technique (IRMPT) for strabismus surgery in TED involves recessing muscles' insertions to positions where they rest without tension. We report and evaluate the long-term outcomes of a large number of patients who underwent surgery using this technique. We also study factors that influence the need for re-operations.

Methods: We reviewed patients' charts for demographic characteristics, history, types of operated muscles, initial surgical outcomes, clinical and reoperation history, and diplopia outcomes at last follow up. Patients were considered to have poor outcomes when persistent diplopia was present in primary and/or reading gazes despite >10 D prism correction or the inability of patients to tolerate prism. Good outcomes were defined as no diplopia in primary and reading gazes with <10 D prism correction. Excellent outcomes were defined as having no diplopia in primary and reading gazes without the use of prisms. Success was defined as having a good or excellent final outcome.

Results: 129 patients were followed for an average of 4.24 ± 5.13 years (range 0.01 – 20.66 years). 95 (73.6%) underwent one surgery. 33 cases required re-operation. Of there, 7 had planned staged surgeries with 100% success. 5 patients experienced disease reactivation and needed reoperation, with 4 having a successful outcome (80%). Of the remaining 21 patients, four required a third procedure, and a single patient needed a fourth. Overall, 93.6% (77.5% excellent and 16.3% good) of patients had a successful outcome. Additional analyses will also be presented.

Conclusion: The IRMPT for treatment of diplopia and strabismus in patients with TED results in a durable relief of double vision in a large majority of patients. Patients with greater horizontal deviations, disease reactivation, and prior interventions are more likely to require re-operations.

Discussant: **Natalie C. Kerr**

SATURDAY 12:00 PM–12:20 PM

EFFECT OF SITUATIONAL JUDGMENT AND VALUE-ALIGNMENT ASSESSMENT DATA ON THE OPHTHALMOLOGY RESIDENCY MATCH PROCESS: METHODS AND PRELIMINARY RESULTS

R. Michael Siatkowski*, **Steven Feldon**, Kai Ding, Justin Dvorak

Purpose: Transition away from USMLE Step I exam scores and course grades in medical school in favor of pass-fail has limited the data available for the residency matching process. In addition, profession-wide DEI initiatives also mandate the need for more holistic review of applicants. This study evaluates the use of the Altus Suite ™ (now Acuity Insights™) on which applicants to interview and how they should be ranked for the 2022-23 match cycle.

Methods: This study received exemption approval by the Western Institutional Review Board as well as the internal review boards of participating programs. All candidates for the match participated in the 3 components of the Altus Suite™: Casper, a situational judgment test; Snapshot, a one-way interview; and Duet, a value alignment assessment between the candidates and programs. Programs self-designated into one of 3 groups for both the decision to interview and the composition of the program rank list. Group 1 utilized Altus data first when making interview and rank list decisions, then used SF Match application data to make their final decision. Group 2 was the reverse order from Group 1. Group 3 allowed Altus data to be used in an ad hoc fashion. Primary outcomes were changes between preliminary and final decisions for interview decisions and placement on the final rank list. Secondary analyses evaluate effects among applicants who identify as URiM, as well as programs' qualitative assessment of the Altus Suite.

Results: Results will become available following the February 1 match deadline and will be reported here.

Conclusion: To be presented at the meeting.

Discussant: **Sean P. Donahue**

AOS 2023

Poster Abstracts

Posters will be displayed on Thursday, May 18 through Saturday, May 20.

Poster authors will be available to discuss their work during guided poster sessions scheduled on Friday, May 19 from 9:45 AM – 10:30 AM and on Saturday, May 20 from 9:15 AM – 10:00 AM.

Poster abstracts are listed in alphabetical order by presenting author's last name.

PLEASE NOTE THE FOLLOWING PROGRAM KEY:

Bold = *AOS Member*
* = *Presenter*
♦ = *Financial Disclosure*

(Posters will indicate relevant financial relationships.)

POSTER SESSION 1 FRIDAY, MAY 19 | 9:45 – 10:30 AM

MONITOR 1	
Nikhila Khandwala	Clinical Characteristics of Axenfeld-Rieger Syndrome in Children
Ken Kitayama	Systemic Disease Burden Mediates Racial and Ethnic Disparities in Incisional Glaucoma Surgical Outcomes: A Causal Mediation Analysis
MONITOR 2	
Victoria Tseng	Racial and Ethnic Differences in the Prevalence of Neovascular Glaucoma in At-Risk Beneficiaries in the California Medicare Population
Sophia Wang	Machine Learning Approaches for Predicting Glaucoma Progression in a Large Multicenter Electronic Health Records Consortium: The Sight Outcomes Research Collaborative (SOURCE)
MONITOR 3	
Teresa Chen	Frequency of Strabismus after Tube Shunt Surgery in the Adult versus Pediatric Population
John Bullock	Ophthalmology and the Nobel Prizes
MONITOR 4	
Anat Galor	Ocular Pain After Refractive Surgery: Preliminary Analysis of Epidemiology and Risk Factors
Penny Asbell	In Vitro Antibiotic Resistance among Presumed Bacterial Keratitis Isolates in the ARMOR Surveillance Study
MONITOR 5	
Massimo Busin	Pre-Descemet Stroma Is Optically Transparent even in the Absence of Corneal Endothelium
Carol Karp	Ocular Surface Squamous Neoplasia: Changes in the Standard of Care 2003 to 2022
MONITOR 6	
Robert Weisenthal	Comparison of the Long Term Results of Descemet's Stripping Automated Endothelial Keratoplasty (DSAEK) and Descemet's Membrane Endothelial Keratoplasty (DMEK) in Fellow Eyes for Treatment of Fuchs Endothelial Dystrophy (FED)
Christopher Leffler	Did Ottoman Traveller Evliya Çelebi Introduce Cataract Aspiration into Western Europe in 1665?
MONITOR 7	
Preston Blomquist	Risk Stratification of Ocular Emergencies Using Smartphone External Photography

POSTER SESSION 2 SATURDAY, MAY 20 | 9:15 – 10:00 AM

MONITOR 1	
Lucie Guo	Synthetic Biology for Ophthalmic Gene Therapy
K. Thiran Jayasundera	Content Generation, Psychometric Validation, and Application in Clinical Practice and Trials of Patient Reported Outcome Measures for Inherited Retinal Diseases
MONITOR 2	
Kent Small	North Carolina Macular Dystrophy (NCMD/MCDR1): Analysis of Our Entire Database, a Model Disease of Non-coding Mutations
Walter Lisch	Lisch Epithelial Corneal Dystrophy is Not a X-chromosomal but an Autosomal Dominant Inherited Disorder
MONITOR 3	
Cameron Parsa	NAION is Caused by Papillary Vitreous Separation
Mary Elizabeth Hartnett	Oxidized Cholesterol Induces RPE to Release Inflammatory Cytokines and VEGF: a Potentially Treatable Cause of Fibrosis in Untreatable AMD
MONITOR 4	
David Wilson	Cell Based Therapy for Retinal Disease
Janet Coleman-Belin	Association between Social Vulnerability Scores and Vision Difficulty in the United States
MONITOR 5	
G***ary Brown***	Healthcare Educational Returns
R***on Adelman***	Gender Bias in Ophthalmology Reimbursement
MONITOR 6	
Brooke Sherry	Stakeholder Perspectives on Barriers and Facilitators to Implementing Sustainability Interventions in Cataract Surgery
Christopher Leffler	Inter-surgeon Variation in Reoperation following Strabismus Surgery among Medicare Beneficiaries: Associations with Adjustable Sutures, Patient and Surgeon Characteristics
MONITOR 7	
Grant Hilliard	Outcomes of Strabismus Surgery in Patients Following Teprotumumab Therapy
Ravi Parikh	Ophthalmologist Turnover: An Analysis of the Physician Workforce the United States

SATURDAY · MONITOR 5

GENDER BIAS IN OPHTHALMOLOGY REIMBURSEMENT

Ron Adelman*, Aidan Gibson, Ava Khosarvi

Purpose: To study the impact of provider gender on Medicare reimbursement across ophthalmologic subspecialties, and the field in entirety.

Methods: We analyzed reports from the Center for Medicare and Medicaid Services (CMS) from 2013-2020 which provide the total reimbursement for each provider by their primary specialty and Medicare Part B Healthcare Common Procedure Coding System (HCPCS) service codes. Ophthalmologists were grouped into glaucoma, cornea, retina, cataract, or comprehensive if the physician performed at least ten procedures from a set of representative HCPCS codes for each given specialty. Within each subspecialty, we grouped the providers by gender and determined the yearly average total reimbursement, average reimbursement per patient, and the total reimbursement per provider per HCPCS code, and the gender ratio.

Results: In 2020 female glaucoma, cornea, retina, and cataract surgeons were reimbursed 68.35%, 60.40%, 64.69% and 73.02% as much as their male counterparts, compared to 63.27%, 60.34%, 72.49% and 57.79% respectively in 2013. When controlled for the number of patients, female glaucoma specialists received 89.58% compared to male glaucoma specialists. This rate was 89.15%, 89.29%, and 94.67% for cornea, retina, and cataract surgeons respectively. In 2020, across the entire specialty, female physicians were reimbursed 48.85% as much as male physicians, compared to 49.65% in 2013.

Conclusion: On average, Medicare total payment per year for a female ophthalmologist was substantially less than a male ophthalmologist. When reimbursement was controlled by subspecialty, this disparity improved to 60-73%, and when controlled for both subspecialty and the number of patients seen the disparity improved to 89-94%. Across the eight years of study, there is only a moderate change in the gender disparity in reimbursement.

FRIDAY · MONITOR 4

IN VITRO ANTIBIOTIC RESISTANCE AMONG PRESUMED BACTERIAL KERATITIS ISOLATES IN THE ARMOR SURVEILLANCE STUDY

Penny A. Asbell•*, Christine M. Sanfilippo, Heleen H. DeCory

Purpose: Bacterial keratitis can cause sight-threatening complications, and infections caused by antibiotic-resistant pathogens can impact treatment success. Data from the Antibiotic Resistance Monitoring in Ocular micRoorganisms (ARMOR) surveillance study provide valuable information on evolving antimicrobial resistance patterns among common ocular bacteria. Here, we report cumulative in vitro resistance rates among presumed keratitis isolates collected in ARMOR from 2009 through 2021.

Methods: Ocular isolates of Staphylococcus aureus, coagulase-negative staphylococci (CoNS), Streptococcus pneumoniae, Haemophilus influenzae, and Pseudomonas aeruginosa were obtained from US clinical centers each year as part of ARMOR. Minimum inhibitory concentrations (MICs) for up to 16 antibiotics were determined and interpreted per Clinical and Laboratory Standards Institute methods and breakpoints. The subset of isolates collected from the cornea were analyzed herein.

Results: A total of 1,989 isolates (565 S. aureus, 705 CoNS, 134 S. pneumoniae, 540 P. aeruginosa, and 35 H. influenzae) were collected from 64 sites across 31 states. Among S. aureus and CoNS respectively, substantial proportions of isolates were resistance to oxacillin/methicillin (33%, 38%), azithromycin (54%, 56%), ciprofloxacin (35%, 33%), tobramycin (17% each) and trimethoprim (5%, 32%). Multidrug resistance (≥3 antibiotic classes) was found in 34% of S. aureus and 39% of CoNS and was >80% among methicillin-resistant strains thereof. Isolates of S. pneumoniae exhibited notable resistance only to azithromycin and oral penicillin (32% and 29%, respectively). While all P. aeruginosa were resistant to polymyxin B, <5% were resistant to other agents including ciprofloxacin. All H. influenzae were susceptible to tested drugs, with the exception of one tetracycline-resistant strain.

Conclusion: In this cumulative analysis of corneal isolates collected in ARMOR, in vitro antibiotic resistance was prevalent among staphylococci (a high proportion of which were MDR) and among pneumococci. These data, along with the ocular pharmacokinetics of tested antibiotics, should be considered when selecting antibiotics for the management of bacterial keratitis infections.

FRIDAY · MONITOR 7

RISK STRATIFICATION OF OCULAR EMERGENCIES USING SMARTPHONE EXTERNAL PHOTOGRAPHY

Preston Blomquist*, Lance Stutz, Aiden Gregston, Linda Hynan, Richard Hession

Purpose: To evaluate the use of smartphone external photography in determining the diagnosis and urgency of patients presenting to the emergency department with an ocular complaint.

Methods: A survey was created using consecutive patient encounters in the Parkland Memorial Hospital Emergency Department with an in-person ophthalmology consult and external and/or anterior segment findings. The diagnosis and severity of the ocular condition was determined by a faculty ophthalmologist of the 33 short clinical vignettes. Faculty and resident ophthalmologists at The University of Texas Southwestern Medical Center were invited to participate. Only half of participants were shown an external photograph of each eye taken with a clip-on 20X macro lens and an iPhone XR (12-megapixel camera). Participants were asked to provide the most likely diagnosis and urgency for each clinical vignette.

Results: There were 15 participants in each group. In the group without external photographs, the correct diagnosis was identified on average in 58.6% ± 7.7% of cases, compared to 67.9% ± 9.2% in the group with photographs (p=0.0105). The correct urgency was identified on average in 55.5% ± 6.8% of cases, and a delay in triage occurred in 15.4% ± 10.2%. There was no statistically significant difference between the photo and no photo groups regarding urgency, and there were no statistically significant differences in all comparisons between faculty and residents. In the 11 cases identified as emergent, the correct urgency was identified more than 80% of the time in both groups.

Conclusion: The addition of high-quality external photographs improved the diagnostic accuracy of patients presenting to the emergency room with abnormal ocular examination findings. However, identifying the correct urgency of these patients did not improve with the addition of external photographs.

SATURDAY · MONITOR 5

HEALTHCARE EDUCATIONAL RETURNS

Gary Brown*, Melissa Brown

Purpose: Business principles are often neglected in medical school and other post-baccalaureate advanced healthcare profession programs. Important business principles that evaluate an investment's financial desirability are Net Present Value (NPV) and Internal Rate of Return (IRR). There are few reports in the literature comparing the financial desirability of the post-baccalaureate (educational) training costs and time required for different physician specialties, as is the case for physician specialties and non-physician advanced healthcare professions. We therefore undertook NPV and IRR analyses in different healthcare professions to assess the financial return from post-baccalaureate educational costs and time invested.

Methods: Nine medical specialties and six post-baccalaureate advanced healthcare professions were evaluated. The NPV quantifies the lifetime financial gain above baccalaureate earnings. The formula is NPV = all post-baccalaureate earnings (training salaries and/or training stipends + annual career practice earnings minus annual baccalaureate earnings lost during practice to age 65) minus all training expenditures (tuitions + interest on tuition loans during training + interest during the amortized payback of loans over the first ten years of career practice + the opportunity cost of baccalaureate salary lost during training). The IRR is similar to the return-on-investment, though it integrates the time value of money, whereas return-on-investment does not. All costs were discounted at $3.97%/year (50-year annual US average). Tuitions and salaries were inflated at the same rate, though interest was not.

Results:

Profession	Training cost	2022 salary	NPV	IRR
Primary care	$530,321	$254,333	$6.1M	18.3%
Psychiatrist	$569,738	$287,000	$7.3M	15.9%
General surg.	$569,738	$402,000	$10.3M	19.8%
Anesthesia	$569,738	$405,000	$11.4M	19.9%
Ophthalmology	$569,738	$417,000	$11.8M	20.3%
Dermatology	$569,738	$438,000	$12.6M	20.9%
Gastroenterol.	$523,627	$453,000	$13.2M	20.3%
Cardiology	$523,627	$497,000	$14.7M	21.3%
Orthopedics	$523,627	$557,000	$16.9M	22.5%
Nurse anesth.	$359,080	$202,470	$4.1M	24.0%
Nurse pract.	$229,646	$118,040	$1.2M	13.7%
Dentist	$548,219	$177,770	$3.9M	15.1%
MBA, insurance	$185,676	$153,460	$3.8M	45.5%
Hospital CEO	$185,676	$153K/$569K	$14.7M	46.6%
Attorney	$321,631	$148,030	$3.1M	16.2%

Conclusion: The IRR for ophthalmologists lies between that of primary care physicians and highly paid procedural physicians such as cardiologists and orthopedic surgeons.

FRIDAY · MONITOR 3

OPHTHALMOLOGY AND THE NOBEL PRIZES

John D. Bullock*

Purpose: Given the importance of sight, it is not surprising that Nobel Prizes (NP's) have been awarded to numerous vision scientists.

Methods: Allvar Gullstrand (1911, the only ophthalmologist-winner for an ocular subject) won a NP for his studies of the optics of the eye.

Results: NP's were awarded to 8 non-ophthalmologists for ophthalmic topics. In 1967, Hartline, Granit, and Wald received prizes "for their discoveries concerning physiological and chemical processes in the eye," and in 1981, Hubel and Wiesel, were honored for their work on visual processing. The immunologist Peter Medawar (1960) discovered the immune-privileged status of the cornea and anterior chamber while the Japanese biochemist Satoshi Ōmura and the Irish parasitologist William Campbell co-developed ivermectin for the treatment of ocular onchocerciasis. Three other fully trained and previously-practicing ophthalmologists have actually received NP's, but for subjects unrelated to ophthalmology. Emil von Behring practiced in Germany for three years before working as a microbiologist/immunologist in Berlin, winning the NP for his development of the diphtheria antitoxin. Fritz Pregl (Austria) switched from ophthalmology to physiological chemistry, analyzing minute quantities of biological compounds. Walter Hess had practiced near Zurich and then studied neurophysiology. He shared the 1949 NP for his discovery of the functional organization of the diencephalon. Other ophthalmologists have been nominated but rejected for NP's including Hjalmar Schiøtz (tonometer [Norway]), Karl Koller (cocaine anesthesia [Austria]), and Jules Gonin (retinal surgery [Swizerland]). Cuban ophthalmologist Carlos Finlay was rejected for a non-ocular subject (transmission of yellow fever by mosquitoes). Ocular disability was a factor in two awards: 1. Rene Prudhomme ("Eye disease", France, 1901, Literature) and Nils Gustaf Dalen (industrial explosion, Sweden, 1912, Physics). NP's were also awarded to 34 laureates for 15 subjects indirectly, but highly significantly, related to ophthalmology.

Conclusion: NP's have contributed greatly to the science of ophthalmology as well as to the overall field of medicine.

FRIDAY · MONITOR 5

PRE-DESCEMET STROMA IS OPTICALLY TRANSPARENT EVEN IN THE ABSENCE OF CORNEAL ENDOTHELIUM

Massimo Busin*, Angeli Christy Yu, Alessandro Ruzza, Diego Ponzin

Purpose: To evaluate optical transparency and thickness of pre-Descemet stroma preserved either by means of organ culture media and silica gel-based tissue dehydration.

Methods: Using a 27-gauge needle, pneumatic dissection was performed in 16 sclerocorneal discs mounted on an anterior artificial chamber. The central 6 mm of the bubble roof was removed by baring the optical zone at the level of pneumatic dissection of pre-Descemet layer. The Descemet membrane-endothelium complex was then stripped off. Tissues were evaluated for optical transparency using a custom-built device measuring light transmission and thickness via anterior segment optical coherence tomography immediately following tissue preparation and 7, 14, 21 and 28 days after preservation via organ culture media without deturgescent agent (n=10) or silica-gel based tissue dehydration (n=6). All tissues were sent for histologic and transmission electron microscopy evaluation.

Results: Following pneumatic dissection, average light transmission was 64 lux and corneal thickness was 34 μm. There were no significant differences in corneas preserved in standard organ culture or tissue dehydration. No significant differences in light transmission and thickness were observed up to 30 days. Pre-Descemet tissue consisted of tightly packed collagen bundles devoid of keratocytes.

Conclusion: Thickness and light transmission through the pre-Descemet layer were not affected by the absence of endothelium. The preclinical study provides evidence that pre-Descemetic tissue can be used as a transparent acellular biologic scaffold.

FRIDAY · MONITOR 3

FREQUENCY OF STRABISMUS AFTER TUBE SHUNT SURGERY IN THE ADULT VERSUS PEDIATRIC POPULATIONS

Teresa Chen[♦*], Maria Guzman Aparicio

Purpose: To determine the frequency of strabismus after tube surgery in adults versus pediatric patients.

Methods: This is a retrospective study. A chart review of Ahmed (New World Medical) and Baerveldt (Abbott Medical Optics, Inc.) surgeries performed by a single surgeon (TCC) in a single institution between September 1998 and September 2021 was made. Pediatric patients were <18 years of age at the time of surgery. Patients were excluded if they had <6 months of follow-up data and concomitant major ocular surgery. The main outcome measure was the presence or absence of strabismus or diplopia lasting more than 6 months after tube shunt surgery.

Results: Three hundred and sixty tube surgeries were performed in 333 eyes of 311 patients: of these, 237 procedures in 223 eyes of 202 patients met the inclusion criteria. Of the 223 eyes, 214 had 1 tube, 8 had 2 tubes, and 1 had 3 tubes inserted. Four eyes had a tube exchange, which comprises 2 surgeries per eye but, in the end, only 1 tube implanted per eye. Of the 202 patients included, 30 had pre-existing strabismus. The remaining 172 patients were 149 (86.6%) adults, and 23 (13.4%) children. Of the pediatric patients, 3 eyes of 3 patients (13%) had new onset strabismus after tube surgery at the last follow-up compared to 0 adults (p-value = <0.001).

Conclusion: After tube shunt surgery, pediatric patients have more problems with new-onset strabismus than adults.

SATURDAY · MONITOR 4

ASSOCIATION BETWEEN SOCIAL VULNERABILITY SCORES AND VISION DIFFICULTY IN THE UNITED STATES

Janet Coleman-Belin*, Deyu Pan, Victoria Tseng, Ken Kitayama, Fei Yu, **Anne Coleman**

Purpose: To examine associations between Centers for Disease Control Social Vulnerability Index (SVI) scores and vision difficulty in the United States population.

Methods: The study included individuals ≥18 years old in the 2016-2020 American Community Survey (ACS). SVI scores were calculated on the county level using 2016-2020 ACS data and analyzed as continuous variables, where higher SVI levels indicated higher levels of social vulnerability. Scores were classified as overall SVI and by 4 themes of socioeconomic status (SVI-SES), household composition and disability (SVI-HCD), minority status and language (SVI-MSL), and housing type and transportation (SVI-HTT). Vision difficulty was defined based on percentage of positive participant responses per county to an ACS question about vision difficulty. Associations between SVI scores and vision difficulty were examined on the county level using linear regression modeling, adjusting for county level demographics related to age, sex, race and ethnicity, education, poverty level, and insurance status.

Results: Of 253,272,570 adult participants of the ACS from 2016-2020, 7,002,640 (2.8%) had vision difficulty, and the mean overall SVI score was 0.5±0.3. In adjusted analyses, each 1% increase in SVI score was associated with an increased prevalence of vision difficulty of 17.2±1.7 per 100,000 individuals for the overall SVI ($p<0.001$), 14.5±1.7 per 100,000 for SVI-SES ($p<0.001$), 15.4±1.2 per 100,000 for SVI-HCD ($p<0.001$), and 9.2±2.6 per 100,000 for SVI-MSL ($p<0.001$). There was no statistically significant association between SVI-HTT score and prevalence of vision difficulty ($p=0.08$).

Conclusion: In the 2016-2020 ACS population, increased social vulnerability was associated with increased likelihood of vision difficulty for most SVI themes on the county level. Further investigation is needed to identify the etiology of these findings and strategies to reduce the burden of vision impairment for individuals with high levels of social vulnerability.

FRIDAY · MONITOR 4

OCULAR PAIN AFTER REFRACTIVE SURGERY: PRELIMINARY ANALYSIS OF EPIDEMIOLOGY AND RISK FACTORS

Anat Galor*, Jason Betz, Hannah Behrens, Brooke Harkness, Richard Stutzman, **Winston Chamberlain**, Marie Perez Blanco, Deborah Hegarty, Sue Aicher

Purpose: To examine the frequency and risk factors for ocular pain after laser assisted in situ keratomileusis (LASIK) and photorefractive keratectomy (PRK).

Methods: Prospective study of individuals undergoing refractive surgery. Participants rated their ocular pain on a 0 – 10 Numerical Rating Scale (NRS) pre-surgery and 1 day, 3 months, and 6 months post-surgery. A clinical examination focused on ocular surface health was performed 3- and 6-months post-surgery. Persistent ocular pain was defined as an NRS score ≥ 3 at both 3- and 6-months post-surgery (cases) and this group was compared to individuals with NRS scores <3 at both time points (controls).

Results: 109 individuals underwent refractive surgery (87% LASIK; 13% PRK) and had 6-months of follow-up. Mean age was 34±8 years (range 23 to 57); 62% self-identified as female, 81% as White, 33% as Hispanic. A few individuals reported ocular pain (NRS ≥ 3) prior to surgery (7%), with the frequency of ocular pain increasing after surgery to 23% (n=25) at 3 months and 24% (n=26) at 6 months. Twelve individuals (11%) reported an NRS ≥ 3 at both time points and comprised the persistent pain group. Factors that predicted persistent pain after surgery in a multivariable analysis were: (a) symptom report of depression prior to surgery (Patient Health Questionnaire-9: PHQ9: odds ratio (OR) 1.2, 95% confidence interval (CI) 1.0-1.5, p=0.03); (b), symptoms report of dry eye prior to surgery (5 item Dry Eye Questionnaire, DEQ5: OR 1.3, 95% CI 1.0-1.6, p=0.05), and (c) post-operative pain intensity on day 1 after surgery (OR: 1.5, 95% CI 1.1-2.0, p=0.01). Ocular surface signs of tear dysfunction were not related to pain complaints. Most individuals (>90%) were completely or somewhat satisfied with their vision at 3 and 6 months.

Conclusion: A proportion of individuals report persistent ocular pain after refractive surgery, with several pre- and peri-operative factors predicting pain after surgery.

SATURDAY · MONITOR 1

SYNTHETIC BIOLOGY FOR OPHTHALMIC GENE THERAPY

Lucie Guo♦*, Jing Bian, Alex Davis, Rain Wen, Pingting Liu, Haoliang Huang, Hannah Kempton, Yang Hu, Sui Wang, Stanley Qi, **Jeffrey Goldberg**

Purpose: CRISPR-based genome targeting has emerged as a revolutionary technology for previously incurable diseases, including many in ophthalmology. However, its scope has been largely limited to inherited diseases caused by single genes. There exists an unmet need to develop gene therapy tools for simultaneous targeting of multiple genomic sites in a "multiplexed" fashion, which could expand the capability of ocular gene therapy to common, polygenic diseases. Additionally, there is an unmet need to develop safer platforms for gene therapy, such as where the dosage of gene therapy can be regulated after in vivo administration.

Methods: To develop a toolkit for "multiplexed" gene therapy, we used structure-guided protein engineering to develop an improved CRISPR/Cas12a enzyme and tested its in vivo capability through AAV-based delivery to retinal ganglion cells as well as subretinal delivery in postnatal mice. We also tested "biosensors" that can detect cellular injury in retinal ganglion cells, compatible with AAV-based gene therapy.

Results: Compared to wildtype Cas12a, our improved dCas12a enzyme ("hyperCas12a") has significantly greater efficacy in gene editing, activation, repression, and base-editing, and including in vivo gene editing in retinal ganglion cells. Delivery of the improved dCas12a-activator with a single array of several CRISPR-RNAs simultaneously activated multiple gene targets in the retina of postnatal mice. We also developed biosensors to respond to cellular injury, as a first step toward building "smart" gene therapy that may be inducible or auto-regulatable.

Conclusion: We anticipate these new synthetic biology tools to be valuable to the ophthalmic gene therapy field, with the potential to expand the scope of ophthalmic therapy beyond rare inherited diseases.

SATURDAY · MONITOR 3

OXIDIZED CHOLESTEROL INDUCES RPE TO RELEASE INFLAMMATORY CYTOKINES AND VEGF: A POTENTIALLY TREATABLE CAUSE OF FIBROSIS IN UNTREATABLE AMD

Mary Elizabeth Hartnett, Aniket Ramshekar*, Haibo Wang, Thaonhi Cung, Chris Wallace-Carrete, Chandler Zaugg, Jasmine Nguyen

Purpose: Oxysterols, amenable to dietary treatment, accumulate in drusen and AMD. We previously found a predominant one, 7-ketocholesterol (7KC), contributes to mesenchymal transition (MT) in choroidal endothelial cells (CECs) and experimental fibrosis. Here we determined if 7KC induced MT in RPE but found RPE instead release inflammatory cytokines and VEGF.

Methods: Cultured human RPE were incubated with 7KC (10 μM) or control and assayed for alpha-smooth muscle actin (αSMA) and fibroblast activation protein (FAP), B-cell lymphoma-2 (BCL-2) and mRNA (BCL-xL), phosphorylated serine 10 in histone H3 (p-histone H3). RPE pretreated with mTOR-inhibitor, rapamycin, and incubated with 7KC or appropriate controls were assayed for: 1) senescence with p21, p16, and β-galactosidase staining; 2) cytokine expression with phospho-NF-κB, total NF-κB, IL-1β, IL-6, VEGF; and 3) RPE integrity by junctional barrier complexes, cadherin/β-catenin, Electric Cell-substrate Impedance Sensing (ECIS); and 4) RPE cell markers, RPE65, CRALBP and BEST1.

Results: Compared to control, 7KC did not induce FAP and αSMA expression in RPE but increased expression of anti-apoptotic BCL-2 BCL-xL, and p-histone H3, aligning with cell cycle arrest at mitosis, and p21 ($p<0.05$), p16 ($p<0.05$, and β-galactosidase staining ($p<0.05$), while retaining RPE markers. 7KC-treated RPE showed increased phospho-NF-κB ($p<0.01$), IL-1β ($p<0.01$), IL-6 ($p<0.001$) and VEGF ($p<0.001$), compromised junctional integrity with reduced cadherin/β-catenin complexes ($p<0.01$) and lower ECIS ($p<0.001$) that were restored with rapamycin-induced mTOR inhibition.

Conclusion: 7KC causes RPE to enter cell cycle arrest with senescence and compromised barrier integrity mediated through mTOR signaling. These findings support the hypothesis that 7KC, which accumulates in drusen, reduces RPE barrier integrity and causes RPE to release inflammatory cytokines and VEGF. VEGF can then attract CECs to migrate toward drusen where they undergo MT and contribute to fibrosis, leading to potential resistance to anti-VEGF in AMD. Future studies to reduce oxidative compounds may limit untreatable vision loss in AMD.

SATURDAY · MONITOR 7

OUTCOMES OF STRABISMUS SURGERY IN PATIENTS FOLLOWING TEPROTUMUMAB THERAPY

Grant Hilliard*, **Natalie Kerr**

Purpose: Teprotumumab was approved for use in Thyroid Eye Disease (TED) in January 2020. To date, no reports have appeared in the literature about the results of patients requiring surgical treatment for symptomatic strabismus in TED following teprotumumab.

Methods: We report 7 sequential patients who had surgery for symptomatic diplopia after teprotumumab. Variables analyzed included elapsed months from last teprotumumab dose to the date of surgery, history of previous orbital decompression, primary preoperative horizontal and vertical deviation, surgical procedure, and 2-month postoperative results.

Results: Mean age of the 7 patients was 54 years (range, 39-73 years). Two patients had orbital decompressions prior to surgery. The mean elapsed time from treatment to surgery was 5 months (range, 2-7 months). The mean preoperative deviation was 18 prism diopters (PD) horizontally (range, 4-50 PD) and 23 PD vertically (range, 4-40 PD). At the 2-month postoperative visit, mean deviation was 5 PD horizontally (range, 0-15 PD) and 6PD vertically (range, 0-15 PD). Two patients received horizontal muscle surgery, three received vertical surgery, and two received bilateral surgery. Three patients had adjustable sutures. Three patients were diplopia-free after 1 surgery. One patient chose prism spectacles to correct residual diplopia and another used head posture to fuse and were considered treatment successes. Two underwent further surgery and were diplopia-free 2 months postoperatively.

Conclusion: Patients requiring strabismus surgery for symptomatic strabismus following teprotumumab achieve good outcomes following surgical treatment for TED.

SATURDAY · MONITOR 1

CONTENT GENERATION, PSYCHOMETRIC VALIDATION, AND APPLICATION IN CLINICAL PRACTICE AND TRIALS OF PATIENT REPORTED OUTCOME MEASURES FOR INHERITED RETINAL DISEASES

K. Thiran Jayasundera♦*, David Musch

Purpose: To evaluate properties and development of the Michigan Retinal Degeneration Questionnaire (MRDQ) and the Michigan Vision-related Anxiety Questionnaire (MVAQ), a patient-reported outcome (PRO) measure designed to evaluate vision-related difficulties, distress, accommodations, and limitations of patients with Inherited Retinal Diseases (IRD) for use in clinical practice and clinical trials.

Methods: Adult patients with a confirmed diagnosis of cone dystrophy, cone-rod dystrophy, macular dystrophy, or rod-cone dystrophy were recruited for content generation and psychometric validation of the MRDQ and MVAQ, adhering to FDA guidelines for construction of PRO measures. Test-retest variability, domain-trait associations, the ability to distinguish different IRD phenotypes, associations between vision-related anxiety and vision-related disabilities, and correlations with the National Eye Institute Visual Functioning Questionnaire 25 (NEI VFQ-25) and the Impact of Vision Impairment (IVI) were obtained.

Results: The MRDQ consists of seven domains (central vision, color vision, contrast sensitivity, scotopic function, photopic peripheral vision, mesopic function and photosensitivity). The MVAQ consists of two domains (cone dysfunction related anxiety, and rod dysfunction related anxiety). Based on item response theory, each domain produces a level of disability or distress ranging from -3 to +3 theta, where an increasing score indicates a higher severity in difficulties, limitations or distress. Initial content items for the MRDQ and MVAQ were drafted through a series of expert panel focus groups, in-depth patient interviews, cognitive interviews, and pilot questionnaire administration. Patients with IRDs participated in open-ended, in-depth interviews to solicit their perspectives on symptoms they related to their visual condition. Transcribed interviews were coded and analyzed in Atlas.ti software and content items were drafted based on grounded theory principles of theme extraction. Following the generation of items, graded response models (GRM) were built for the domains of the MRDQ and MVAQ. One-way ANOVA testing was significant for distinguishing among IRD phenotypes in domains of MRDQ/MVAQ. Cone-function anxiety correlated with Central Vision upon controlling for visual acuity, rod-function anxiety correlated with Scotopic Function upon controlling for visual field area, and all domains in MRDQ and MVAQ had significant correlations with NEI VFQ-25 and IVI composite scores.

Conclusion: Patients with IRDs have addressable needs that result from the progression of their disease and worsening visual function. The MRDQ and MVAQ provide validated PROs for use in clinical practice to measure functional deficits in everyday life for patients with a specific IRD phenotypic expressions and evaluate interventions with targeted low vision rehabilitation and psychotherapy. These PROs are currently incorporated as outcome measures in ongoing IRD clinical trials.

FRIDAY · MONITOR 5

OCULAR SURFACE SQUAMOUS NEOPLASIA: CHANGES IN THE STANDARD OF CARE 2003 TO 2022

Jason Greenfield, Adam Cohen, **Anat Galor**, **James Chodosh**, Donald Stone, **Carol Karp**♦*

Purpose: To elucidate treatment preferences for ocular surface squamous neoplasia (OSSN) and to examine the changes in treatment modalities over the past two decades.

Methods: An electronic survey consisting of 24 questions was distributed on the management of OSSN. Ophthalmologists who are members of the Cornea Society, The Ocular Microbiology and Immunology Group (OMIG), Keranet, Pancornea, and cornea specialist groups in India, Thailand, and Japan were surveyed. Participants' medical and surgical treatment preferences were assessed, and the results were compared to surveys administered in 2003 and 2012.

Results: A total of 285 individuals responded to the survey; 90% of respondents were self-classified as cornea specialists. Seventy three percent reported using primary topical monotherapy to treat OSSN as compared to 58% in 2012 ($p=0.008$). Compared to 2003, the percentage use of topical interferon significantly increased ($p<0.0001$) from 14% to 55%, 5-fluorouracil increased ($p<0.0001$) from 5% to 23%, and mitomycin C decreased ($p<0.0001$) from 76% to 19% as a primary monotherapy. The frequency of performing excision without the use of postoperative adjunctive medical therapy decreased significantly ($p<0.0001$), from 66% to 26% for lesions less than 2 millimeters, 64% to 12% for lesions between 2 and 8 millimeters, and 47% to 5% for lesions greater than 8 millimeters from 2003 to 2022. More clinicians initiated topical immuno/chemotherapy without performing a biopsy as compared to 2003 (31% vs 11%, $p<0.0001$).

Conclusion: These results demonstrate a paradigm shift in the management of OSSN. The use of primary medical therapy as a first approach has significantly increased, with a reduction in the frequency of performing surgical excision alone.

FRIDAY · MONITOR 1

CLINICAL CHARACTERISTICS OF AXENFELD-RIEGER SYNDROME IN CHILDREN

Nikhila Khandwala*, Divya Sree Ramya Achanta, Pooja Jadon, Sneha Barur, Anil Kumar Mandal, Muralidhar Ramappa, **Deepak Edward**

Purpose: Axenfeld-Rieger Syndrome (ARS) is a disorder defined by anterior segment dysgenesis and systemic associations. There are limited studies on ARS in children. The purpose of this study is to analyze the clinical profile of ARS in a pediatric cohort.

Methods: This was a retrospective study of ARS patients presenting to LVP Eye Institute, Hyderabad, India. Data recorded included demographics, anterior, posterior segment findings, and systemic associations. Diagnostic criteria included presence of ocular and systemic findings associated with ARS.

Results: A total of 365 patients (695 eyes) were diagnosed with bilateral ARS, with female patients accounting for 54%. Average age at presentation was 13.8 years (1 day- 61 years). In 15% (109 patients), family history of ARS was elicited with systemic associations in 14% (52 patients). The corneal findings included posterior embryotoxon (40%, 284 eyes), megalocornea (10%, 69 eyes), microcornea (11%, 78 eyes), corneal scarring (13%, 88 eyes), and corneal haze (5%, 34 eyes). 86% (600 eyes) had iris abnormalities including anterior synechiae/iris processes, irregular iris stroma, and atrophy, and 3.5% (24 eyes) with partial or complete aniridia. 42% (295 eyes) had an irregular pupil, polycoria, or corectopia and 7% (50 eyes) had cataract and 1% (4 eyes) with lens subluxation. Secondary glaucoma was present in 41% (285) eyes and was more commonly associated with iris changes (93%).

Conclusion: In this ARS pediatric cohort, ocular findings included corneal, iris, pupil and angle abnormalities, similar to what has been cited in patients of all ages.1 ,2 Megalocornea and microcornea were unique. The 15% rate of family history of ARS was lower than previously cited (38-70%), suggesting the need for genetic testing in this cohort.3 The rate of secondary glaucoma in children was similar to that cited in all patients with ARS-related glaucoma suggesting that glaucoma may develop early and the need for regular screening in children.

FRIDAY · MONITOR 1

SYSTEMIC DISEASE BURDEN MEDIATES RACIAL AND ETHNIC DISPARITIES IN INCISIONAL GLAUCOMA SURGICAL OUTCOMES: A CAUSAL MEDIATION ANALYSIS

Ken Kitayama*, Victoria Tseng, Fei Yu, **Anne Coleman**

Purpose: To estimate the proportion of the racial/ethnic disparity in glaucoma surgical outcomes eliminated by theoretically intervening on systemic disease burden as measured by the Charlson comorbidity index (CCI).

Methods: A retrospective cohort was constructed using the entire population of 2016-2018 CA fee-for-service Medicare beneficiaries with a claim for incisional glaucoma surgery (trabeculectomy, tube shunt, EX-PRESS shunt). The exposure was race/ethnicity, stratified into: Non-Latinx White, Black, Latino, Asian, and Other. The mediator was CCI dichotomized to low (0-3)/high (4+) based on 19 medical conditions. Time to failure event (the primary outcome of interest) was defined as revision of index surgery or reoperation. Follow-up extended through 2019. Time-to-event was modeled using Cox proportional hazards with age and sex as covariates. Causal mediation analysis was used to estimate the total effect (TE) of the entire racial/ethnic disparity and the controlled direct effect (CDE) for the remaining disparity after fixing CCI to low.

Results: Among 6,524 beneficiaries in the final sample (non-Latinx White:52.3% [reference group], Black:9.7%, Asian:14.7%, Latinx:19.7%, Other:3.7%), 60.0% (n=3,912) had low CCI and 24.4% (n=1,593) had a failure event. The TE estimates suggested greater failure risk in Black (hazard ratio [HR]:1.12, p=.19), Asian (HR:1.22, p<.01), Latino (HR:1.21, p<.01), and other race and ethnicity beneficiaries (HR:1.30, p=.04). The CDE estimates showed no significant disparities after fixing CCI to low for Black (HR:1.10, p=0.43), Asian (HR:1.13, p=0.18), Hispanic (HR:1.14, p=0.13), and Other (HR:1.17, p=0.34) groups. The proportion of the racial/ethnic disparity that could be eliminated by intervening on CCI was 21.3% for Black, 38.6% for Asian, 34.9% for Latino, and 43.0% for other race/ethnicity beneficiaries.

Conclusion: There was increased risk of glaucoma surgical failure in racially and ethnically minoritized CA Medicare beneficiaries. This disparity can be mitigated by intervening on systemic disease burden. Future studies are needed to identify targets to reduce disparities.

FRIDAY · MONITOR 6

DID OTTOMAN TRAVELLER EVLIYA ÇELEBI INTRODUCE CATARACT ASPIRATION INTO WESTERN EUROPE IN 1665?

Christopher Leffler*

Purpose: To review the history of cataract aspiration in the Middle East and Europe in the medieval and Renaissance periods, including a description of cataract aspiration in Southeastern Anatolia in 1655 which has not previously been discussed in the ophthalmology history literature.

Methods: The description of cataract aspiration by Ottoman traveller Evliya Çelebi from Southeastern Anatolia in 1655 was reviewed, along with similar descriptions by Austrian surgeons after Çelebi visited Viennese hospitals during peace talks in 1665.

Results: Ottoman traveller Evliya Çelebi described cataract aspiration at Bitlis in 1655. He then visited hospitals in Vienna at peace talks with the Habsburgs in 1665. In Vienna, Çelebi spoke with Habsburg surgeons, observed surgeries, and referred to the advanced ophthalmology in Vienna. By 1669, shortly after Çelebi's visit to Vienna, cataract aspiration was attributed to Habsburg surgeon Rocco Mattioli. Breaking up the crystalline lens with a fine brush prior to aspiration was also described, as a European innovation. These ideas were published by Mattioli's contacts in Amsterdam and culminated in the earliest identified vitrectomy by suction in 1690.

Conclusion: Cataract aspiration was still occurring in the Middle East in the mid-1600s, several centuries after the latest previously identified instance. European authors for all practical purposes had ignored the medieval Arabic descriptions of the procedure prior to 1665. The Europeans began to draw pictures of the procedure, and to actually attempt similar procedures, after Ottoman traveller, who described the procedure in Anatolia, visited Vienna in 1665.

SATURDAY · MONITOR 6

INTER-SURGEON VARIATION IN REOPERATION FOLLOWING STRABISMUS SURGERY AMONG MEDICARE BENEFICIARIES: ASSOCIATIONS WITH ADJUSTABLE SUTURES, PATIENT AND SURGEON CHARACTERISTICS

Christopher Leffler*, Alicia Woock, Meagan Shinbashi, Melissa Suggs

Purpose: The objective of this study was to quantify inter-surgeon variation in strabismus surgery reoperation rates in a large national database of provider payments, and to explore associations of reoperation rate with practice type and volume, surgical techniques, and characteristics of the patient population.

Methods: Fee-for-service payments to providers for Medicare beneficiaries having strabismus surgery between 2012 and 2020 were retrospectively analyzed to identify reoperations in the same calendar year. The adjustable-suture technique was considered to be available to the patient if the patient's surgeon billed for adjustable sutures. Predictors of the rate of reoperation for each surgeon were determined by multivariable linear regression.

Results: Among 141 surgeons, the reoperation rate for 1-horizontal muscle surgery varied between 0.0% and 30.8%. Due to the presence of high-volume surgeons with high reoperation rates, just 11 surgeons contributed half of the reoperation events for 1-horizontal muscle surgery in this national database. Use of adjustable sutures, surgeon gender, and surgical volume were not independently associated with surgeon reoperation rate. Associations of reoperation with patient characteristics, such as age and poverty, were explored. In a multivariable model, surgeons in the South and those who predominantly operated in the earlier years of the database (2012-16) tended to have a higher reoperation rate ($p<0.05$). Still, the multivariable model could explain only 12.0% of the variation in surgeon reoperation rate.

Conclusion: Patient-level analyses which ignore inter-surgeon variation will be dominated by the practices of a small number of high-volume, high-reoperation surgeons. There are order-of-magnitude variations in reoperation rates among strabismus surgeons, the cause of which remains largely unexplained.

SATURDAY · MONITOR 2

LISCH EPITHELIAL CORNEAL DYSTROPHY IS NOT A X-CHROMOSOMAL BUT AN AUTOSOMAL DOMINANT INHERITED DISORDER

Walter Lisch*

Purpose: To identify the genetic etiology of Lisch epithelial corneal dystrophy (LECD), MIM #300778

Methods: To submit blood samples and oral cavity swabs for whole exome and genome sequencing of 28 LECD patients including the original family with ten affected individuals, six individuals from two novel families, and twelve simplex cases from Hanau, Aarhus, Tuebingen, Dortmund, Glasgow, Miami, and Los Angeles to the Genetic Institutes of Innsbruck (Janecke), Seattle (Bamshad), and Los Angeles (Chung and Aldave).

Results: There was an identification of five heterozygous, rare (MAF<6x10 high minus 5 in gnom AD) variants in MCOLN1, explaining six of nine family members. Three variants, c.514C>T(p.Arg172*), c.576C>A(p.Cys 192*), and c.406-2A>G are predicted to be loss-of-function and two were missense, c.776>C(p.Leu259Pro) in a proband and affected father and c.694A>C(p.Thr232Pro) in a proband.

Conclusion: LECD is an autosomal dominant inherited disorder on chromosome 19. Some carriers of MCOLN1 loss-of-function mutations present with LECD.

SATURDAY · MONITOR 7

OPHTHALMOLOGIST TURNOVER: AN ANALYSIS OF THE PHYSICIAN WORKFORCE THE UNITED STATES

Ravi Parikh*, Prem Patel, Amar Sheth, Parth Patel, Harris Ahmed, John Markle, Tedi Begaj, **James Tsai**

Purpose: To determine frequency of turnover among ophthalmologists and to determine physician and practice characteristics associated with turnover nationally.

Methods: This cross-sectional study used data from the Centers for Medicare & Medicaid Services PhysicianCompare Database (2014–2021). Ophthalmologists were selected by National Provider Identifier (NPI). Data extracted included gender, location, medical school graduation year, unique practice identifier, practice size, and practice name. Practices were categorized as university-affiliated if the name included "univ, college, faculty, or school" and ophthalmology-exclusive if the name included "eye", "cataract", "ophth", "oculo", "cornea", "retina", "glaucoma"; otherwise, practices were non-university and multi-specialty. Per prior methodology, we excluded ophthalmologists likely in training (within 6 years of medical school graduation), those practicing outside of the 50 US states and the District of Columbia, and those who billed <1000 MedicareRVU in 2014. Turnover was determined to occur when an ophthalmologist (identified by NPI) changed group affiliations (defined by practice identifier) from one year to the next. In group practices, multivariable logistic regression was performed to determine characteristics associated with turnover.

Results: We examined turnover among 13,255 ophthalmologists affiliated with 3,306 practices. Overall, 34.1% of ophthalmologists were observed to separate from their 2014 position by 2021. Annual turnover rates ranged from 3.7% in 2017 to 19.4% in 2018, with an average rate of 9.4%. New York (48.7%) had the highest cumulative turnover, whereas New Hampshire (16.9%) had the lowest. Factors associated with turnover included Northeast location (aOR: 1.48; 95% CI: 1.35–1.72), small practice size (2-4 members; aOR: 1.24;95% CI: 1.05–1.47), university-affiliation (aOR: 1.5; 95% CI: 1.28–1.77), and multi-specialty practice (aOR:1.61; 95% CI: 1.44–1.80; $p<0.05$ for all). Females (aOR: 1.16; 95% CI: 1.04–1.31) and those practicing for 0-5years (aOR: 4.35; 95% CI: 3.64–5.19), 6-10 years (aOR: 2.63; 95% CI: 2.20–3.15), 11-19 years (aOR: 2.06; 95% CI: 1.75–2.43), and 20-29 years (aOR: 1.42; 95% CI: 1.20–1.68) were more likely to turnover ($p<0.05$).

Conclusion: Over 1 in 3 ophthalmologists have changed clinical positions from 2014-2021. Turnover occurred most likely in the first 5 years after training, small practice size (2-4 members), university affiliation, and multi-specialty practice. Annual turnover rates peaked prior to the COVID19 pandemic.

SATURDAY · MONITOR 3

NAION IS CAUSED BY PAPILLARY VITREOUS SEPARATION

Cameron Parsa*, Mostafa Sanjari, Khalil Falavarjani, Ali Akbarzadeh, Kaveh Aghdam

Purpose: It has been proposed that brisk vitreous separation would fracture viscoelastic (age-related) axonal cytoskeletons, particularly in small discs with vitreous most adherent to central vessels and adjacent axons, to produce so-called NAION.1,2 If so, all those with NAION should demonstrate peripapillary or total vitreous separation.

Methods: 27 consecutive patients with NAION underwent SD-OCT vitreous examination within two weeks of symptom onset. 32 healthy age-matched controls with small cup-to-disc ratios, 11 patients with papillitis, and 32 patients with papilledema were also examined.

Results: In the 27 patients with NAION, 17 (62.9%) had stage 4, one (3.7%) had stage 3, 3 (11.1%) had stage 2, and 6 (22.2%) had stage 1 vitreous detachment. All demonstrated total (17/27, 62.9%) or peripapillary (10/27, 37.0%) vitreous detachment.

In those with papilledema, 15 (46.8%) had stage 4, 2 (6.2%) had stage 2, 8 (25%) had stage 1, and 7 (21.8%) had stage 0 detachment (4 with vitreous fully attached).

In those with papillitis, 5 (45.4%) had stage 4, 5 (45.4%) had stage 1, and 1 had stage 0 detachment. Three with stage 1 or 0 (27.2%) had no peripapillary detachment.

In healthy controls with "discs-at risk," 12 (37.5%) had stage 4, 1 (3.1%) had stage 3, 4 (12.5%) had stage 2, 13 (40.6%) had stage 1, and 2 (6.2%) had stage 0 detachment. 5/15 with stage 1 or 0 (15.6%) had vitreous fully attached at the disc.

Conclusion: Unlike an age-matched population, or those with disc swelling from other causes, all patients with NAION demonstrate total or peripapillary vitreous separation. Prior studies encompassing a further 143 patients had also revealed such ubiquitous detachment in NAION, 3-5 but had not included controls. Findings support abrupt peripapillary vitreous separation, precocious in diabetes,6 as causative for fracture of age-related viscoelastic axonal cytoskeletons,7, 8 producing so-called NAION.

SATURDAY · MONITOR 6

STAKEHOLDER PERSPECTIVES ON BARRIERS AND FACILITATORS TO IMPLEMENTING SUSTAINABILITY INTERVENTIONS IN CATARACT SURGERY

Brooke Sherry*, Maria De Los Angeles Ramos Cadena, Christina Prescott, **Joel Schuman**, Cassandra Thiel

Purpose: Cataract surgery emits significant greenhouse gases, and implementing sustainability interventions in ophthalmology requires the engagement of various stakeholders. Our study assesses attitudes toward sustainability interventions and identifies perceived barriers and facilitators to implementation at one health system-affiliated ambulatory surgical center in the northeast US.

Methods: A list of sustainability interventions for US cataract surgery was developed using previous literature and clinical observations. We developed a semi-structured interview guide to gather stakeholder opinions for the following intervention domains: eliminating/reducing supplies, reusable supplies, pharmaceuticals, and process changes. Relevant stakeholders at NYU Langone Health were identified, including clinical staff, departmental and system administrators, infection control & supply chain personnel. Each 30-min interview is recorded and transcribed and will be reviewed & coded for themes of barriers and facilitators to implementing these sustainability interventions.

Results: TBD

Conclusion: TBD

SATURDAY · MONITOR 2

NORTH CAROLINA MACULAR DYSTROPHY (NCMD/MCDR1): ANALYSIS OF OUR ENTIRE DATABASE, A MODEL DISEASE OF NON-CODING MUTATIONS

Kent Small*

Purpose: Note: A group of 41 authors named the NCMD Consortium has contributed to this research. We reported the first 5 mutations in 12 NCMD families with 141 subjects. The purpose of this study is to clinically and molecularly study our entire NCMD database to determine if our initial findings continue to be substantiated.

Methods: Ophthalmic examinations and whole genome sequencing (WGS) and/or targeted DNA Sanger sequencing was performed on our entire dataset of 55 families with 384 subjects. Junction PCR and Sanger sequencing was used to confirm point mutations and characterize duplications involving the MCDR1/MCDR3/PRDM13 locus.

Results: Of the total 384 subjects evaluated to date, 272 were found to be affected having DNA sequence changes consistent with MCDR1 on chromosome 6 or MCDR3 on chromosome 5. Unaffected family member sequences were 117 subjects. In addition to our 12 initial families, we report the findings of an additional 43 families with 78 subjects affected and 41 unaffected. Eight of these new families, 35 subjects, were found to have the original "V1" Chr6:99593030G>T mutation, in a non-coding region of the DNASE1 site upstream of PRDM13. Fourteen families, 50 subjects, had the "V2" mutation Chr6:99593111G>C in the same DNASE1 site. One Asian family with 2 subjects had our previously reported Asian "V3" Chr6:99593164C>T mutation in the same DNASE1 site. Two new single nucleotide variants (SNVs) have recently been reported by us from our dataset, Ch6:99599064A>G in four members of one Czech family and Chr6:99959303G>C in four members of a Mexican family. A new tandem duplication Chr6:99560265-99616492 involving the same DNASE1 site, was recently reported by us in a Turkish family. Two novel non-coding point mutations at chr6:g.99598914T>C and chr6:g.99598926G>A (hg38) in the non-coding region of the DNase I site were found in two Korean families. A previously unreported geographic origin for this phenotype.

Conclusion: North Carolina Macular Dystrophy (NCMD) is more prevalent than typically thought with a worldwide distribution making the name of this disease a gross misnomer. Continued identification of subjects and families and their mutations supports our initial discovery of mutations. Our group has found 10 of 15 total NCMD mutations. All of the mutations (SNVs and duplications) appear to involve DNASE1 sites in non-coding regions. This suggests that this DNASE1 site is a mutational hot spot and confirms our original findings that it is critical in regulating PRDM13.

FRIDAY · MONITOR 2

RACIAL AND ETHNIC DIFFERENCES IN THE PREVALENCE OF NEOVASCULAR GLAUCOMA IN AT-RISK BENEFICIARIES IN THE CALIFORNIA MEDICARE POPULATION

Victoria Tseng♦*, Ken Kitayama, Fei Yu, **Anne Coleman**

Purpose: Neovascular glaucoma (NVG) is a potentially blinding complication of retinal vascular disease. The purpose of the present study was to examine racial and ethnic differences in the prevalence of NVG in at-risk beneficiaries in the California Medicare population.

Methods: The study included all 2019 California Medicare beneficiaries ≥65 years old with proliferative diabetic retinopathy (PDR), retinal vein occlusion (RVO), or ocular ischemic syndrome (OIS). Race and ethnicity were defined as Non-Hispanic White, Black, Hispanic, Asian, and Other based on the Research Triangle Institute race code. The presence of NVG was defined by International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes. Associations between race and ethnicity and prevalence of NVG in patients with PDR, RVO, or OIS were examined using logistic regression modeling, adjusting for age, sex, and Charlson Comorbidity Index.

Results: There were 42,895 California Medicare beneficiaries in 2019 with PDR, RVO, or OIS, of whom 1,883 (4.4%) had NVG. Racial and ethnic distribution of the study population included 20,585 (48.0%) Non-Hispanic White, 2,180 (5.1%) Black, 6,243 (14.6%) Asian, 12,113 (28.2%) Hispanic, and 1,774 (4.1%) Other beneficiaries. In adjusted analyses, compared to Non-Hispanic White beneficiaries with PDR, RVO, or OIS, those who were Black (adjusted odds ratio [aOR]=1.75, 95% confidence interval [CI]=1.44, 2.13) and Hispanic (aOR=1.62, 95% CI=1.45, 1.81) had higher odds of NVG. There were no statistically significant associations between Asian or Other race and ethnicity and odds of NVG.

Conclusion: In the 2019 California Medicare population, at-risk beneficiaries who were Black and Hispanic had higher likelihood of NVG compared to Non-Hispanic White beneficiaries. Further studies are needed to examine the etiology for these differences and to reduce potential racial and ethnic disparities for this blinding condition.

FRIDAY · MONITOR 2

MACHINE LEARNING APPROACHES FOR PREDICTING GLAUCOMA PROGRESSION IN A LARGE MULTICENTER ELECTRONIC HEALTH RECORDS CONSORTIUM: THE SIGHT OUTCOMES RESEARCH COLLABORATIVE (SOURCE)

Sophia Wang*, **Joshua Stein**

Purpose: Advances in artificial intelligence have enabled the development of predictive models for glaucoma. However, most work is single-center and uncertainty exists regarding the generalizability of such models. The purpose of this study was to build and evaluate machine learning (ML) approaches to predict glaucoma progression requiring surgery using data from a large multicenter consortium of electronic health records (EHR).

Methods: Structured EHR data from 5 academic eye centers participating in SOURCE were identified, including demographics, diagnosis codes, medications, and clinical information (intraocular pressure, visual acuity, refractive status, and central corneal thickness). We developed machine learning models to predict whether glaucoma patients (identified by ICD codes) would progress to glaucoma surgery (identified by CPT codes) using the following modeling approaches: 1) penalized logistic regression (lasso, ridge, and elastic net); 2) random forest. One site was reserved as an "external site" test set (N=2574); of the patients from the remaining sites, 3000 each were randomly selected to be in development and test sets, with the remaining 34747 reserved for model training. Evaluation metrics included area under the receiver operating characteristic curve (AUROC) on the test set and the external site.

Results: 55444 (12.8%) of 43321 patients underwent glaucoma surgery. Overall, the AUROC ranged from 0.651-0.675 on the random test set and from 0.623-0.673 on the external test site, with the random forest model performing best on both sets. There was a greater performance decrease from the random test set to the external test site for the penalized regression models than for the random forest model.

Conclusion: ML models developed using EHR data can predict whether glaucoma patients will need surgery. Performance of our predictive models was similar to prior models trained on structured EHR data from a single center. Caution should accompany deployment of predictive models to populations on sites external to the original training set. Additional research is needed to investigate the impact of protected class characteristics such as race or gender on model performance and fairness.

FRIDAY · MONITOR 6

COMPARISON OF THE LONG-TERM RESULTS OF DESCEMET'S STRIPPING AUTOMATED ENDOTHELIAL KERATOPLASTY (DSAEK) AND DESCEMET'S MEMBRANE ENDOTHELIAL KERATOPLASTY (DMEK) IN FELLOW EYES FOR TREATMENT OF FUCHS ENDOTHELIAL DYSTROPHY (FED).

Robert Weisenthal*

Purpose: To compare the long-term results of Descemet's stripping automated endothelial keratoplasty (DSAEK) and Descemet's membrane endothelial keratoplasty (DMEK) in fellow eyes for treatment of Fuchs endothelial dystrophy (FED).

Methods: Two-centered, retrospective case series of 64 patients (128 eyes) with DSAEK followed by DMEK. The main outcomes measured were BSCVA and duration of time to achieve BSCVA as well as eye preference.

Results: Preoperative median logarithm of the minimum angle of resolution (LogMAR) BSCVA was similar in eyes
receiving DMEK 0.36±0.26 and DSAEK 0.42±0.34 (P = 0.266)]. Average follow up time needed for the DMEK eyes to achieve BSCVA was faster than that of DSAEK (277 days versus 490 days, P = 0.0014). With long term follow-up BSCVA of the DMEK eyes [0.09±0.10 logMAR and DSAEK eyes [0.11 ±0.16 logMAR did not show a statistically significant difference (P = 0.069). Twenty two of the 64 preferred the DMEK eye, 17 patients preferred the DSAEK eye (P= 0.423) while 25 patients did not have a preference. In the DMEK group the average spherical equivalent was -0.08 compared to DSAEK group at 0.06. [P = 0.2854].

Conclusion: In our fellow eye study with long term follow-up DMEK and DSAEK had comparable levels of BSCVA and patient satisfaction. The DMEK eyes reached their BSCVA sooner, however the DSAEK eyes improved over a longer time frame. A greater number of patients had 20/25 and 20/20 vision in the DMEK group, however the difference was not statistically significant.

SATURDAY · MONITOR 4

CELL BASED THERAPY FOR RETINAL DISEASE

David Wilson*, Jonathan Stoddard, Martha Neuringer, Trevor McGill

Purpose: There are several reports and ongoing clinical trials of implantation of cell suspensions or cell sheets in patients with retinal disease; but, as yet there are no techniques for successful cell replacement. This study elucidates the factors limiting the success of cell-based therapy.

Methods: The present study was conducted in rhesus macaques and conformed to ARVO guidelines. Subretinal injections were performed through a 38-gauge cannula utilizing an automated infusion to deliver a target volume of 100 microliters. The infusion consisted of saline(n=3) or Green Fluorescent Protein (GFP) labeled allogenic(n=3) or autologous(n=3) IPSC derived RPE cells. Postoperative imaging consisted of multimodal photography and optical coherence tomography. Microscopy for correlation with imaging was performed at 1- and 3-week time points.

Results: Saline: Injection of saline alone created a "debris zone" of photoreceptor outer segments and amputated pigment containing RPE microvilli. This debris zone impaired the restoration of the normal photoreceptor-RPE interface. Histopathologic examination revealed there was an increase in number and distribution of microglial cells. Allogenic RPE cells: Transplanted cells were easily recognized with autofluorescence photography. The number of cells diminished rapidly so that few were present by 3 weeks. Histopathologic findings revealed a more intense increase in the number of microglial cells. In addition, there was a prominent infiltrate of B & T cells. Autologous RPE cells: Cells remained identifiable within the subretinal space up to the 3-week time point, but the number markedly diminished over time. Fewer microglia and mononuclear cells were present compared to allogenic transplants. Histopathologic examination revealed that the GFP positive cells remained in the retina or subretinal space, with minimal incorporation into the RPE monolayer.

Conclusion: Injury of the retina, immune response, and inadequate cellular integration limit cell-based approaches to the treatment of retinal disease. Human trials must address these challenges to be successful.

Notes

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