

Wills Eye Resident Series: A patient is referred to Wills for an ominous limbal mass, p. 71

# REVIEW<sup>®</sup> *of* OPTHALMOLOGY

November 2023 • reviewofophthalmology.com

Clinical advice you can trust

**GLAUCOMA MANAGEMENT**  
Cyclodialysis Clefts with MIGS  
PAGE 17

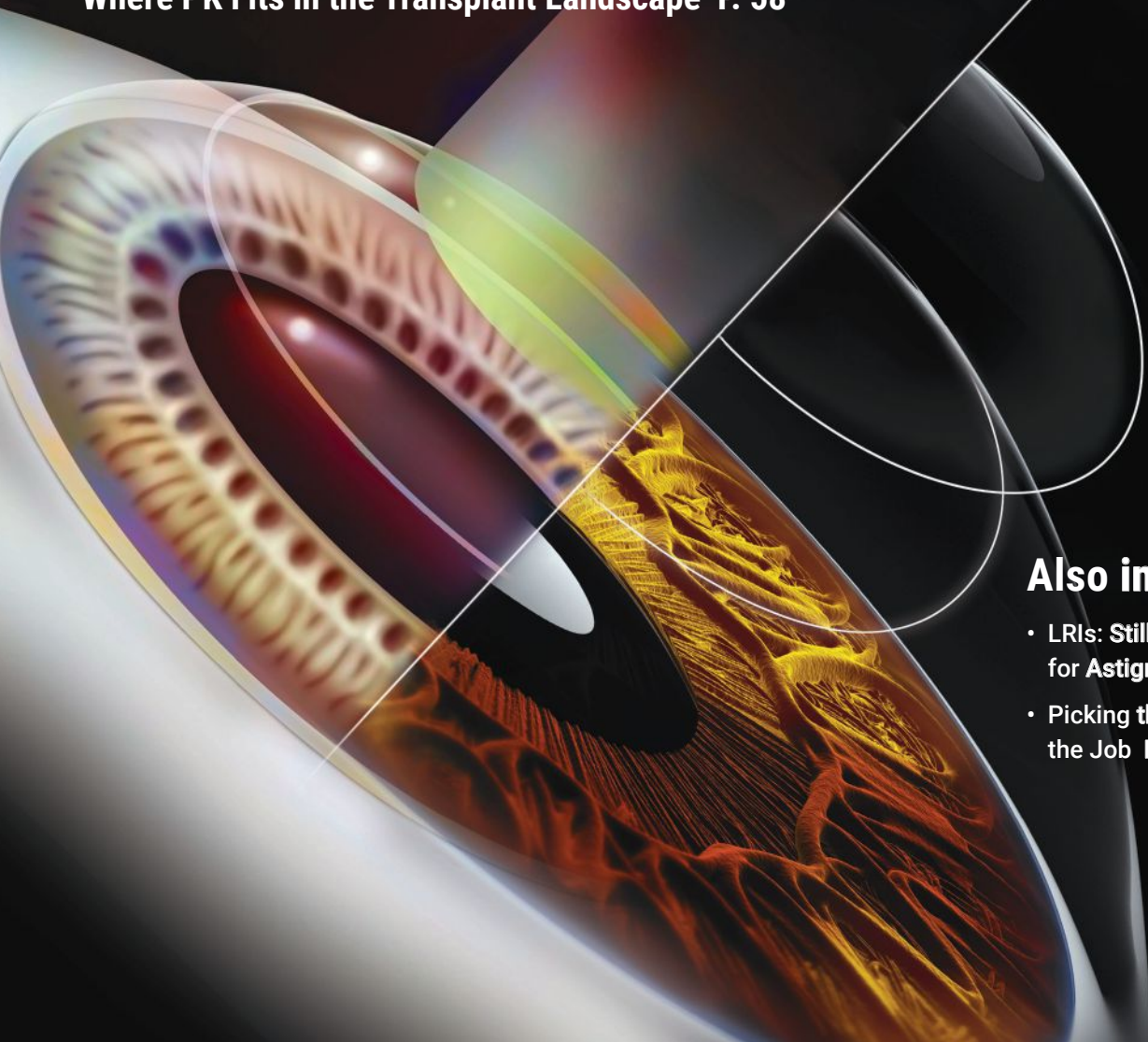
**REFRACTIVE/CATARACT RUNDOWN**  
Pterygia in Cataract Patients  
PAGE 28

**RETINAL INSIDER**  
OCTA in Neurodegenerative Disease  
PAGE 64

## The Wide World of **CORNEAL PROCEDURES**

Cross-linking Best Practices P. 46

Where PK Fits in the Transplant Landscape P. 58



### Also inside

- LRIs: Still a Valuable Asset for Astigmatism P. 34
- Picking the Right MIGS for the Job P. 54



TONO-PEN AVIA®

Reichert

mmHg

13.95

DATA

AMETEK

Tono-Pen AVIA® Tonometer

# TRUSTED TONOMETRY. RELIABLE REFRACTION.

We share your passion for personalizing and improving glaucoma care and vision testing. For nearly two centuries, we've delivered innovative, precise, and efficient diagnostic devices to help you provide better patient care.

BUY NOW



WATCH MORE AT [REICHERT.COM](https://www.reichert.com)



Reichert® 7CR Auto Tonometer + IOPcc



Phoroptor® VRx Digital Refraction System with ClearChart® Digital Acuity









Ocular Response Analyzer® G3 with Corneal Hysteresis + IOPcc

**Reichert**  
**AMETEK**

*passionate about eye care*

© 2023 AMETEK, Inc. & Reichert, Inc. (10-2023) · Reichert, Tono-Pen AVIA, Phoroptor VRx, ClearChart, and Ocular Response Analyzer are registered trademarks of Reichert, Inc.

Designed & assembled in USA      

## Patient Education Websites May Hinder More than Help

For better or worse, patients often go online to gain medical information or to make decisions about their condition. Therefore, it's necessary for patient-oriented websites to be readable to the layperson or have complementary patient education video content to promote better health literacy. Website accessibility accommodations are especially important to cataract surgery candidates, as these patients already have vision difficulties and may have other medical comorbidities due to older age that may limit their access online.

Researchers based at The Wilmer Eye Institute at Johns Hopkins University School of Medicine in Baltimore have determined that accessibility and readability measures need to be improved among informational patient-oriented health websites, especially for cataract surgery.<sup>1</sup> The average reading level of the top 100 patient-oriented websites regarding cataract surgery was approximately the 12th-grade level, which is far above the American Medical Association-recommended 6th-grade level and the average 8th-grade reading level in the U.S. population.

Wilmer cornea specialist Esen Akpek, the study's corresponding author, credits her mentees at the Institute for the idea. "I practice at a tertiary-care center and, most of the time, patients are somewhat educated about their condition—but not always," Dr. Akpek says. "So, it's a different kind of skillset to provide them with information in a

meaningful, understandable way, and to not scare them about surgery, but at the same time inform them about the surgery's risks. Also, we have to be able to recommend a lens implant while not influencing them to choose one implant over another.



It's an art, actually, which I hadn't realized until I started mentoring students and residents. These individuals sometimes take time off from their education and come and work for me for a year or two.

"It was actually their idea," Dr. Akpek continues, "because I sometimes have trouble explaining things without using medical terms too much, to explain using lay language to present an accurate representation of pros and cons and the like."

Dr. Akpek says accurate explanations can also counteract any wrong information patients may have learned about eye surgery.

"A lot of the time, patients have done some Googling, and come in

with misinformation or a misunderstanding," she says. "So, we wondered if the available information was understandable. Is the information suitable for the purposes of education? That's when we started looking at the availability of online information."

The study, published in *Ophthalmology*, performed an incognito search for "cataract surgery" using a search engine. The top 100 patient-oriented cataract surgery websites that came up were included and categorized as institutional, private practice or medical organization according to authorship. Each site was assessed for readability using four standardized reading grade-level formulas. Accessibility was assessed through multilingual availability, accessibility-menu availability, complementary educational-video availability, and conformance and adherence to guidelines for web content accessibility. The team sorted 32, 55 and 13 sites to institutions, private practice and other medical organizations, respectively. These categories included the following sources of information:

- Institution: academic centers, medical societies and governmental websites;
- Private practice: for-profit medical entities providing care to patients;
- Other medical organizations: standalone health information service websites, health magazines, insurance companies and pharmaceutical or device firms).

The overall mean reading grade



# BRIGHTER LOOKING EYES WITH ONE DROP

## The Conversation Eye Care Providers Should Be Having with Patients



### Melissa Toyos, MD

Practices at Toyos Clinic located in Tennessee, Mississippi, and New York

Aesthetics are an important patient concern that can affect how they feel about themselves and around other people. Patients commonly use products and services that promise aesthetic enhancement, including lash extensions, eyelash growth treatments, colored contact lenses, eye makeup, eye creams, and serums. Increasingly, patients also seek out redness-relieving eye drops to improve the appearance of their eyes.

### Ocular Redness: A Key Patient Concern

Demand is substantial: 4 in 10 sales in the over-the-counter (OTC) eye drop category are for redness relievers.<sup>1</sup> Because ocular redness is often caused by "minor" eye irritations, patients may not recognize it as a valid concern that they can discuss with their eye care provider (ECP) and are, therefore, not always professionally counseled on which redness reliever is best for them. Without their ECP's input, patients can sometimes lean on potentially unreliable sources, such as the store shelf, their peers, commercials, or the internet. Herein lies an opportunity to educate patients and guide them through the enormous ocular redness market while also addressing the root cause of their symptoms.

### LUMIFY®: A Clinically Proven Approach to Treating Ocular Redness

LUMIFY® (brimonidine tartrate ophthalmic solution) 0.025% drops are indicated for relieving redness of the eye due to minor eye irritations.<sup>2</sup> Most redness relievers are  $\alpha$ 1- or  $\alpha$ 1/ $\alpha$ 2-adrenergic receptor agonists;  $\alpha$ 1-adrenergic receptor agonism constricts corneal arterioles, hindering oxygen delivery to the cornea, which causes rebound redness. Brimonidine tartrate, by contrast, is selective for the  $\alpha$ 2-adrenergic receptor, primarily constricting ocular surface venules, which

do not affect ocular surface oxygen delivery and therefore is not associated with high levels of rebound redness.<sup>3</sup>

In 6 clinical studies with over 600 patients, low-dose brimonidine tartrate demonstrated a 1 minute onset of action, which persisted for up to 8 hours.<sup>4</sup> It had a favorable safety profile and, consistent with its mechanism of action, a low incidence of rebound redness (1.2%).<sup>4,5,6</sup> Adverse event rates did not significantly differ from control, and the most common adverse events in brimonidine-treated eyes were reduced visual acuity (4.0%) and conjunctival redness (2.6%).<sup>5</sup>

### Opportunity for ECPs to Step In

Market research indicates that patients report using of redness relievers an average of 3 days per week.<sup>7</sup> Ocular redness is a key concern for many patients, but the OTC eye care market contains an often overwhelming array of products. Understanding and communicating the benefits and challenges of available products is key to helping patients narrow down which products—out of everything on the shelf—might work best for them.

**LUMIFY® provides safe and effective redness relief for my patients dealing with minor eye irritations**

LUMIFY® is a redness reliever drop differentiated in its mechanism of action, rapid effects, and minimal rebound redness. LUMIFY® provides patients with excellent redness relief. In recommending a product as efficacious and reliable as LUMIFY®, ECPs can establish themselves as trusted professionals who can



### Incorporating ocular aesthetics into the patient conversation



Ask patients if they are happy with how their eyes look and feel



Ask patients if they use OTC eye care products and if they are satisfied with them



Consider that the aesthetic aspect of eye care may be just as important to a patient as the clinical aspect



Be ready and willing to provide OTC recommendations

address patients' needs—both clinical and aesthetic. This can lead not only to improved patient outcomes and satisfaction but could also enhance trust in their relationship with their ECP.

1. IQVIA Sales Data, Latest 52 weeks ending 6/18/2023
2. LUMIFY® [Drug facts]. Bausch & Lomb Incorporated, Bridgewater, NJ.
3. Corboz MR, Rivelli MA, Varty L, et al. Pharmacological characterization of postjunctional  $\alpha$ -adrenoceptors in human nasal mucosa. *Am J Rhinol.* 2005;19(5):495-502.
4. McLaurin E, Cavet ME, Gomes PJ, Ciolino JB. Brimonidine ophthalmic solution 0.025% for reduction of ocular redness: a randomized clinical trial. *Optom Vis Sci.* 2018;95(3):264-271.
5. Ackerman SL, Torkildsen GL, McLaurin E, Vittitow JL. Low-dose brimonidine for relief of ocular redness: integrated analysis of four clinical trials. *Clin Exp Optom.* 2019;102(2):131-139.
6. Torkildsen GL, Sanfilippo CM, DeCory HH, Gomes PJ. Evaluation of efficacy and safety of brimonidine tartrate ophthalmic solution, 0.025% for treatment of ocular redness. *Curr Eye Res.* 2018;43(1):43-51.
7. Data on file. Bausch & Lomb. Rochester, NY

was 11.8, with higher reading levels observed in private practice websites compared to institutions and medical organizations combined (12.1 vs. 11.4). Fewer private practice websites had multiple language options compared to institutional and medical organization websites combined (5.5 percent vs. 20 percent). More private practice websites had accessibility menus than institutions and medical organizations combined (27.3 percent vs. 8.9 percent). Notably, 85 percent of websites violated what's called the perceivable principle, which is the notion that "information and user interface components must be presented in a way that all users can recognize and understand," according to experts in accessibility.

"These issues may negatively impact patient experiences by leading to medical misinformation, surgical hesitancy or refusal, increased frustration and poor satisfaction post-surgery," the researchers wrote in their paper. "Cataract surgery can be made more equitable and understandable within the general population by providing usable online information to prospective recipients."

Dr. Akpek says the accessibility of the information is even more critical in the ophthalmic realm, as opposed to patients researching heart surgery or information from another specialty, since the patients are dealing with vision issues. "It's especially important to us as ophthalmologists because we deal with vision," she says. "So, if the contrast or font size can't be modified for patients with issues such as cataract or AMD, then the simple availability of the information may not mean that much, even if it's accurate, because patients simply may not be able to view it."

She adds that, in contrast to tertiary-care patients who usually come in armed with some knowledge of their condition and potential surgery, improvements in patient education could really make a difference for patients earlier in their eye-care journey. "Being able to educate patients in this way is key, especially in primary eye-care settings like optometry and general ophthalmology. Good websites should be able to inform the patients about what cataracts are, how to instill eye drops after surgery, and such, which would

save chair time for me, allowing us to talk more about such things as the risks and benefits of surgery."

Dr. Akpek says that, if a practice could do one thing to help make their online information more useful, she thinks it would be a good thing for schedulers to provide online links to patients prior to them coming in. "Not everyone will read it, or understand it, but if some of them have some preliminary fund of knowledge before they come in for an evaluation, I think that would be helpful for both sides," she says. "And if the information we're asking the patient to read is accurate, understandable and adjustable for their disabilities—visual and otherwise—I think that would be even more awesome."

The team proposed that an area of future research may include surveying cataract surgery candidates to evaluate whether these websites provide information that adequately addresses their needs.

1. Lin MX, Li G Cui D, et al. Usability of patient-education oriented cataract surgery websites. *Ophthalmology*. October 16, 2023. [Epub ahead of print].

## Orasis Presbyopia Drop Gets Approval

Come the new year, ophthalmologists will have another medical option for presbyopia. Soon to join Allergan's Vuity (pilocarpine 1.25%) on the market is another pilocarpine drop, this one at a lower concentration of 0.4%. Called Qlōsi (pronounced "CLOH-see"), the drug's FDA approval was announced in mid-October by Orasis Pharmaceuticals. The new drop is approved for daily or b.i.d. dosing as needed for patients with presbyopia. Given Qlōsi's lower concentration, cli-

nicians will be curious to see whether it results in fewer adverse effects than Vuity. Another potential plus: the formulation is preservative-free, Orasis says.

In the drug's two Phase III clinical trials, involving more than 600 patients, Orasis reports that the pupil-constricting drop demonstrated efficacy 20 minutes after administration and—with the benefit of a second dose two to three hours after the first—can last up to eight hours, as

measured on day 15. Both trials also met their primary and key secondary endpoints on day eight, achieving a gain of at least three lines in distance-corrected near visual acuity without losing one line or more in distance visual acuity. The company adds in its press release that the drop had no impact on night vision.

Headache and instillation site pain were among the most common treatment-related adverse events, affecting 6.8 percent and 5.8 percent of participants, respectively. Moderate treatment-related adverse events were reported by 1.3 percent of participants, and all other adverse events were mild, the company reports.

Nick Mamalis, MD, co-director of

*(Continued on p. 12)*

### CORRECTIONS

In the September article, "Dry-Eye Treatments Continue to Evolve," the maker of Ivizia was incorrectly listed as Similasan. The drug's maker is Thea.

In the October article, "Tarso-conjunctival Flaps for Severe Keratitis," author David Morcos was incorrectly identified as David Morcos, DO. His correct title is David Morcos, BA. Review regrets the errors.

## CONTRIBUTORS

### CHIEF MEDICAL EDITOR

Mark H. Blecher, MD

### CONTACT LENSES

Penny Asbell, MD

### CORNEA / ANTERIOR SEGMENT

Thomas John, MD

### GLAUCOMA MANAGEMENT

Peter Netland, MD, PHD  
Kuldev Singh, MD

### MEDICARE Q & A

Mary Pat Johnson,  
COMT, CPC

### PEDIATRIC PATIENT

Janine Collinge, MD

### PLASTIC POINTERS

April Lao, MD

### REFRACTIVE SURGERY

Arturo S. Chayet, MD

### RETINAL INSIDER

Carl Regillo, MD, FACS  
Yoshihiro Yonekawa, MD

### TECHNOLOGY UPDATE

Steven T. Charles, MD  
Michael Colvard, MD

### WILLS RESIDENT CASE SERIES

Collin Rozanski, MD

## ADVISORY BOARD

**PENNY A. ASBELL, MD**, MEMPHIS, TENN.

**BRANDON AYRES, MD**, PHILADELPHIA

**SURENDRA BASTI, MD**, CHICAGO

**WILLIAM I. BOND, MD**, PEKIN, ILL.

**ALAN N. CARLSON, MD**, DURHAM, N.C.

**Y. RALPH CHU, MD**, EDINA, MINN.

**ADAM J. COHEN, MD**, CHICAGO

**JANINE COLLINGE, MD**, FARMINGTON, CONN.

**UDAY DEVGAN, MD, FACS**, LOS ANGELES

**ERIC DONNENFELD, MD**, ROCKVILLE CENTRE, N.Y.

**DANIEL S. DURRIE, MD**, KANSAS CITY, MO.

**ROBERT EPSTEIN, MD**, MCHENRY, ILL.

**ROBERT D. FECHTNER, MD**, NEWARK, N.J.

**BRIAN FRANCIS, MD** Los Angeles

**JAMES P. GILLS, MD**, TARPON SPRINGS, FLA.

**HARRY GRABOW, MD**, SARASOTA, FLA.

**DOUGLAS K. GRAYSON, MD**, NEW YORK CITY

**DAVID R. HARDTEN, MD**, MINNEAPOLIS

**SARA J. HAUG, MD, PHD**, DURANGO, COLO.

**KENNETH J. HOFFER, MD**, SANTA MONICA, CALIF.

**JACK T. HOLLADAY, MD, MSEE**, HOUSTON

**JOHN D. HUNKELER, MD**, KANSAS CITY, MO.

**THOMAS JOHN, MD**, TINLEY PARK, ILL.

**ROBERT M. KERSHNER, MD, MS**, PALM BEACH GARDENS, FLA.

**GUY M. KEZIRIAN, MD**, PARADISE VALLEY, ARIZ.

**SUMITRA KHANDLWAL, MD**, HOUSTON

**TERRY KIM, MD**, DURHAM, N.C.

**BRAD KLIGMAN, MD**, MANHASSET, N.Y.

**TOMMY KORN, MD**, SAN DIEGO

**APRIL LAO, MD**, MEMPHIS

**DAVID A. LEE, MD**, HOUSTON

**FRANCIS S. MAH, MD**, LA JOLLA, CALIF.

**NICK MAMALIS, MD**, SALT LAKE CITY

**EDWARD MANCHE, MD**, PALO ALTO, CALIF.

**MIKE S. MCFARLAND, MD**, PINE BLUFF, ARK.

**JEFFREY B. MORRIS, MD, MPH**, ENCINITAS, CALIF.

**KEVIN MILLER, MD**, LOS ANGELES

**MAJID MOSHIRFAR, MD**, DRAPER, UTAH

**MARLENE R. MOSTER, MD**, PHILADELPHIA

**ROBERT J. NOECKER, MD**, FAIRFIELD, CONN.

**ROBERT OSHER, MD**, CINCINNATI

**MARK PACKER, MD**, WEST PALM BEACH, FLA.

**CHRISTOPHER J. RAPUANO, MD**, PHILADELPHIA

**AUGUST READER III, MD**, SAN FRANCISCO

**TONY REALINI, MD, MPH**, MORGANTOWN, W.V.

**KENNETH J. ROSENTHAL, MD**, GREAT NECK, N.Y.

**ERIC ROTHCHILD, MD**, DELRAY BEACH, FLA.

**SHERI ROWEN, MD**, BALTIMORE

**INGRID U. SCOTT, MD, MPH**, HERSHEY, PA.

**JOEL SCHUMAN, MD**, PITTSBURGH

**GAURAV SHAH, MD**, ST. LOUIS

**DAVID R. STAGER JR., MD**, DALLAS

**KARL STONECIPHER, MD**, GREENSBORO, N.C.

**JAMES C. TSAI, MD**, NEW YORK CITY

**VANCE THOMPSON, MD**, SIOUX FALLS, S.D.

**FARRELL C. TYSON, MD**, CAPE CORAL, FLA.

**R. BRUCE WALLACE III, MD**, ALEXANDRIA, LA.



### BUSINESS OFFICES

19 CAMPUS BOULEVARD, SUITE 101  
NEWTOWN SQUARE, PA 19073  
SUBSCRIPTION INQUIRIES (877) 529-1746  
(USA ONLY); OUTSIDE USA, CALL (847) 763-9630

### BUSINESS STAFF

PUBLISHER

**MICHAEL HOSTER**

(610) 492-1028 MHOSTER@JOBSON.COM

SENIOR MANAGER, STRATEGIC ACCOUNTS

**MICHELE BARRETT**

(610) 492-1014 MBARRETT@JOBSON.COM

REGIONAL SALES MANAGER

**JONATHAN DARDINE**

(610) 492-1030 JDARDINE@JOBSON.COM

DIGITAL MARKETING MANAGER

**MATT EGGER**

(610) 492-1029 MEGGER@JOBSON.COM

CLASSIFIED ADVERTISING

(888)-498-1460

PRODUCTION MANAGER

**KAREN LALLONE**

(610) 492-1010 KLALLONE@JOBSON.COM

SUBSCRIPTIONS

\$63 A YEAR, \$99 (U.S.) IN CANADA,  
\$158 (U.S.) IN ALL OTHER COUNTRIES.

SUBSCRIPTIONS E-MAIL:

REVOPHTHALMOLOGY@CAMBEYWEST.COM

### CIRCULATION

PO BOX 71, CONGERS, NY 10920-0071

(877) 529-1746

OUTSIDE USA: (845) 267-3065

SENIOR CIRCULATION MANAGER

**HAMILTON MAHER**

(212) 219-7870 hmaher@jhihealth.com

CEO, INFORMATION GROUP SERVICES

**BILL SCOTT**

SENIOR VICE PRESIDENT, OPERATIONS

**JEFF LEVITZ**

VICE PRESIDENT, HUMAN RESOURCES

**TAMMY GARCIA**

VICE PRESIDENT, CREATIVE SERVICES & PRODUCTION

**MONICA TETTAMANZI**

DIRECTOR, PRODUCTION/MANUFACTURING

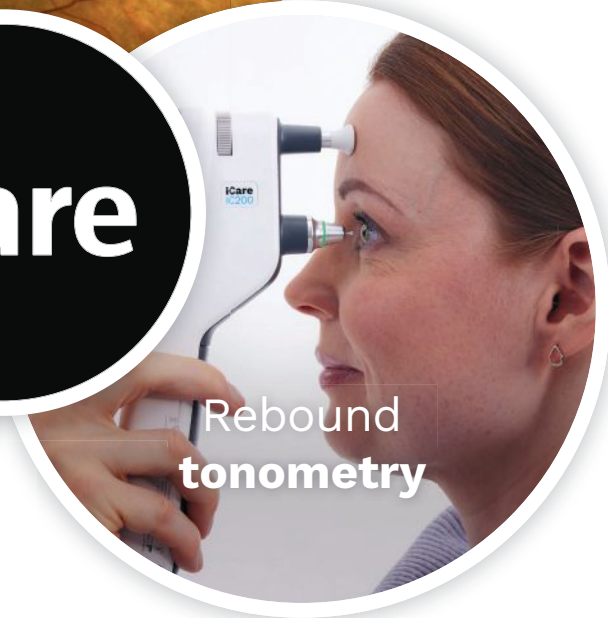
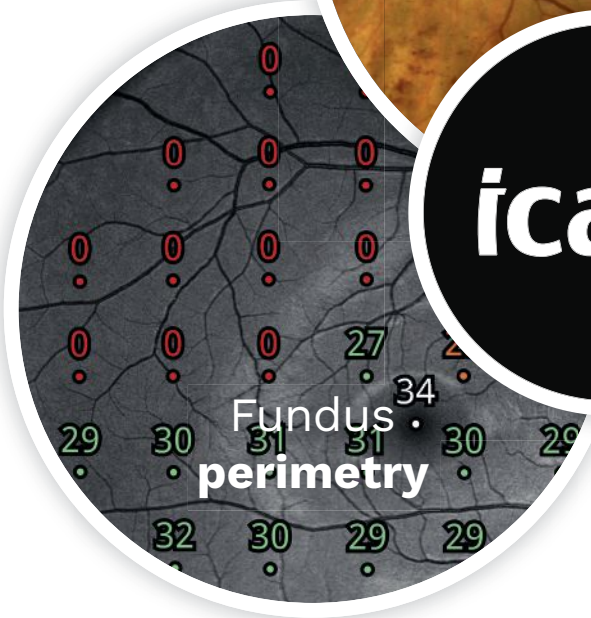
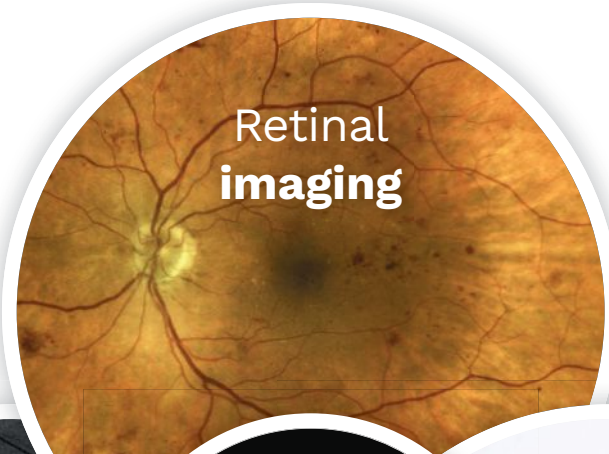
**REBECCA SLEBODNIK**

VICE PRESIDENT, CIRCULATION

**JARED SONNERS**

299 Market St. 2 Gateway Center - 4th Floor  
Newark NJ 07102

REVIEW OF OPHTHALMOLOGY (ISSN 1081-0226; USPS No. 0012-345) is published monthly, 12 times per year by Jobson Medical Information, LLC/WebMD 283 - 299 Market St. 2 Gateway Center - 4th Floor Newark NJ 07102. Periodicals postage paid at New York, NY and additional mailing offices. Postmaster: Send address changes to Review of Ophthalmology, PO Box 71, Congers, NY 10929-0071. Subscription Prices: US One Year \$63.00, US Two Year \$112.00, Canada One Year \$99.00, Canada Two Year \$181.00, Int'l One Year \$158.00, Int'l Two Year \$274.00. For subscription information call (877) 529-1746 (USA only); outside USA, call (845-267-3065. Or email us at revophthalmology@cambeywest.com. Canada Post: Publications Mail Agreement #40612608. Canada Returns to be sent to Bleuchip International, P.O. Box 25542, London, ON N6C 6B2.



**You know us for tonometry.**  
**Get to know iCare for**  
**imaging and perimetry.**



Discover the next level of eye care  
with our full line of devices.

Scan or visit [www.icare-world.com/USA](http://www.icare-world.com/USA)





# FEATURES

Vol. XXX, No. 11 • November 2023

**Catch Up on the Latest News**  
Read *Review's* weekly newsletter  
online at [reviewofophthalmology.com](http://reviewofophthalmology.com).

**46**

## **Cross-linking: Best Practices**

Stabilizing the cornea takes significant work—in and out of the chair. Here, veteran surgeons share their top tips for cross-linking patients.

**Christine Yue Leonard**  
*Senior Associate Editor*

**58**

## **Where PK Fits in the Transplant Landscape**

Since the development of endothelial keratoplasty, penetrating keratoplasty cases began to drop. Cornea specialists weigh in on this trend and where PK fits into their armamentarium.

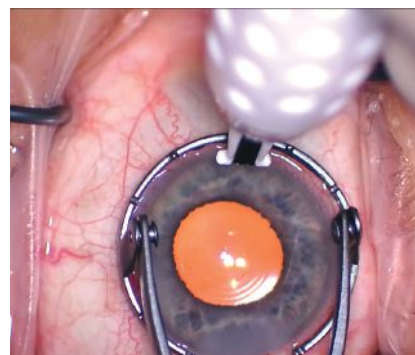
**Andrew Beers**  
*Associate Editor*

**34**

## **LRIs: Still A Valuable Asset for Astigmatism**

Despite advances in toric IOL technology, experienced cataract surgeons say limbal relaxing incisions are still a worthwhile technique to perform.

**Liz Hunter, Senior Editor**



**54**

## **How to Select the Right MIGS for the Job**

Considerations include severity of glaucoma, IOP and the number of medications the patient is taking.

**Michelle Stephenson**  
*Contributing Editor*



# DEPARTMENTS

November 2023

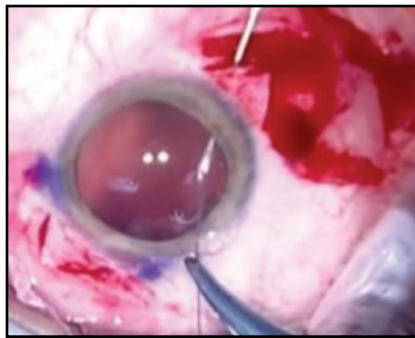
## 4 News

## 14

EDITOR'S PAGE

### One Size Does not Fit All

Walter Bethke  
Editor in Chief



## 17

GLAUCOMA MANAGEMENT

### Cyclodialysis Clefts With MIGS

Repair techniques vary, but prevention is the best cure. Here's how to manage this complication.

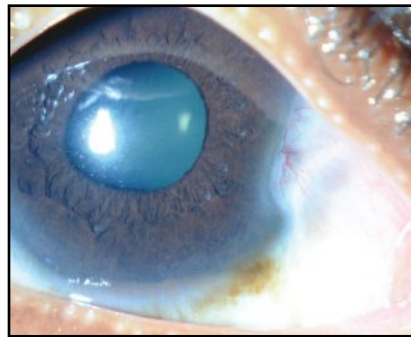
Won I. Kim, MD

## 27

THE FORUM

### If You're Not Part of the Solution...

Mark H. Blecher, MD  
Chief Medical Editor



## 28

REFRACTIVE/CATARACT RUNDOWN

### Addressing Pterygia in Cataract Patients

These conjunctival lesions can impact keratometry, often making staged surgery the best choice for patient outcomes.

Liz Hunter, Senior Editor

## 63

AD INDEX

## 64

RETINAL INSIDER

### Neurodegenerative Diseases and OCTA

This imaging method can help elucidate retinal disease, monitor progression and possibly advance therapy.

Joshua Woo, BA, Sejal Patel, Sharon Fekrat, MD, FASRS, and Dilraj S. Grewal, MD, FASRS

## 69

RESEARCH REVIEW

### Complications of Cataract Surgery in Wet AMD



## 71

WILLS EYE RESIDENT CASE SERIES

### A 78-year-old man is referred to Wills Eye Hospital for an ominous limbal mass.

Bailey M. Harrison, MD, Ralph C. Eagle, Jr., MD, and Zeba A. Syed, MD

 VISIT US ON SOCIAL MEDIA

Facebook [www.facebook.com/RevOphth](http://www.facebook.com/RevOphth)  
Twitter/X [twitter.com/RevOphth](https://twitter.com/RevOphth)  
Instagram [@revophth](https://www.instagram.com/revophth)

NOW AVAILABLE  
TO PRESCRIBE



Learn more at  
[XDEMZYHCP.com](https://XDEMZYHCP.com)

**xdemvy**<sup>™</sup>  
(lotilaner ophthalmic  
solution) 0.25%

# Might over mites

in just 6 weeks

1st &  
only

FDA-APPROVED TREATMENT FOR  
DEMODEX BLEPHARITIS (DB)

## INDICATIONS AND USAGE

XDEMZY (lotilaner ophthalmic solution) 0.25% is indicated for the treatment of *Demodex* blepharitis.

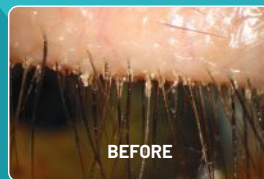
## IMPORTANT SAFETY INFORMATION:

## WARNINGS AND PRECAUTIONS

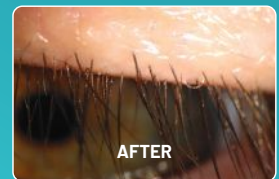
**Risk of Contamination:** Do not allow the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to minimize contamination of the solution. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

**Use with Contact Lenses:** XDEMZY contains potassium sorbate, which may discolor soft contact lenses. Contact lenses should be removed prior to instillation of XDEMZY and may be reinserted 15 minutes following its administration.

## Real results



BEFORE



AFTER

44% and 55% of patients taking XDEMZY in SATURN-1 (N=209) and SATURN-2 (N=193), respectively, achieved a significant improvement in their eyelids (reduction of collarettes to no more than 2 collarettes per upper lid) at Day 43 vs 7% (N=204) and 12% (N=200) of patients taking vehicle (P<0.01 in each trial).\*

All images are of actual patients who participated in clinical trials for Tarsus Pharmaceuticals.

**ADVERSE REACTIONS:** The most common adverse reaction with XDEMZY was instillation site stinging and burning which was reported in 10% of patients. Other ocular adverse reactions reported in less than 2% of patients were chalazion/hordeolum and punctate keratitis.

**Please see next page for a Brief Summary of the full Prescribing Information.**

**Reference:** XDEMZY [prescribing information]. Tarsus Pharmaceuticals, Inc; 2023.

\*The safety and efficacy of XDEMZY for the treatment of DB were evaluated in a total of 833 patients (415 of whom received XDEMZY) in two 6-week, randomized, multicenter, double-masked, vehicle-controlled studies (SATURN-1 and SATURN-2). Patients were randomized to either XDEMZY or vehicle at a 1:1 ratio, dosed twice daily in each eye for 6 weeks. All patients enrolled were diagnosed with DB. The primary efficacy endpoint was defined as the proportion of patients with collarette reduction to no more than 2 collarettes per upper eyelid at Day 43 (SATURN-1: XDEMZY N=209, vehicle N=204, P<0.01; SATURN-2: XDEMZY N=193, vehicle N=200, P<0.01).

© 2023 Tarsus Pharmaceuticals, Inc. All rights reserved.  
Tarsus, XDEMZY, and the associated logos are trademarks of  
Tarsus Pharmaceuticals, Inc. US--2300405 9/23



**XDEMYV™ (lotilaner ophthalmic solution) 0.25%, for topical ophthalmic use**

**BRIEF SUMMARY OF PRESCRIBING INFORMATION**  
Please see the XDEMYV™ package insert for full Prescribing Information.

**INDICATIONS AND USAGE**  
XDEMYV is indicated for the treatment of Demodex blepharitis.

**CONTRAINDICATIONS**  
None.

**WARNINGS AND PRECAUTIONS**  
**Risk of Contamination** Do not allow the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to minimize contamination of the solution. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

**Use with Contact Lenses** Contact lenses should be removed prior to instillation of XDEMYV and may be reinserted 15 minutes following its administration.

**ADVERSE REACTIONS**  
Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

XDEMYV was evaluated in 833 patients with Demodex blepharitis in two randomized, double-masked, vehicle-controlled studies (Saturn-1 and Saturn-2) with 42 days of treatment. The most common ocular adverse reaction observed in controlled clinical studies with XDEMYV was instillation site stinging and burning which was reported in 10% of patients. Other ocular adverse reactions reported in less than 2% of patients were chalazion/hordeolum and punctate keratitis.

**USE IN SPECIFIC POPULATIONS**  
**Pregnancy:** Risk Summary There are no available data on XDEMYV use in pregnant women to inform any drug associated risk; however, systemic exposure to lotilaner from ocular administration is low. In animal reproduction studies, lotilaner did not produce malformations at clinically relevant doses.

**Data Animal Data** In an oral embryofetal developmental study in pregnant rats dosed during organogenesis from gestation days 6–19, increased post-implantation loss, reduced fetal pup weight, and incomplete skeletal ossification were observed at 50 mg/kg/day (approximately 1390 times the recommended human ophthalmic dose (RHOD) on a body surface area basis) in the presence of maternal toxicity (i.e., decreased body weight and food consumption). A rare malformation of situs inversus of the thoracic and abdominal viscera occurred in 1 fetus from a pregnant rat receiving 50 mg/kg/day; whether this finding was treatment-related could not be excluded. No maternal or embryofetal toxicity was observed at 18 mg/kg/day (approximately 501 times the RHOD on a body surface area basis). In an oral embryofetal development study in pregnant rabbits dosed during organogenesis from gestation days 7–19, no embryofetal toxicity or teratogenic findings were observed at 20 mg/kg/day (approximately 580-times the RHOD on an AUC basis), even in the presence of maternal toxicity (i.e., decreased food consumption and body weight).

In an oral two-generation reproductive toxicity study, F0 male and female rats were administered lotilaner at doses up to 40 mg/kg/day for 10 weeks before pairing and during the 2-week pairing period (3 weeks for males). Dosing for F0 females continued through lactation day 22. F1 male and female rats were administered lotilaner at 1 and 5 mg/kg/day post-weaning from day 23 for 10 weeks before pairing and during the 2-week pairing period (3 weeks for males). Dosing for F1 prenatals females continued through lactation day 22. There were no clear adverse effects on the F1 generation, and a slightly lower mean body weight during lactation was noted for F2 pups at 5 mg/kg/day. The no observed adverse effect level (NOAEL) was determined to be 5 mg/kg/day

(approximately 139 times the RHOD on a body surface area basis).

**Lactation:** Risk Summary There are no data on the presence of XDEMYV in human milk, the effects on the breastfed infant, or the effects on milk production. However, systemic exposure to lotilaner following 6 weeks of topical ocular administration is low and is >99% plasma protein bound, thus it is not known whether measurable levels of lotilaner would be present in maternal milk following topical ocular administration. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for XDEMYV and any potential adverse effects on the breast-fed child from XDEMYV.

**Pediatric Use:** Safety and effectiveness in pediatric patients below the age of 18 years have not been established.

**Geriatric Use:** No overall differences in safety or effectiveness have been observed between elderly and other adult patients.

**NONCLINICAL TOXICOLOGY**  
**Carcinogenesis, Mutagenesis, Impairment of Fertility**  
**Carcinogenesis** Long-term studies in animals have not been performed to evaluate the carcinogenic potential of lotilaner.

**Mutagenesis** Lotilaner was not genotoxic in the following assays: Ames assay for bacterial gene mutation, *in vitro* chromosomal aberration assay in cultured human peripheral blood lymphocytes, and *in vivo* rat micronucleus test.

**Impairment of fertility** In a two-generation study of reproductive performance in rats, F0 male and female rats were administered lotilaner at oral doses of 40 mg/kg/day for 80 days reduced to 20 mg/kg/day for 47–50 supplementary days. Reduced pregnancy rates and decreased implantation rates were observed in F0 females at doses 20 mg/kg/day (approximately 556 times the RHOD on a body surface area basis), which were also associated with maternal toxicity (i.e., decreased body weight and food consumption). No effects on fertility were observed in F0 females at the dose of 5 mg/kg/day (approximately 139 times the MRHOD on a body surface area basis). No effects on fertility were observed in F0 males at the oral dose of 20 mg/kg/day (approximately 556 times the RHOD on a body surface area basis), and no effects on fertility were observed in F1 males and females at the oral dose of 5 mg/kg/day (approximately 139 times the RHOD on a body surface area basis).

**PATIENT COUNSELING INFORMATION**  
**Handling the Container** Instruct patients to avoid allowing the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to minimize contamination of the solution. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

**When to Seek Physician Advice** Advise patients that if they develop an intercurrent ocular condition (e.g., trauma or infection), have ocular surgery, or develop any ocular reactions, particularly conjunctivitis and eyelid reactions, they should immediately seek their physician's advice concerning the continued use of XDEMYV.

**Use with Contact Lenses** Advise patients that XDEMYV contains potassium sorbate, which may discolor soft contact lenses. Contact lenses should be removed prior to instillation of XDEMYV and may be reinserted 15 minutes following its administration.

**Use with Other Ophthalmic Drugs** Advise patients that if more than one topical ophthalmic drug is being used, the drugs should be administered at least 5 minutes between applications.

**Missed Dose** Advise patients that if one dose is missed, treatment should continue with the next dose.

**RX only**

© 2023 Tarsus Pharmaceuticals, Inc. All rights reserved.

XDEMYV is a trademark of Tarsus Pharmaceuticals, Inc.

US–2300345 9/23

## REVIEW NEWS

(Continued from p. 6)

the Intermountain Ocular Research Center at the University of Utah's Moran Eye Center, says he expects patients' and physicians' experience with Vuity will inform their use of the new drop. "I think what will happen is it'll be the same group of people who will benefit," he says. "What I learned [with Vuity] is that a lot of my wife's friends, now in their 60s, wanted to use it and insisted I write them prescriptions. But then it didn't do anything. People in that older age range don't have accommodative reserve and also have smaller pupils. So a medication like a low-dose pilocarpine that works to shrink the pupil to increase the range of focus, in these patients who have a smaller pupil to begin with, it keeps the potential for increasing that range lower. I think people realized that if you have some accommodative reserve, then you can get results from it. When they do the studies, though, they do get a good response from patients in the age range where you'd expect to see it—40s and 50s—and I think with a low dose of the pilocarpine, the side effects are low. With these low-dose pilocarpines, you don't get headache from accommodative spasm or some of the other symptoms you'd get with the old high-dose pilocarpine. I think the experience [with this new drug] will be similar to the previous one: These drops will work well in younger presbyopes rather than older presbyopes."

Orasis says the drug will be commercially available in the first half of 2024, Orasis says.

## Anti-VEGF for AMD in the Setting of DR

The relationship between diabetes and age-related macular degeneration is both complex and controversial. Even though some authors have reported diabetes as a risk factor for AMD (i.e., especially for wet AMD), other studies didn't find any correlation between these two disorders. Importantly, diabetic retinopathy and wet AMD share treatment options, as anti-VEGF intravitreal injections are used to treat both AMD-associated macular neovascularization and diabetic macular edema.

A recent optical coherence tomography angiography study conducted in Italy aimed at assessing whether the presence of diabetes and diabetic retinopathy could impact the baseline characteristics of treatment-naïve AMD-associated type 1 macular neovascularization.<sup>1</sup> Also, the researchers assessed longitudinal changes occurring in type 1 macular neovascularization during anti-VEGF therapy in order to understand whether the

(Continued on p. 16)

**izervay**<sup>™</sup>  
(avacincaptad pegol  
intravitreal solution) 2 mg

# Join us for a collaborative discussion on how IZERVAY<sup>™</sup> may benefit your patients

Webinar Event  
**December 12, 2023**

For your convenience, this program will be broadcast twice

6:00 PM - 7:00 PM ET (60 minutes)

9:00 PM - 10:00 PM ET (60 minutes)

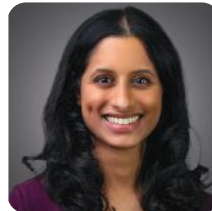
**You will learn:**

- How to detect the imaging biomarkers
- Efficacy and safety for IZERVAY
- Treatment considerations for patients

## Presenters



**Diana Shechtman OD, FFAO**  
Consultative Optometrist  
Eye Centers of South Florida  
Miami, FL



**Priya Vakharia MD**  
Retina Specialist  
Retina Vitreous Associates of Florida  
Tampa, FL



**REGISTER NOW**

Scan this QR code to register  
or visit <https://mngh.co/16D48F>

This presentation is from Iveric Bio, an Astellas Company, and Drs. Shechtman and Vakharia are being compensated by Iveric for their time. Continuing medical education credits are not available in connection with this program.

IVERIC bio, Inc., An Astellas Company  
8 Campus Drive Parsippany-Troy Hills, NJ 07054

Copyright ©2023 IVERIC bio, Inc., An Astellas Company.  
All rights reserved. US-AP-2300337 10/23

**REVIEW**<sup>®</sup>  
of OPTHALMOLOGY

**IVERIC**  
**BIO**  
An Astellas Company



## EDITORIAL STAFF

**Editor in Chief**  
**Walter Bethke**

(610) 492-1024  
wbethke@jobson.com

**Senior Editor**  
**Liz Hunter**

(610) 492-1025  
ehunter@jobson.com

**Senior Associate Editor**  
**Christine Leonard**

(610) 492-1008  
cleonard@jobson.com

**Associate Editor**  
**Leanne Spiegle**

(610) 492-1026  
lspiegle@jobson.com

**Associate Editor**  
**Andrew Beers**

(570) 856-5156  
abeers@jobson.com

**Chief Medical Editor**  
**Mark H. Blecher, MD**

**Senior Art Director**  
**Jared Araujo**

(610) 492-1032  
jaraujo@jobson.com

**Graphic Designer**  
**Lynne O'Connor**

(267) 566-6007  
lyoconnor@jobson.com

**Business Offices**

19 Campus Boulevard, Suite 101  
Newtown Square, PA 19073  
(610) 492-1000  
Fax: (610) 492-1039

**Subscription inquiries:**

United States – (877) 529-1746  
Outside U.S. – (845) 267-3065  
E-mail:

revophthalmology@cambeywest.com  
Website: www.reviewofophthalmology.com



# One Size Does Not Fit All

In the early 16th century, people's clothing usually consisted of what they made themselves, wore used clothes or, if they were wealthy, could take an already existing pattern or design and have it tailored. For the commoner, if the pants were too loose you could cinch your belt tighter, too long and maybe you or your wife could hem them a bit. Then, around the end of the 16th and into the 17th century, some shops allowed you to come in and select the fabric, design, pattern and everything else for a piece of clothing from scratch, and after your measurements were taken, the material you picked was set aside and other customers were informed that it was already "spoken for" or, as they would say it back then, "bespoke."

Now, it seems a lot of things are bespoke, from clothes (of course) to artisanal food and drink "experiences." Also, as our corneal cover focus points out, even surgery is bespoke. However, rather than it being an effort to put on airs like someone who's in search of bespoke birthday candles, a bespoke surgery actually has concrete benefits for the patient and the surgeon.

In the past, if a patient had a serious corneal problem, either in the anterior or the posterior, all roads usually led to penetrating keratoplasty. Though penetrating keratoplasty is an effective procedure, it leaves the patient with varying degrees of astigmatism, rejection issues and possibly the need for further surgeries.

Now, however, surgeons can customize their intervention based on a patient's specific condition.

As surgeons we spoke to for our update on corneal collagen cross-linking (*pg. 46*) attest, in some cases advanced

keratoconus often meant a relentless march toward a penetrating keratoplasty and its attendant risks. But now, that march can be slowed or arrested in some patients. "We know that cross-linking is effective and that preventing the development of visually devastating keratoconus is a significant quality of life enhancer ... It's very meaningful to that patient and family," says Omaha's Brandon Baartman, MD, in the article.

And, on the posterior side of the cornea, the strides made in endothelial transplants have been remarkable. The ability to preserve vital layers of the cornea while just replacing the endothelium has saved a lot of patients from having to go through the penetrating keratoplasty healing and follow-up process.

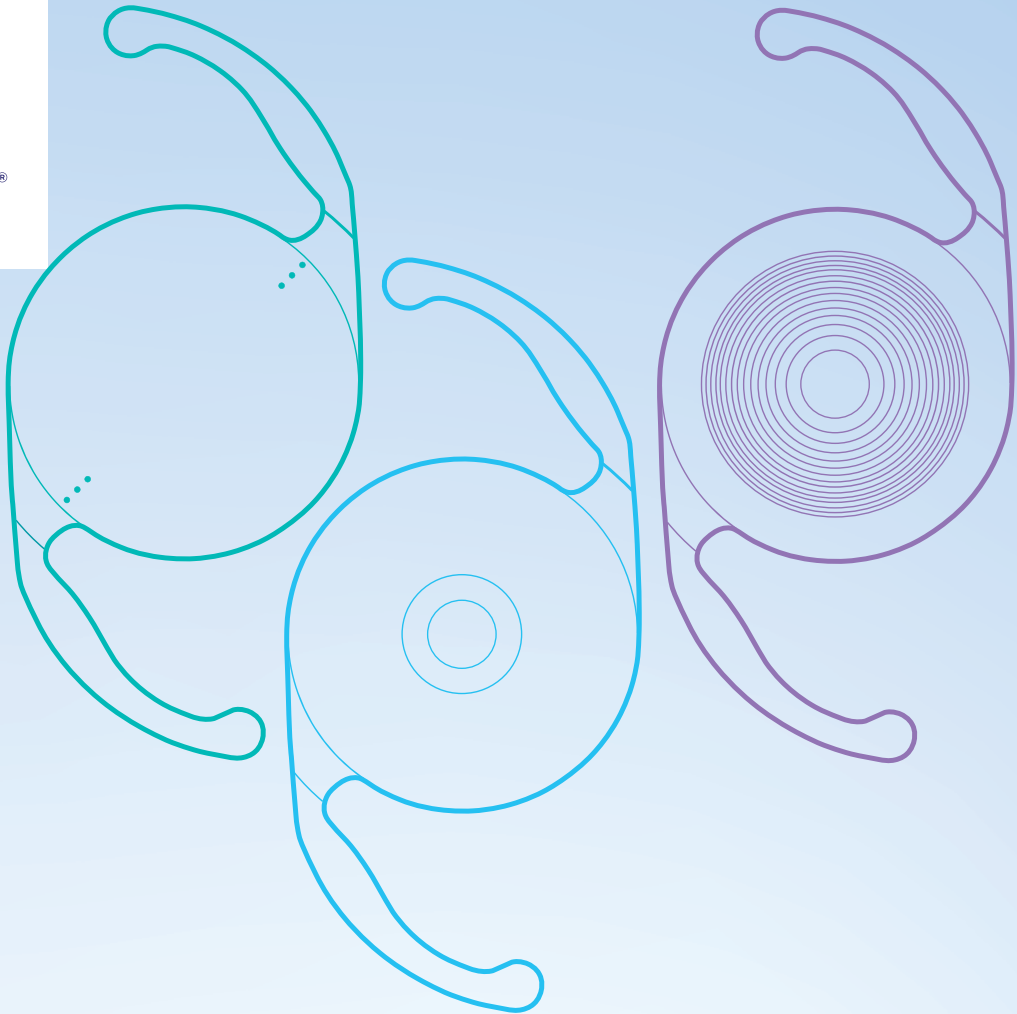
However, as our feature on transplantation on page 58 points out, the "big gun" of penetrating keratoplasty is still there for certain patients who need its invasive—but effective—ability to restore a cornea to health. Sometimes, as the corneal surgeons in the article point out, if the scarring or corneal involvement is just too much, a penetrating keratoplasty can still save the day—and the stitching will be just as precise as that in your new suit from Savile Row.

— *Walter Bethke*  
*Editor in Chief*

1. Bespoke. <https://en.wikipedia.org/wiki/Bespoke>. Accessed October 21, 2023.



**CLAREON®**  
COLLECTION



## THE CLAREON® COLLECTION IS COMPLETE

### CLAREON® TORIC

Glistening-free\* BioMaterial with unrivaled rotational stability† and predictable performance.1-6

### CLAREON® VIVITY®

The first and only non-diffractive wavefront shaping PCIOL with exceptional clarity,2,3\* monofocal-quality distance visual acuity, excellent intermediate vision, and functional near vision.†‡

### CLAREON® PANOPTIX®

A full range of vision with exceptional clarity that lasts.7,8\*

**45%**§ of patients are willing to upgrade to an ATIOL, however, only **18%**|| are currently receiving one. Educate your patients on Alcon ATIOLs to meet their expectations.9

[Learn more at ClareonIOL.com](https://www.alcon.com/CLAREONIOL.com)

\* Defined as modified Miyata grade 0, <25mv/mm<sup>2</sup> over 3 years (n=138), and over 9 years (n=20), respectively. ATIOL=Advanced Technology IOL.

† In vitro comparison, P <0.05.

‡ Results from a prospective, randomized, parallel group, subject- and assessor-masked, multisite trial of 107 subjects bilaterally implanted with the AcrySof® IQ Vivity® Extended Vision IOL and 113 with the AcrySof® IQ IOL with 6 months follow-up.

¶ Snellen VA was converted from logMAR VA. A Snellen notation of 20/20-2 or better indicates a logMAR VA of 0.04 or better, which means 3 or more of the 5 ETDRS chart letters in the line were identified correctly.

§ N=297.

|| Q4 2022.

## IMPORTANT PRODUCT INFORMATION: CLAREON® FAMILY OF IOLS

**CAUTION:** Federal law restricts these devices to sale by or on the order of a physician.

**INDICATION:** The family of **Clareon® intraocular lenses (IOLs)** includes the **Clareon® Aspheric Hydrophobic Acrylic** and **Clareon® Aspheric Toric IOLs**, the **Clareon® PanOptix® Trifocal Hydrophobic IOL**, **Clareon® PanOptix® Toric**, **Clareon® Vivivity® Extended Vision Hydrophobic Posterior Chamber IOL** and **Clareon® Vivivity® Toric IOLs**. Each of these IOLs is indicated for visual correction of aphakia in adult patients following cataract surgery. In addition, the **Clareon® Toric IOLs** are indicated to correct pre-existing corneal astigmatism at the time of cataract surgery. The **Clareon® PanOptix®** lens mitigates the effects of presbyopia by providing improved intermediate and near visual acuity, while maintaining comparable distance visual acuity with a reduced need for eyeglasses, compared to a monofocal IOL. The **Clareon® Vivivity®** lens mitigates the effects of presbyopia by providing an extended depth of focus. Compared to an aspheric monofocal IOL, the lens provides improved intermediate and near visual acuity, while maintaining comparable distance visual acuity. All of these IOLs are intended for placement in the capsular bag.

### WARNINGS / PRECAUTIONS:

**General cautions for all Clareon® IOLs:** Careful preoperative evaluation and sound clinical judgment should be used by the surgeon to decide the risk / benefit ratio before implanting any IOL in a patient with any of the conditions described in the Directions for Use that accompany each IOL. Physicians should target emmetropia, and ensure that IOL centration is achieved.

For the **Clareon® Aspheric Toric**, **PanOptix® Toric** and **Vivivity® Toric IOLs**, the lens should not be implanted if the posterior capsule is ruptured, if the zonules are damaged, or if a primary posterior capsulotomy is planned. Rotation can reduce astigmatic correction; if necessary lens repositioning should occur as early as possible prior to lens encapsulation.

For the **Clareon® PanOptix® IOL**, some visual effects may be expected due to the superposition of focused and unfocused multiple images. These may include some perceptions of halos or starbursts, as well as other visual symptoms. As with other multifocal IOLs, there is a possibility that visual symptoms may be significant enough that the patient will request explant of the multifocal IOL. A reduction in contrast sensitivity as compared to a monofocal IOL may be experienced by some patients and may be more prevalent in low lighting conditions. Therefore, patients implanted with multifocal IOLs should exercise caution when driving at night or in poor visibility conditions. Patients should be advised that unexpected outcomes could lead to continued spectacle dependence or the need for secondary surgical intervention (e.g., intraocular lens replacement or repositioning). As with other multifocal IOLs, patients may need glasses when reading small print or looking at small objects. Posterior capsule opacification (PCO), may significantly affect the vision of patients with multifocal IOLs sooner in its progression than patients with monofocal IOLs.

For the **Clareon® Vivivity® IOL**, most patients implanted with the **Vivivity® IOL** are likely to experience significant loss of contrast sensitivity as compared to a monofocal IOL. Therefore, it is essential that prospective patients be fully informed of this risk before giving their consent for implantation of the **Clareon® Vivivity® IOL**. In addition, patients should be warned that they will need to exercise caution when engaging in activities that require good vision in dimly lit environments, such as driving at night or in poor visibility conditions, especially in the presence of oncoming traffic. It is possible to experience very bothersome visual disturbances, significant enough that the patient could request explant of the IOL. In the parent AcrySof® IQ Vivivity® IOL clinical study, 1% to 2% of AcrySof® IQ Vivivity® IOL patients reported very bothersome starbursts, halos, blurred vision, or dark area visual disturbances; however, no explants were reported.

Prior to surgery, physicians should provide prospective patients with a copy of the Patient Information Brochure available from Alcon informing them of possible risks and benefits associated with these IOLs.

**ATTENTION:** Reference the Directions for Use labeling for each IOL for a complete listing of indications, warnings, and precautions.

**REFERENCES:** 1. Werner L, Thatthamla I, Ong M, et al. Evaluation of clarity characteristics in a new hydrophobic acrylic IOL. *J Cataract Refract Surg.* 2019;45:1490-1497. 2. Oshika T, Fujita Y, Inamura M, Miyata K. Mid-term and long-term clinical assessments of a new 1-piece hydrophobic acrylic IOL with hydroxyethyl methacrylate. *J Cataract Refract Surg.* 2020 May;46(5):682-687. 3. Maxwell A, Suryakumar R. Long-term effectiveness and safety of a three-piece acrylic hydrophobic intraocular lens modified with hydroxyethyl-methacrylate: an open-label, 3-year follow-up study. *Clin Ophthalmol.* 2018;12:2031-2037. 4. Alcon Data on File, 2017. 5. Lane S, Collins S, Das KK, Maass S, Thatthamla I, Schatz H, Van Noy S, Jain R. Evaluation of intraocular lens mechanical stability. *J Cataract Refract Surg.* 2019 Apr;45(4):501-506. 6. Clareon® Vivivity® Extended Vision Hydrophobic IOL (CNWET0) Directions for Use – US. 7. Clareon® PanOptix® Trifocal Hydrophobic Acrylic IOL Model: CNWTT0 DFU. 8. Lehmann R, Maxwell A, Lubeck DM, Fong R, Walters TR, Fakadej A. Effectiveness and Safety of the Clareon® Monofocal Intraocular Lens: Outcomes from a 12-Month Single-Arm Clinical Study in a Large Sample. *Clin Ophthalmol.* 2021;15:1647-1657. Published 2021 Apr 20. 9. Alcon Data on File, 2022.

## REVIEW NEWS

*(Continued from p. 12)*

presence of diabetes and diabetic retinopathy may impact such modifications. The team found that mild nonproliferative diabetic retinopathy eyes responded differently to wet AMD treatment. In particular, the diabetic group showed limited contraction of the macular neovascular lesion area after intravitreal therapy.

The study enrolled 50 treatment-naïve eyes with a diagnosis of wet AMD and type 1 macular neovascularization, of which 20 were affected by mild diabetic retinopathy. En face OCTA were examined for the macular neovascular lesion area (mm<sup>2</sup>), the macular neovascularization flow area (mm<sup>2</sup>), the central macular thickness and the best-corrected visual acuity. The OCTA acquisition was performed before the aflibercept loading phase (consisting of three monthly injections) and then one month after the last injection of the loading phase.

All morpho-functional parameters showed a significant change at the end of the study period compared with values in both groups. Furthermore, the researchers found a greater reduction of macular neovascularization after the loading phase in eyes without diabetic retinopathy. In the remaining parameters, no significant changes were found between the two groups. The study revealed a smaller reduction of macular neovascularization area after the loading dose of anti-VEGF therapy in eyes with diabetic retinopathy.

The researchers proposed two co-existing mechanisms behind the finding: (1) the presence of diabetic retinopathy in eyes affected by wet age-related macular degeneration could lead to higher levels of vascular endothelial growth factor, and therefore a worse response to treatment in terms of macular neovascularization downsizing; (2) diabetic retinopathy is known to be associated with choroidal hypoperfusion that might contribute to the macular neovascularization persisting as a mechanism of defense to the retinal pigment epithelium and outer retina ischemia.

“These results provide evidence that the diabetic retinopathy impact might play a fundamental role not only in the development and progression of macular neovascularization but also in evaluating reaction to anti-angiogenic therapy,” the researchers concluded in their paper. “Future larger studies using swept-source optical coherence tomography angiography and longer follow-up are needed to support our preliminary findings.” ◀

1. Viggiano P, Landini L, Grassi MO, et al. Effects of diabetic retinopathy on longitudinal morphological changes in AMD-associated type 1 macular neovascularization. *Sci Rep* 2023;13:1:16337.





EDITED BY KULDEV SINGH, MD, MPH,  
AND PETER A. NETLAND, MD, PHD

## GLAUCOMA MANAGEMENT

# Cyclodialysis Clefts With MIGS

*Repair techniques vary, but prevention is the best cure. Here's how to manage this complication.*

WON I. KIM, MD  
BETHESDA, MD.

**C**yclodialysis clefts occur when the longitudinal ciliary muscle fibers separate from the scleral spur,<sup>1</sup> forming a pathway from the anterior chamber to the supra-choroidal space. The subsequent increased uveoscleral outflow may result in hypotony maculopathy and other sequelae such as anterior chamber shallowing, choroidal effusions, retinal folds and vision loss.<sup>2</sup>

Cyclodialysis clefts can arise as a complication of any minimally invasive glaucoma surgery, but they're most likely to occur with goniotomy. Fortunately, this is rare. A review of the FDA's MAUDE database<sup>3</sup> found 30 case reports of clefts associated with Cypass (which is now off the market), iStent and Xen over a 10-year span, which is a very small number considering the thousands of MIGS surgeries performed every year.

Here, I'll discuss how to avoid cyclodialysis clefts with MIGS, as well as the non-surgical and surgical approaches to repair.

### Preoperative Considerations

To minimize the chances of this complication occurring, identify patients who may be at higher risk. Risk factors include patients with a

suboptimal gonioscopic view (e.g., due to corneal opacities, edema, arcus or scarring); patients with very lightly pigmented trabecular meshwork whose angle anatomy may be misidentified; and uncooperative patients, such as those who might cough or jerk their head suddenly in the middle of surgery.

### Intraoperative Considerations

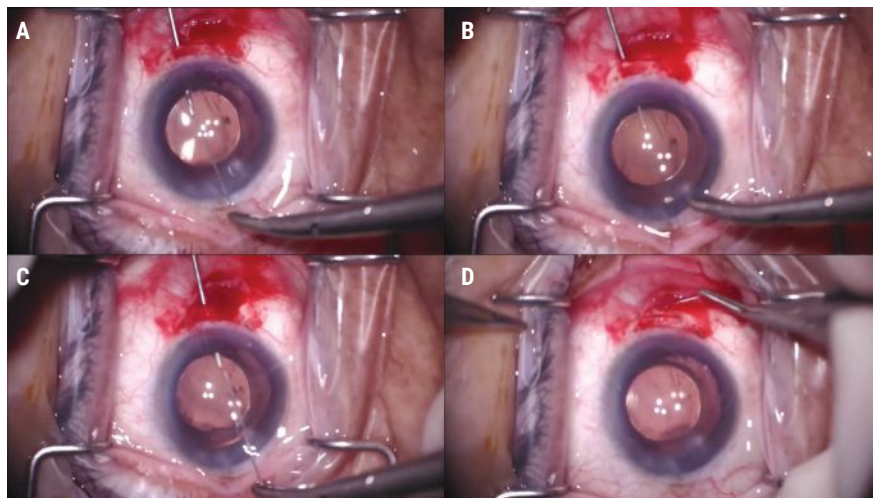
The right tools and tricks can make a difference. Here are three intraoperative strategies that can help:

- For eyes with lightly pigmented

trabecular meshwork, consider using trypan blue to stain the tissue. Trypan blue is readily available and easy to incorporate into the surgery.

- Consider a retrobulbar block in a patient who's uncooperative to get complete akinesia of the eye and decrease the risk of a movement-related complication.

- Novice surgeons who may not have as much experience using intraoperative gonioscopy may press down too hard on the eye with their off hand, creating corneal striae that impede the view of the angle, subsequently increasing the risk for a complication. If you're training a resident, consider using a hands-free gonio lens that couples itself with the corneal surface such as the Ocular SecureFlex HF Surgical Gonio. Another option is the Transcend Vold Gonio (Volk) which is designed to have the goniolens float freely on the corneal surface, so even if the surgeon is pressing down on the eye, the



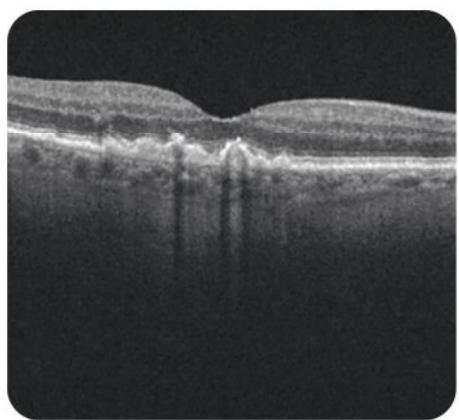
Reza Razeghinejad, MD

**Figure 1.** In the "Bucket Handle" closure by Reza Razeghinejad, MD, a 27-ga. needle is passed through a scleral groove 1.5 mm posterior to the limbus under a peritomy which passes into the ciliary sulcus and docks with the long straight needle of a Prolene suture passed across the anterior chamber through a clear cornea wound. This is repeated with the other end of the Prolene. Tying reapproximates the ciliary body and buries the knot in the groove.

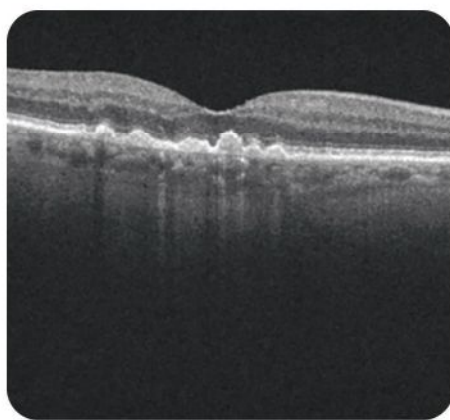
This article has no commercial sponsorship.

Dr. Singh is a professor of ophthalmology and chief of the Glaucoma Division at Stanford University School of Medicine. He is a consultant to Alcon, Allergan, Santen, Sight Sciences, Glaukos and Ivantis. Dr. Netland is Vernah Scott Moyston Professor and Chair at the University of Virginia in Charlottesville.

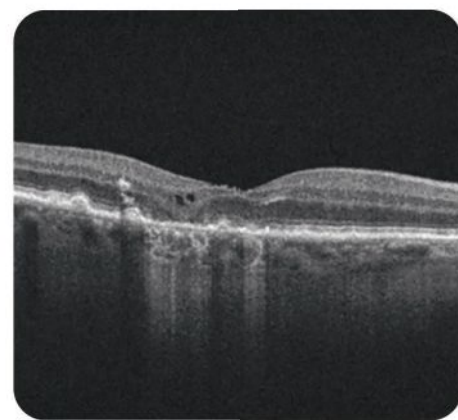
# GEOGRAPHIC ATROPHY (GA) CAN PROGRESS FASTER THAN YOU THINK<sup>1</sup>



**Baseline**



**Month 3**



**Month 6**

1. Boyer D, Schmidt-Erfurth U, van Lookeren Campagne M, et al. The pathophysiology of geographic atrophy secondary to age-related macular degeneration and the complement pathway as a therapeutic target. *Retina*. 2017;37(5);819-835.

## INDICATION

IZERVAY™ (avacincaptad pegol intravitreal solution) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD)

## IMPORTANT SAFETY INFORMATION

### CONTRAINDICATIONS

IZERVAY is contraindicated in patients with ocular or periocular infections and in patients with active intraocular inflammation.

### WARNINGS AND PRECAUTIONS

#### Endophthalmitis and Retinal Detachments

Intravitreal injections, including those with IZERVAY, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering IZERVAY in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.

# EVERY MONTH MATTERS WHEN TREATING GA

  
**izervay**<sup>™</sup>  
(avacincaptad pegol  
intravitreal solution) 2 mg



Learn more at  
[IZERVAYcp.com](https://www.izervaycp.com)

## Neovascular AMD

In clinical trials, use of IZERVAY was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (7% when administered monthly and 4% in the sham group) by Month 12. Patients receiving IZERVAY should be monitored for signs of neovascular AMD.

## Increase in Intraocular Pressure

Transient increases in intraocular pressure (IOP) may occur after any intravitreal injection, including with IZERVAY. Perfusion of the optic nerve head should be monitored following the injection and managed appropriately.

## ADVERSE REACTIONS

Most common adverse reactions (incidence  $\geq 5\%$ ) reported in patients receiving IZERVAY were conjunctival hemorrhage, increased IOP, blurred vision, and neovascular age-related macular degeneration.

**Please see full Prescribing Information for more information.**

Copyright © 2023 IVERIC bio, Inc. An Astellas Company.  
All rights reserved. US-AP-2300334 10/23

**IVERIC  
BIO**  
An Astellas Company

## IZERVAY™ (avacincaptad pegol intravitreal solution)

Rx only

**Brief Summary:** This information is not comprehensive. Visit IZERVAYecp.com to obtain the FDA-approved product labeling or call 609-474-6755.

### 1 INDICATIONS AND USAGE

IZERVAY is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

### 2 DOSAGE AND ADMINISTRATION

#### 2.1 General Dosing Information

IZERVAY must be administered by a qualified physician.

#### 2.2 Recommended Dosage

The recommended dose for IZERVAY is 2 mg (0.1 mL of 20 mg/mL solution) administered by intravitreal injection to each affected eye once monthly (approximately every 28 ± 7 days) for up to 12 months.

#### 2.4 Injection Procedure

Only 0.1 mL (2 mg) should be administered to deliver a single dose. Any excess volume should be disposed.

Prior to the intravitreal injection, patients should be monitored for elevated intraocular pressure (IOP) using tonometry. If necessary, ocular hypotensive medication can be given to lower the IOP.

The intravitreal injection procedure must be carried out under controlled aseptic conditions, which includes the use of surgical hand disinfection, sterile gloves, a sterile drape, and a sterile eyelid speculum (or equivalent). Adequate anesthesia and a broad-spectrum topical microbicide should be given prior to the injection.

Inject slowly until the rubber stopper reaches the end of the syringe to deliver the volume of 0.1 mL. Confirm delivery of the full dose by checking that the rubber stopper has reached the end of the syringe barrel.

Immediately following the intravitreal injection, patients should be monitored for elevation in intraocular pressure (IOP). Appropriate monitoring may consist of a check for perfusion of the optic nerve head or tonometry.

Following intravitreal injection, patients should be instructed to report any symptoms suggestive of endophthalmitis (e.g., eye pain, redness of the eye, photophobia, blurring of vision) without delay.

Each vial and syringe should only be used for the treatment of a single eye. If the contralateral eye requires treatment, a new vial and syringe should be used and the sterile field, syringe, gloves, drapes, eyelid speculum, filter needle, and injection needle should be changed before IZERVAY is administered to the other eye. Repeat the same procedure steps as above.

Any unused medicinal product or waste material should be disposed of in accordance with local regulations.

### 3 DOSAGE FORMS AND STRENGTHS

Intravitreal solution: 20 mg/mL clear to slightly opalescent, colorless to slightly yellow solution in a single-dose vial.

### 4 CONTRAINDICATIONS

#### 4.1 Ocular or Periocular Infections

IZERVAY is contraindicated in patients with ocular or periocular infections.

#### 4.2 Active Intraocular Inflammation

IZERVAY is contraindicated in patients with active intraocular inflammation.

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Endophthalmitis and Retinal Detachments

Intravitreal injections may be associated with endophthalmitis and retinal detachments. Proper aseptic injection techniques must always be used when administering IZERVAY in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay, to permit prompt and appropriate management.

#### 5.2 Neovascular AMD

In clinical trials, use of IZERVAY was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (7% when administered monthly and 4% in the sham group) by Month 12. Patients receiving IZERVAY should be monitored for signs of neovascular AMD.

#### 5.3 Increase in Intraocular Pressure

Transient increases in intraocular pressure (IOP) have been observed after an intravitreal injection, including with IZERVAY. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

### 6 ADVERSE REACTIONS

The following potentially serious adverse reactions are described elsewhere in the labeling:

- Ocular and periocular infections
- Neovascular AMD
- Active intraocular inflammation
- Increase in intraocular pressure
- Endophthalmitis and retinal detachments

#### 6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of avacincaptad pegol was evaluated in 733 patients with AMD in two sham-

controlled studies (GATHER1 and GATHER2). Of these patients, 292 were treated with intravitreal IZERVAY 2 mg (0.1 mL of 20 mg/mL solution). Three hundred thirty-two (332) patients were assigned to sham.

Adverse reactions reported in ≥2% of patients who received treatment with IZERVAY pooled across GATHER1 and GATHER2, are listed below in Table 1.

**Table 1: Common Ocular Adverse Reactions (≥2%) and greater than Sham in Study Eye**

Adverse Drug Reactions	IZERVAY N = 292	Sham N = 332
Conjunctival hemorrhage	13%	9%
Increased IOP	9%	1%
Choroidal neovascularization	7%	4%
Blurred vision*	8%	5%
Eye pain	4%	3%
Vitreous floaters	2%	<1%
Blepharitis	2%	<1%

\* Blurred vision includes visual impairment, vision blurred, visual acuity reduced, visual acuity reduced transiently.

### 8 USE IN SPECIFIC POPULATIONS

#### 8.1 Pregnancy

##### Risk Summary

There are no adequate and well-controlled studies of IZERVAY administration in pregnant women. The use of IZERVAY may be considered following an assessment of the risks and benefits.

Administration of avacincaptad pegol to pregnant rats and rabbits throughout the period of organogenesis resulted in no evidence of adverse effects to the fetus or pregnant female at intravenous (IV) doses 5.1 times and 3.2 times the human exposure (based on AUC) at the maximum recommended human dose (MRHD) of 2 mg once monthly, respectively.

In the U.S. general population, the estimated background risks of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15%-20%, respectively.

##### Animal Data

An embryo fetal developmental toxicity study was conducted with pregnant rats. Pregnant rats received daily intravenous (IV) injections of avacincaptad pegol from day 6 to day 17 of gestation at 0.1, 0.4, 1.2 mg/kg/day. No maternal or embryofetal adverse effects were observed at any dose evaluated. An increase in the incidence of a non-adverse skeletal variation, described as short thoracolumbar (ossification site without distal cartilage) supernumerary ribs, was observed at all doses evaluated. The clinical relevance of this finding is unknown. Plasma exposures at the high dose were 5.1 times the MRHD, based on Area Under the Curve (AUC).

An embryo fetal developmental toxicity study was conducted with pregnant rabbits. Pregnant rabbits received daily IV injections of avacincaptad pegol from day 7 to day 19 of gestation at 0.12, 0.4, 1.2 mg/kg/day. No maternal or embryofetal adverse effects were observed at any dose evaluated. Plasma exposure in pregnant rabbits at the highest dose of 1.2 mg/kg/day was 3.2 times the human exposure at the MRHD, based on AUC.

#### 8.2 Lactation

There is no information regarding the presence of avacincaptad pegol in human milk, the effects of the drug on the breastfed infant or on milk production.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for IZERVAY and any potential adverse effects on the breastfed infant from IZERVAY.

#### 8.4 Pediatric Use

Safety and effectiveness of IZERVAY in pediatric patients have not been established.

#### 8.5 Geriatric Use

Of the total number of patients who received IZERVAY in the two clinical trials, 90% (263/292) were ≥65 years and 61% (178/292) were ≥75 years of age. No significant differences in efficacy or safety of avacincaptad pegol were seen with increasing age in these studies. No dose adjustment is required in patients 65 years and above.

### 17 PATIENT COUNSELING INFORMATION

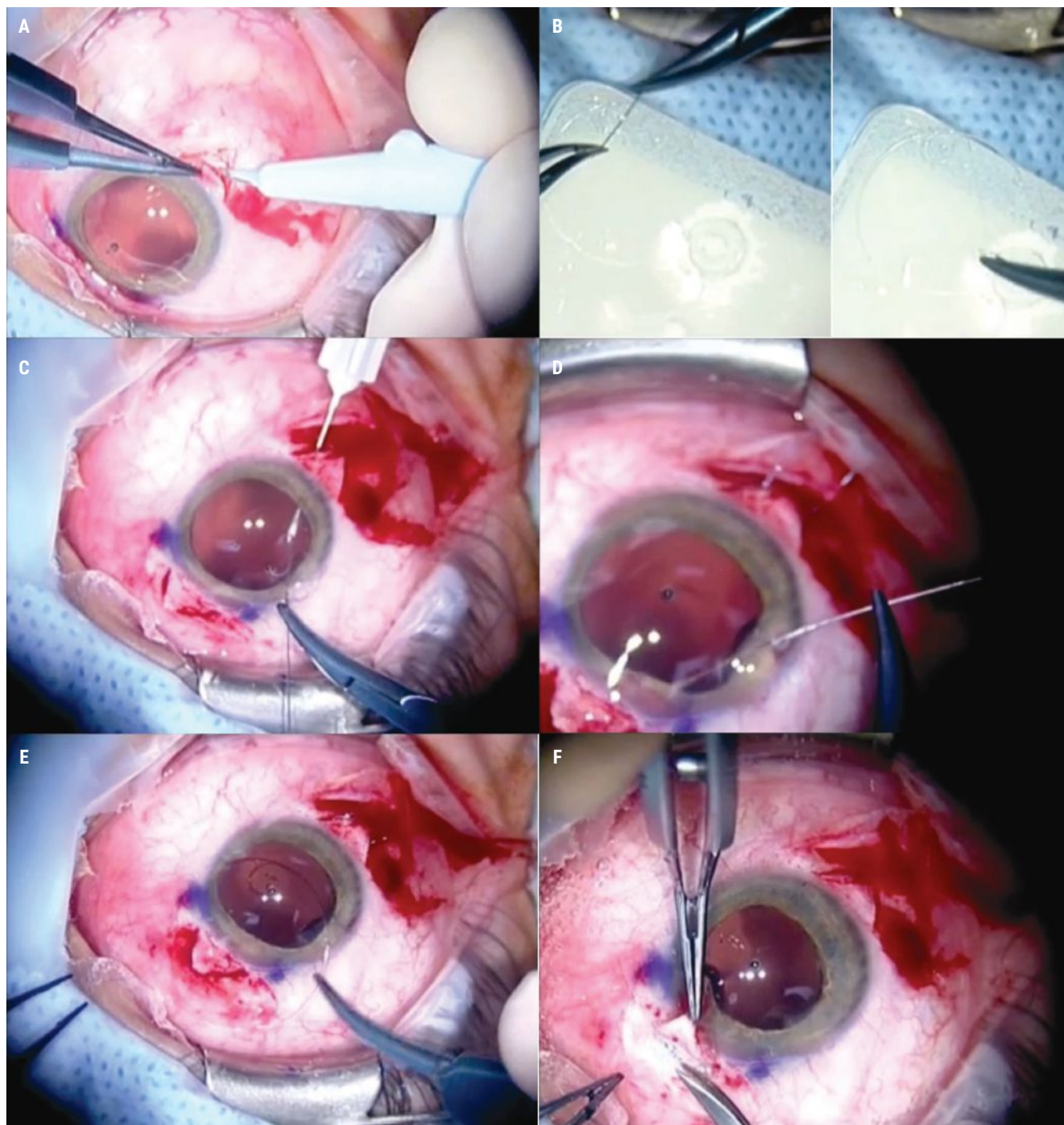
Advise patients that following IZERVAY administration, patients are at risk of developing neovascular AMD, endophthalmitis, elevated intraocular pressure and retinal detachments. If the eye becomes red, sensitive to light, painful, or if a patient develops a change in vision, instruct the patient to seek immediate care from an ophthalmologist.

Patients may experience temporary visual disturbances and blurring after an intravitreal injection with IZERVAY and the associated eye examinations. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

Manufactured by:

IVERIC bio, Inc., An Astellas Company, Parsippany, NJ 07054

©2023 IVERIC bio, Inc., An Astellas Company. IZERVAY is a trademark of IVERIC bio, Inc., An Astellas Company.



**Figure 2.** In this CTR-assisted closure for large clefts, David DiLoreto, MD, PhD, and Shakeel Shareef, MD, use a modified Cianni ring. You first create scleral flaps 180 degrees apart. Then, pass the Prolene suture into the eyelet and tie it to the eyelet. Dock the long straight needles into the 27-ga. hypodermics passed into the sulcus under the scleral flaps. This is repeated with the other eyelet. Then, carefully tuck the ring into the ciliary sulcus. You can then tie the sutures, providing circumferential tension from the ring, and allowing for closure of very large clefts.

gonio lens won't compress the cornea and cause corneal striae.

### Non-surgical Management

If the cleft is small (less than one

clock hour), the management decision is pretty easy: Most surgeons will opt to observe. If left alone, a cleft of this size will probably close on its own. Spending extra time in

the operating room to perform a primary closure is usually unnecessary.

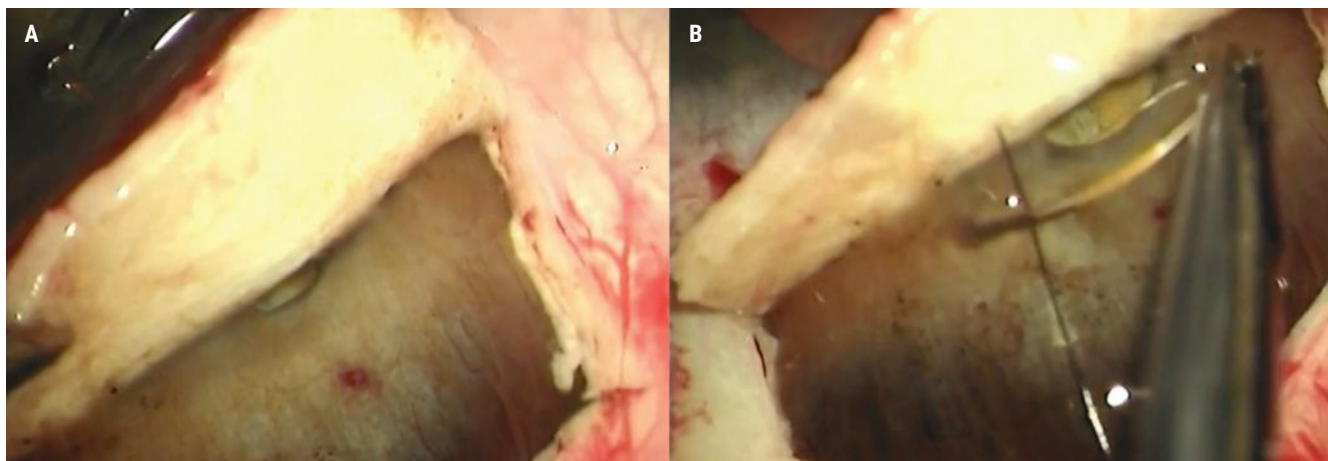
Here are some options to consider for encouraging spontaneous closure:

- *Reduce the amount of postoper-*



Michele Lim, MD

**Figure 3.** This *ab-interno* closure procedure by Michele Lim, MD, doesn't involve docking. A long needle of a Prolene suture is passed across the anterior chamber, piercing the far peripheral iris and angle. The needle is passed out through the sclera. This is repeated with the second needle of the double-armed Prolene suture. The suture is tied and the knot is buried.



Keith Barton, MD

**Figure 4.** In this *ab-externo* direct closure through a full thickness scleral flap by Keith Barton, MD, there's unimpeded flow of aqueous through the suprachoroidal space. The surgeon identifies the cleft under the scleral flap and closes it under direct visualization with 9-0 nylon.

*ative steroid.* This allows some more inflammation in the eye.

- **Administer topical atropine drops once or twice daily for several weeks.** Atropine drops will dilate the pupil and relax the ciliary muscle, making it more likely that the ciliary muscle will be in close proximity to the scleral wall.

- **Laser the cleft using a diode laser.** This produces some inflammation to encourage closure. Use higher power, large spot size and long duration. Suggested power settings for 100 spots in overlapping rows: 700 to 900 mW, 200- $\mu$ m spot size, 500 milliseconds duration.

Surgeons may differ in their approach for larger clefts. For a cleft that's two clock hours or more, some may choose to close it primarily and others may elect to give the cleft a chance to close on its own before taking the patient back the operating

room. In general, larger cleft size is a preoperative risk factor for spontaneous closure failure.<sup>4</sup>

### Timing of Surgical Repair

Permanent visual acuity decrease from hypotony maculopathy may occur without timely intervention. So, how long should you wait before heading to the operating room? It's a tricky question. The general recommendation is to intervene within the first three months—perhaps give the cleft a month and a half to close on its own, and if it hasn't by then, make plans to return to the operating room.

This three-month recommendation comes from a small study of nine patients who had hypotony maculopathy after trabeculectomy.<sup>5</sup> Six eyes had vision restored after undergoing surgery to elevate the IOP. Three eyes didn't return to preoperative vision;

these eyes all had hypotony for more than three and a half months.

However, there are documented cases of vision being restored with surgical repair even years after hypotony. In one report of 32 eyes, postoperative visual acuities were significantly better than preoperative acuities, even when surgical repair was done 54 months after trauma.<sup>6</sup> This same study noted that mean IOP was 3.2 mmHg regardless of cleft size, and that larger clefts took longer for postoperative elevated IOP to normalize after direct cycloplexy.

Nevertheless, we can't know which eyes will recover vision and which won't, so timely surgical repair is advised.

### Surgical Repair Techniques

Here are four approaches to consider:

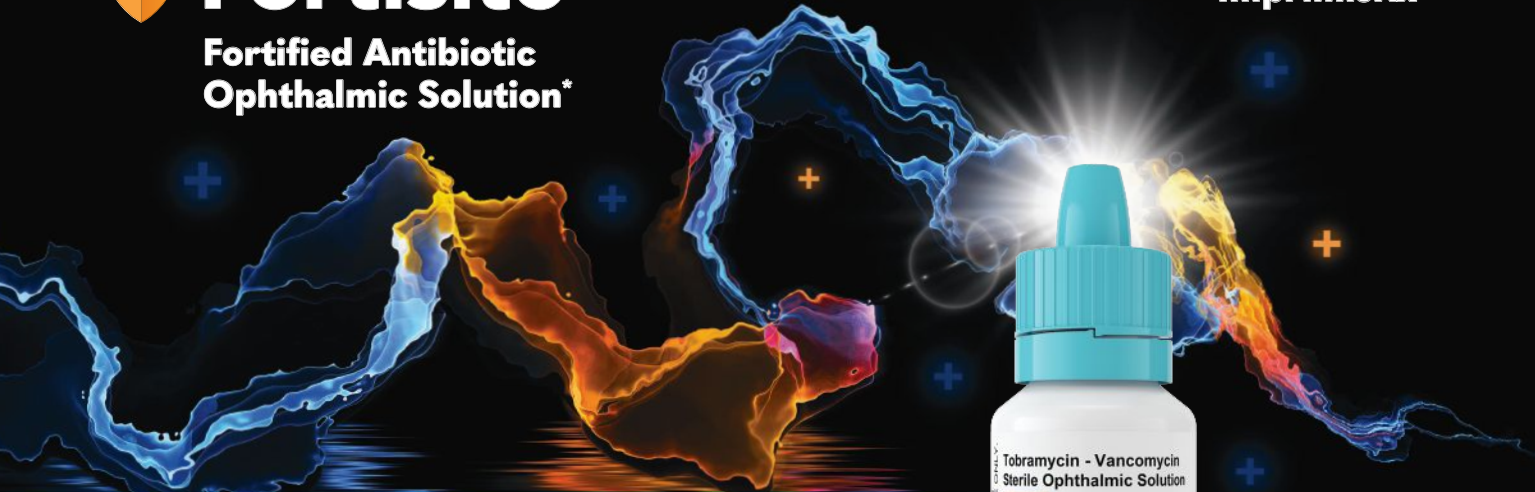
- **"Bucket Handle" docking technique.** This technique requires that



# Fortisite™

**Fortified Antibiotic  
Ophthalmic Solution\***

**Available only from  
ImprimisRx®**



## Expanding our Fortisite® Portfolio:



We're excited to announce the expansion of our portfolio with new and upcoming formulations. These additions join our existing Fortisite portfolio of fortified antibiotics. Additional options are now available to you and your patients.

### Fortisite Formulations:

<b>NEW!</b>	<b>Tobramycin 1% and Vancomycin 2.5%</b> Ophthalmic Solution
<b>Current</b>	<b>Tobramycin 1.5% and Vancomycin 5%</b> Ophthalmic Solution
<b>COMING SOON!</b>	<b>Vancomycin 2.5%</b> Ophthalmic Solution
	<b>Vancomycin 5%</b> Ophthalmic Solution



100% Replacement  
Guarantee on  
Expired Product\*\*



Same-Day  
Shipping and Easy  
Ordering\*\*\*



Refrigerated;  
Never Frozen<sup>†,1,2</sup>



Quality  
Tested<sup>††</sup>



Scan to order now or visit  
[order.imprimisrx.com/fortisite](https://order.imprimisrx.com/fortisite)

Customer Care  
**844-446-6979**

\*For professional use only. ImprimisRx specializes in customizing medications to meet unique patient and practitioner needs. No compounded medication is reviewed by the FDA for safety and efficacy. ImprimisRx does not compound essential copies of commercially available products. These ingredients carry risks. Visit [imprimisrx.com/productinformation](https://imprimisrx.com/productinformation) for full product details. References available upon request.

\*\*Replacement guarantee applies to product that expires before providing to patient.

\*\*\*Same-day shipping applies to orders submitted by 3 PM EST Monday-Friday.

†Beyond use date is 150 days refrigerated versus 45 days frozen based on completed stability studies.

††Every batch is tested for potency and sterility at our FDA-registered laboratory.

References. 1. Data on file. 2. United States Pharmacopeia <797> Pharmaceutical compounding—sterile preparations. (2022). USP-NF, Rockville, MD.

ImprimisRx and Fortisite are registered trademarks of Harrow IP, LLC. ©2023 ImprimisRx. All Rights Reserved. FORTI-00044 10/23

**imprimis**   
A HARROW COMPANY

the patient be pseudophakic. It's suitable for small- to moderate-sized cyclodialysis clefts and involves mostly internal closure with some minor external dissection.

First, make a conjunctival dissection. Then, carve a partial thickness scleral groove parallel to the limbus and 1.5 mm posterior to the limbus. Make a clear corneal incision opposite the scleral groove and fill the anterior chamber with viscoelastic. Next, pass a 27-ga. hypodermic needle through the scleral groove into the ciliary sulcus just past the outer extent of the cyclodialysis cleft. Then, pass the long straight needle of a double armed Prolene suture across the anterior chamber through the clear cornea wound and dock it with the 27-ga. hypodermic needle (Figure 1A).

Withdraw the 27-ga. needle, bringing the long needle and Prolene suture along with it (Figure 1B). Repeat this docking technique with the other needle of the double-armed Prolene suture on the opposite side of the cyclodialysis cleft (Figure 1C).

Tying the suture reapproximates the ciliary body to the scleral wall and buries the knot into the scleral groove to prevent erosion. You then close the conjunctiva (Figure 1D).

• **Modified Cionni ring closure.** This capsular tension ring-assisted technique also requires that the patient be pseudophakic. It's suitable for large cyclodialysis clefts and involves mostly internal closure with some minor external dissection.

First, open the conjunctiva in two sections 180 degrees apart. Create partial thickness scleral flaps 180 degrees apart (Figure 2A). Then, pass the Prolene suture into both eyelets of the Cionni ring and tie them to the eyelets (Figure 2B).

Dock the long straight needles of the Prolene suture into the 27-ga. hypodermics passed into the sulcus under the scleral flaps. This is repeated with both needles of the double-armed Prolene (Figure 2C).

Perform this docking procedure 180 degrees away under the second scleral flap for the Prolene suture that was tied to the second eyelet of the modified Cionni ring (Figure 2D). Then, tuck the modified Cionni ring into the ciliary sulcus (Figure 2E).

You can then tie the sutures with the knots buried under the scleral flaps to prevent erosion (Figure 2F). This gives a circumferential tension with the ring allowing for closure of very large cyclodialysis clefts.

• **Ab interno closure without docking.** This technique is suitable for phakic patients. It's good for small cyclodialysis clefts and involves mostly internal closure with some minor external dissection. Some peripheral anterior synechiae and corneal ectasia will be created.

First, open the conjunctiva, create a clear corneal incision and fill the anterior chamber with viscoelastic. Pass a long needle of a Prolene suture across the anterior chamber, piercing through far peripheral iris and through the anterior chamber angle (Figure 3A).

Bring the needle out through the sclera. Repeat this process with the second needle of the double-armed Prolene suture (Figure 3B). Tie the suture and bury the knot (Figure 3C). Finally, close the conjunctiva.

• **Ab externo direct closure.** This technique is also suitable for phakic patients. It requires a large conjunctival dissection and scleral flap dissection. It's especially helpful if the cyclodialysis cleft is difficult to visualize.

First, a full thickness scleral flap is created. Lifting it reveals the area of the cyclodialysis cleft (Figure 4A). Suture is passed through the scleral flap and across the tissue posterior to the defect and tied, closing the defect (Figure 4B). The scleral flap and conjunctiva are then closed.

## Postoperative Patient Counseling

Once the cleft is closed, it takes

about 24 to 48 hours for the body's natural outflow system to reset itself. During this time, the patient's IOP may increase to pressures as high as 50 or 60 mmHg. Glaucoma drops are used to bring down the pressure during this period.

It's very important to warn patients that there's a high chance that successful closure of the cleft may be accompanied by a dramatic and often painful IOP elevation. This IOP elevation is usually self-limited but may rarely require filtering surgery. It's thought that the longer a patient has had a cyclodialysis cleft and therefore a non-functional outflow pathway, the longer the eye will take to normalize.

In summary, cyclodialysis clefts with MIGS are rare. We can take proactive steps to prevent them from happening. Waiting a few months and applying diode laser for spontaneous closure is reasonable. Plan to return to the OR for closure within three months of onset, and be sure to prepare the patient for a postoperative IOP spike. ◀

- Ioannidis AS, Barton K. Cyclodialysis cleft: Causes and repair. *Curr Opin Ophthalmol* 2010;21:2:150-154.
- Agrawal P, Shah P. Long-term outcomes following the surgical repair of traumatic cyclodialysis clefts. *Eye* 2013;27:1347.
- Duong A, et al. Adverse events associated with microinvasive glaucoma surgery reported to the Food and Drug Administration. *Ophthalmol Glaucoma* 2021;4:433-435.
- Ioannidis A et al. The evaluation and surgical management of cyclodialysis clefts that have failed to respond to conservative management. *British Journal of Ophthalmology* 2014;0:1.
- Cohen S, Flynn H, Palmberg P, Gass D, Grajewski A. Treatment of hypotony maculopathy after trabeculectomy. *Ophthalmic Surgery, Lasers & Imaging* 1995;26:435.
- Hwang J, Ahn K, Kim C, Park K, Kee C. Ultrasonic biomicroscopic evaluation of cyclodialysis before and after direct cyclohexy. *Archives of Ophthalmology* 2008;126:9:1222.

## ABOUT THE AUTHOR



**Dr. Kim** is in private practice with Eye Doctors of Washington in the D.C. area. He has no related financial disclosures.



For the treatment of all stages  
of neurotrophic keratitis (NK)



## NOT JUST ANY SOLUTION A RESOLUTION

### Complete and long-lasting resolution of NK for most patients\*1-4

- **Up to 72% of patients** achieved complete corneal healing in clinical trials\*\*1-3
- **80% of these patients** remained healed at 1 year (REPARO trial)\*4

\* Resolution was evaluated in clinical trials as complete corneal healing, defined as the absence of staining in the lesion area and no persistent staining in the rest of the cornea after 8 weeks of treatment and as <0.5-mm lesion staining at 48-week follow-up.<sup>1,3</sup>

† Key study findings were after 8 weeks of treatment, 6 times daily. REPARO (Study NGF0212): 52 European patients with neurotrophic keratitis (NK) in 1 eye per group; 72% of patients completely healed; vehicle response rate 33.3%. Study NGF0214: 24 US patients with NK in 1 or both eyes per group; 65.2% completely healed; vehicle response rate 16.7%.<sup>2,3</sup>

### Important Safety Information WARNINGS AND PRECAUTIONS

#### Use with Contact Lens

Contact lenses should be removed before applying OXERVATE because the presence of a contact lens (either therapeutic or corrective) could theoretically limit the distribution of cenergermin-bkbj onto the area of the corneal lesion. Lenses may be reinserted 15 minutes after administration.

#### Eye Discomfort

OXERVATE may cause mild to moderate eye discomfort such as eye pain during treatment. The patient should be advised to contact their doctor if a more serious eye reaction occurs.

#### ADVERSE REACTIONS

In clinical trials, the most common adverse reaction was eye pain following instillation which was reported in approximately 16% of patients. Other adverse reactions occurring in 1% to 10% of OXERVATE patients and more frequently than in the vehicle-treated patients included corneal deposits, foreign body sensation, ocular hyperemia, ocular inflammation and tearing.

#### USE IN SPECIFIC POPULATIONS

##### Pregnancy

There are no data from the use of OXERVATE in pregnant women to inform any drug associated risks.

##### Lactation

The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for OXERVATE, and any potential adverse effects on the breastfed infant from OXERVATE.

##### Pediatric Use

The safety and effectiveness of OXERVATE have been established in the pediatric population. Use of OXERVATE in pediatric patients 2 years of age and older is supported by evidence from adequate and well-controlled trials of OXERVATE in adults with additional safety data in children.

##### INDICATION

OXERVATE® (cenergermin-bkbj) ophthalmic solution 0.002% (20 mcg/mL) is indicated for the treatment of neurotrophic keratitis.

##### DOSAGE AND ADMINISTRATION

Instill one drop of OXERVATE in the affected eye(s), 6 times a day at 2-hour intervals for eight weeks.

**To report ADVERSE REACTIONS, contact Dompé U.S. Inc. at 1-833-366-7387 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

**Please see the Brief Summary of full Prescribing Information for OXERVATE on the following page.**

**References:** 1. OXERVATE® (cenergermin-bkbj) ophthalmic solution 0.002% (20 mcg/mL) [US package insert]. Boston, MA; Dompé U.S. Inc.; 2019. 2. Bonini S, et al. *Ophthalmology*. 2018;125:1332-1343. 3. Pflugfelder SC, et al. *Ophthalmology*. 2020;127:14-26. 4. Data on File. Clinical Study Report (NGF0212). Dompé U.S. Inc., 2016.

**oxervate**®   
(cenergermin-bkbj ophthalmic  
solution) 0.002% (20 mcg/mL)



## Brief Summary of full Prescribing Information

Consult the full Prescribing Information for complete product information, available at [www.oxervate.com/prescribing-information](http://www.oxervate.com/prescribing-information).

### INDICATIONS AND USAGE

OXERVATE® (cenegermin-bkbj) ophthalmic solution 0.002% is indicated for the treatment of neurotrophic keratitis.

### DOSAGE AND ADMINISTRATION

#### General Dosing Information

Contact lenses should be removed before applying OXERVATE and may be reinserted 15 minutes after administration.

If a dose is missed, treatment should be continued as normal, at the next scheduled administration.

If more than one topical ophthalmic product is being used, administer the eye drops at least 15 minutes apart to avoid diluting products. Administer OXERVATE 15 minutes prior to using any eye ointment, gel or other viscous eye drops.

#### Recommended Dosage and Dose Administration

Instill one drop of OXERVATE in the affected eye(s), 6 times a day at 2-hour intervals for eight weeks.

### WARNINGS AND PRECAUTIONS

#### Use with Contact Lens

Contact lenses should be removed before applying OXERVATE because the presence of a contact lens (either therapeutic or corrective) could theoretically limit the distribution of cenegermin-bkbj onto the area of the corneal lesion. Lenses may be reinserted 15 minutes after administration.

#### Eye Discomfort

OXERVATE may cause mild to moderate eye discomfort such as eye pain during treatment. The patient should be advised to contact their doctor if a more serious eye reaction occurs.

### ADVERSE REACTIONS

#### Clinical Studies Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

In two clinical trials of patients with neurotrophic keratitis, a total of 101 patients received cenegermin-bkbj eye drops at 20 mcg/mL at a frequency of 6 times daily in the affected eye(s) for a duration of 8 weeks. The mean age of the population was 61 to 65 years of age (18 to 95). The majority of the treated patients were female (61%). The most common adverse reaction was eye pain following instillation which was reported in approximately 16% of patients. Other adverse reactions occurring in 1-10% of OXERVATE patients and more frequently than in the vehicle-treated patients included corneal deposits, foreign body sensation, ocular hyperemia, ocular inflammation and tearing.

### USE IN SPECIFIC POPULATIONS

#### Pregnancy

##### Risk Summary

There are no data from the use of OXERVATE in pregnant women to inform any drug associated risks.

Administration of cenegermin-bkbj to pregnant rats or rabbits during the period of organogenesis did not produce adverse fetal effects at clinically relevant doses. In a pre- and postnatal development study, administration of cenegermin-bkbj to pregnant rats throughout gestation and lactation did not produce adverse effects in offspring at clinically relevant doses.

#### Lactation

##### Risk Summary

There are no data on the presence of OXERVATE in human milk, the effects on breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for OXERVATE, and any potential adverse effects on the breastfed infant from OXERVATE.

#### Pediatric Use

The safety and effectiveness of OXERVATE have been established in the pediatric population. Use of OXERVATE in this population is supported by evidence from adequate and well-controlled trials of OXERVATE in adults with additional safety data in pediatric patients from 2 years of age and older.

#### Geriatric Use

Of the total number of subjects in clinical studies of OXERVATE, 43.5 % were 65 years old and over. No overall differences in safety or effectiveness were observed between elderly and younger adult patients.

### NONCLINICAL TOXICOLOGY

#### Carcinogenesis, Mutagenesis, Impairment of Fertility

##### Carcinogenesis and Mutagenesis

Animal studies have not been conducted to determine the carcinogenic and mutagenic potential of cenegermin-bkbj.

##### Impairment of fertility

Daily subcutaneous administration of cenegermin-bkbj to male and female rats for at least 14 days prior to mating, and at least 18 days post-coitum had no effect on fertility parameters in male or female rats at doses up to 267 mcg/kg/day (1709 times the MRHOD).

In general toxicology studies, subcutaneous and ocular administration of cenegermin-bkbj in females was associated with ovarian findings including persistent estrus, ovarian follicular cysts, atrophy/reduction of corpora lutea, and changes in ovarian weight at doses greater than or equal to 19 mcg/kg/day (119 times the MRHOD).





# If You're Not Part of the Solution ...

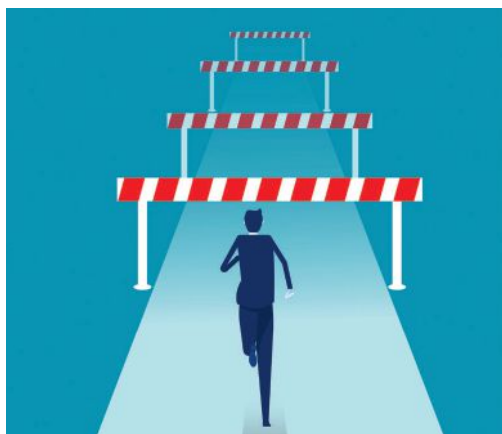
*Musings on life, medicine and the practice of ophthalmology.*

**MARK H. BLECHER**  
CHIEF MEDICAL EDITOR

“If you're not part of the solution, you're part of the problem.” This is a timeworn aphorism in business and in life. It's sort of related to

the saying “Those who can, do. And those who can't, just get in the way.” (It was actually “teach,” but that's not my point.) We all know people who just get in the way. Some are actively obstructing; others are just obstacles, passive and oblivious as always. When I first took my new administrative role at Wills, it was very exciting to bring fresh eyes to a venerated institution, and to identify and address people and processes that might need optimizing, educating and engaging. There were wins both big and small. When I arrived, my position didn't exist, so there was lots of new ground to cover. There were lots of obvious—to me anyway—is-  
sues that I could help address quickly. Now, as I approach three years in this job, most of the easy wins are behind me. There's still a lot to do, as with any large institution. It's a living thing, always changing. And, of course, the environment we live and work in is always changing, too. So, there's no lack of fires to put out. But overall, a few of the remaining bigger issues are both long-standing and recalcitrant. I guess if they were easy, they would've been addressed long ago.

These aren't just operational issues, but recalcitrant people, too. I guess I should expect to have to struggle at times, as it isn't always easy; there are long-established behaviors, workflows, expectations, abuses. Again, this isn't unique to where I work but now it's



in my wheelhouse. I'm occasionally frustrated. It pings my ADHD when an issue needs a longer time horizon to fix. I'm an “on the list, off the list” kind of guy, which is not always a good way to be. Some situations/people require more engagement and more conversation to achieve even small movement. Some seem impossible to fix. But how do you know when you've crossed that line? And if they're impossible, what's the next step?

Systems and workflows can be easily changed if the people involved want to or are compelled to change them. Some individuals, not so much. Of

course, the diversity of personalities is endless. Some are eager and open to changes or suggestions. Some are happy to be involved in the process. Others are resistant, arrogant or angry—maybe all three. I frequently joke that I failed Psych in med school. I didn't. But I don't really consider myself the most empathic individual and struggle to understand people who make life difficult. I should be more understanding, given the work I'm now doing, and maybe I am a bit better these days because I have to be. But when, despite your best efforts, individuals are unmoved and obstructionist, what's your next move? You could say just fire them, which in many cases should be true. But, it's rarely that easy. Aside from HR issues, you have to consider the impact of dismissing someone, anyone, would have on the organization. Consider the impact it would have on coworkers, work flow and even reputation. From a humanitarian viewpoint, that should be the last resort. But I fear that alas, there is a limit to my personal tolerance for those who not only don't want to help the organization move forward but are sabotaging your efforts.

I have to stop feeling like it's a personal failure when I can't resolve every intractable situation or every difficult individual. I do have to stop, but I don't have to stop trying. All the great work being done here, involving so many outstanding people, helping so many patients. At the end of a challenging day, that's what I have to remember. That's why I came out of retirement and why I get up every morning. It can be easy to lose your perspective when facing seemingly impossible issues, but that's just part of life. And I'd rather be part of the solution, than walk away from the problem. ◀



EDITED BY ARTURO CHAYET, MD

## REFRACTIVE/CATARACT RUNDOWN

# Addressing Pterygia in Cataract Patients

*These conjunctival lesions can impact keratometry, often making staged surgery the best choice for patient outcomes.*

LIZ HUNTER  
SENIOR EDITOR

Every cataract surgeon understands the role the cornea plays in refractive outcomes for their patients. The more pristine, the better measurements can be obtained and the more likely patients will be happy. One condition that can interfere with this process is a pterygium.<sup>1</sup> Not all pterygia are created equal, though, and surgeons should consider several factors to determine whether or not to remove one, and when.

“A pterygium is basically scar tissue that can be very small and mild and not really cause much problem at all,” says Christopher J. Rapuano, MD, Chief of Wills Eye Hospital’s Cornea Service. “It can be stable over time, or it can progress slowly, and more so when people are younger and not as much when people are older. Pterygia can sometimes run in families but oftentimes they are related to ultraviolet exposure, chronic trauma, chronic dry eye, and exposure to environmental factors, including sun, wind and sand. They tend to be more common in those who live closer to the equator.”

Pterygia are most commonly found on the nasal side of the eye. “They can be temporal, but they’re usually either at the 3 or the 9 o’clock position and occasionally they can be both nasal and temporal,” continues Dr. Rapuano.

“In some severe cases you’ll see nasal and temporal pterygia that connect in the middle. Because they’re elevated, pterygia can cause some irritation and extra dryness, which causes inflammation, redness and irritation. Patients’ eyes will appear red all the time. It can cause discomfort and cosmetically it doesn’t look good.”



**Excising pterygia doesn’t prevent it from returning in the future and the chosen surgical technique for removal can impact the recurrence rate.**



Some cornea specialists say a small, asymptomatic pterygium that doesn’t bother the patient could be left alone and may not affect refractive outcomes after the cataract surgery. “Typically, lesions smaller than 3 mm don’t tend to create irregularities of the cornea,” says Ellen Koo, MD, an associate professor of clinical ophthalmology at Bascom Palmer Eye Institute.

However, Dr. Rapuano says it’s important to closely look at corneal curvature before making this decision. “In those who have small pterygia that aren’t causing redness, pain or

decreased vision, the question is, should they be removed prior to cataract surgery? And the answer generally is, if it seems to be affecting the corneal curvature, then they should be removed,” he says. “You really want a good, stable, regular corneal curvature for cataract surgery.”

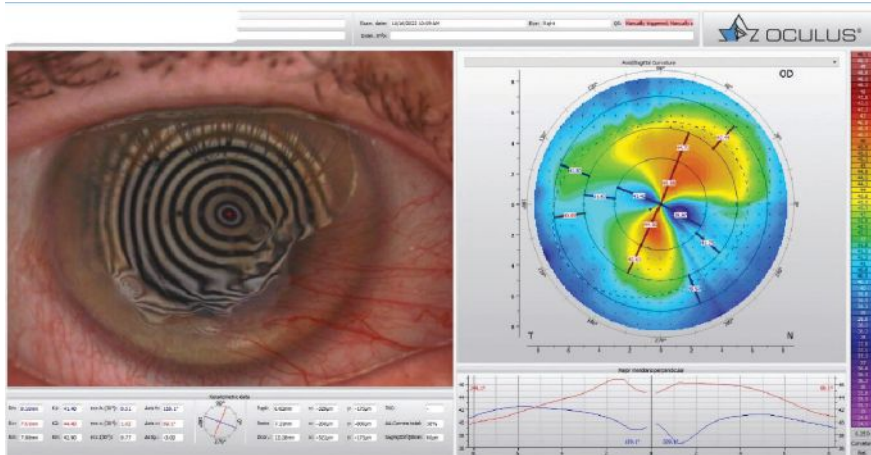
Although larger pterygia are more likely to cause a change in astigmatism, it’s not always about the size of the lesion.

“You can have a smaller pterygium that’s causing more astigmatism than you expected and a larger one that may not be causing much, so we can be a little bit deceived just by the size of it,” says Leela V. Raju, MD, a clinical associate professor at NYU Langone Eye Center. “I don’t believe we generally need a rule of addressing all pterygia before cataract surgery because some can look very fine and thin, and those may not cause as much astigmatism as some of the thicker-looking pterygia. I wouldn’t base it on size, but I would look at how—for lack of a better word—‘beefy’ the pterygium looks. Some that look very thick or red, they might have an increased chance of causing more astigmatism than these very thin ones that you can almost see through at the slit lamp.

“However, if you look at the tomography and it doesn’t show a large amount of astigmatism and it’s not bothering the patient, you could have a discussion about leaving it alone or removing it at the time of cataract surgery, with the understanding that it’s likely we won’t be able to correct all of the astigmatism,” she continues. “Some people are very happy wearing glasses afterwards, and they prefer it in some cases, so make sure that they know their options and make sure you’ve documented the conversation really well.”

This article has no commercial sponsorship.

Dr. Chayet is considered a pioneer in refractive and cataract surgery, and is the medical director of the Codet Vision Institute in Tijuana, Mexico. He is a clinical investigator for RxSight, LensGen and ForSight Vision6.



**Topography showing a large nasal pterygium and the resulting irregular astigmatism.**

## Techniques for Removing the Pterygium

Excising pterygia doesn't prevent them from returning in the future and the chosen surgical technique for removal can impact the recurrence rate.

"The recurrence rate can be as low as 5 percent in the best of hands and in some studies it's 10 or 15 percent," says Dr. Rapuano. "The standard technique that most cornea specialists will use is a conjunctival autograft placed in the area where we just removed the pterygium. We'll use some fibrin glue and oftentimes a few dissolvable sutures to secure it in place. If you do that it has a very low recurrence rate, less than 5 percent."

Removing Tenon's fascia is another component of success in this technique, says Dr. Koo. "With the excision, usually we start with the blunt dissection of the lesion and it often peels off without much effort once you find the right plane," she says. "During the harvest of the conjunctival autograft, it's important that there's minimum Tenon's in the autograft to ensure optimal healing, as well as the cosmesis aspect afterwards. Some people do use the conjunctival pedicle rotation technique, meaning you leave a little pedicle that's still attached from the harvest site and simply rotate that to the site of excised pterygium. The principle of that is to provide a viable autograft and that's also a great technique."

Dr. Raju also uses a conjunctival autograft as her primary technique. "I do a decent amount of Tenon's resection," she says. "I think it's important to remove Tenon's, even hooking the muscle. Getting the Tenon's around the edges of the muscle is important."

An amniotic membrane graft is another technique some choose to perform. "Excision of the lesion with amniotic membrane graft is also considered acceptable, especially in cases where there's not enough viable conjunctiva or there's a need for glaucoma surgery, but the recurrence rate for that is thought to be higher than for the technique with a conjunctival autograft," says Dr. Koo.

In some cases, mitomycin-C could be appropriate, say experts. "Some of the pterygia that I see in New York are in patients who have grown up in much sunnier climates, and their pterygia can look very thick," Dr. Raju says. "In those primary cases I will use mitomycin-C because they definitely have a higher risk of recurrence, even if you do a really good Tenon's resection. Otherwise, I generally reserve any mitomycin-C for recurrent pterygia, or if it's temporal I often do mitomycin-C and maybe even add in amniotic membrane along with a conjunctival autograft because that's not the regular location for them, which makes me think there's something else going on. Anything you can do to reduce inflammation after the procedure is going to

help make sure that you'll have better outcomes and less recurrences."

However, mitomycin-C comes with some risks, adds Dr. Koo. "If using mitomycin-C, you want to limit the concentration to 0.02% and limit the time usage, along with making sure that the ocular surface is flushed really well so that there's no mitomycin-C remaining," she says. "Mitomycin-C is associated with a lower recurrence rate, and is very helpful for cases of recurrent pterygia. That said, intraoperative usage of mitomycin-C does carry risks, and these include risks of delayed epithelialization, scleral thinning or even scleral melt."

## Healing and Next Steps

"After surgery, patients are placed on steroids and carefully monitored in the ensuing weeks and we usually wait at least three months before obtaining biometry," says Dr. Koo. "In that time period, when they're coming back for their follow ups, I do obtain serial topography because you want to achieve stability at the time of cataract surgery consideration.

"With removal of the pterygium you should see a reversal of that induced corneal astigmatism," she continues. "There are some instances where the pterygium itself affects the Bowman's layer and can lead to some level of scarring even after excision. That may be reflected in the final topography, but most of the time we should see marked improvement of the irregular astigmatism. The main goal is to achieve stability and to make sure you can have at least a couple reproducible topographies."

Dr. Raju looks for agreement in her measurements before proceeding with the cataract surgery. "Hopefully I've had measurements that have been agreeing with each other in a two-week period," she says. "For instance, you could do measurements at four weeks and six weeks, or six and eight weeks after pterygium surgery to see that you've got agreement, but once again, I think it's very important to let the patient know that we really want

**SYFOVRE**<sup>®</sup>  
(pegcetacoplan injection)  
15 mg / 0.1 mL

GA unravels so much

**Save retinal  
tissue by slowing  
progression**<sup>1-3</sup>



## INDICATION

SYFOVRE<sup>®</sup> (pegcetacoplan injection) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

## IMPORTANT SAFETY INFORMATION

### CONTRAINDICATIONS

- SYFOVRE is contraindicated in patients with ocular or periocular infections, and in patients with active intraocular inflammation

### WARNINGS AND PRECAUTIONS

#### ● Endophthalmitis and Retinal Detachments

- Intravitreal injections, including those with SYFOVRE, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering SYFOVRE to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.

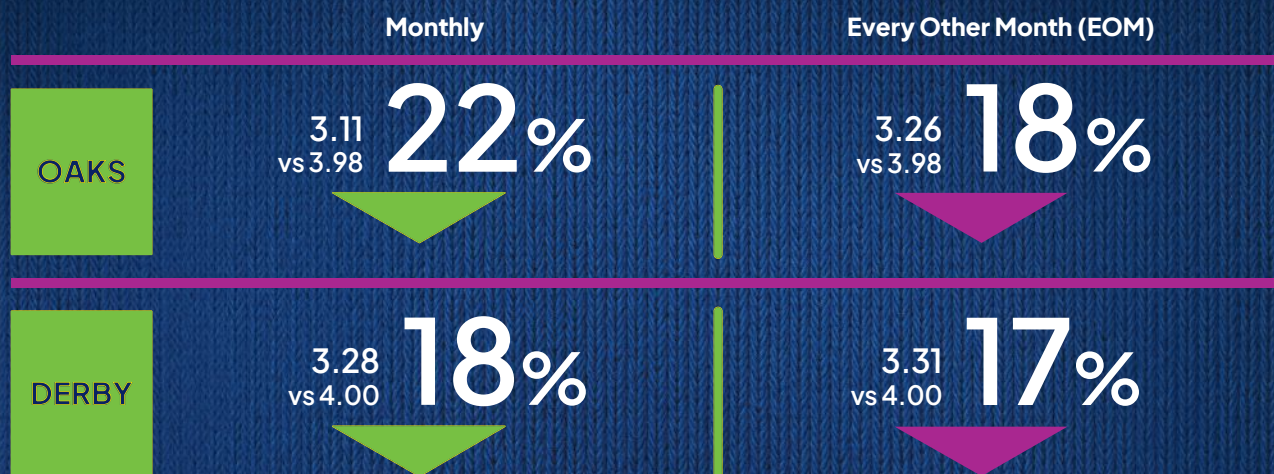
#### ● Neovascular AMD

- In clinical trials, use of SYFOVRE was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (12% when administered monthly, 7% when administered every other month and 3% in the control group) by Month 24. Patients receiving SYFOVRE should be monitored for signs of neovascular AMD. In case anti-Vascular Endothelial Growth Factor (anti-VEGF) is required, it should be given separately from SYFOVRE administration.

#### ● Intraocular Inflammation

- In clinical trials, use of SYFOVRE was associated with episodes of intraocular inflammation including: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, and anterior chamber flare. After inflammation resolves, patients may resume treatment with SYFOVRE.

# SYFOVRE achieved continuous reductions in mean lesion growth rate\* (mm<sup>2</sup>) vs sham pooled from baseline to Month 24<sup>1</sup>



SE in trials (monthly, EOM, sham pooled): OAKS: 0.15, 0.13, 0.14; DERBY: 0.13, 0.13, 0.17.

\*Slope for baseline to Month 24 is an average of slope of baseline to Month 6, Month 6 to Month 12, Month 12 to Month 18, and Month 18 to Month 24.<sup>1</sup>

Based on a mixed effects model for repeated measures assuming a piecewise linear trend in time with knots at Month 6, Month 12, and Month 18.<sup>1</sup>

GA=geographic atrophy; SE=standard error.



Explore the long-term data

## IMPORTANT SAFETY INFORMATION (CONT'D)

### WARNINGS AND PRECAUTIONS (CONT'D)

- **Increased Intraocular Pressure**

- Acute increase in IOP may occur within minutes of any intravitreal injection, including with SYFOVRE. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

### ADVERSE REACTIONS

- Most common adverse reactions (incidence ≥5%) are ocular discomfort, neovascular age-related macular degeneration, vitreous floaters, conjunctival hemorrhage.

**Trial Design:** SYFOVRE safety and efficacy were assessed in OAKS (N=637) and DERBY (N=621), multi-center, 24-month, Phase 3, randomized, double-masked trials. Patients with GA (atrophic nonexudative age-related macular degeneration), with or without subfoveal involvement, secondary to AMD were randomly assigned (2:2:1:1) to receive 15 mg/0.1 mL intravitreal SYFOVRE monthly, SYFOVRE EOM, sham monthly, or sham EOM for 24 months. Change from baseline in the total area of GA lesions in the study eye (mm<sup>2</sup>) was measured by fundus autofluorescence (FAF).<sup>1,4</sup>

**References:** 1. SYFOVRE (pegcetacoplan injection) [package insert]. Waltham, MA: Apellis Pharmaceuticals, Inc.; 2023. 2. Pfau M, von der Emde L, de Sisternes L, et al. Progression of photoreceptor degeneration in geographic atrophy secondary to age-related macular degeneration. *JAMA Ophthalmol.* 2020;138(10):1026–1034. 3. Bird AC, Phillips RL, Hageman GS. Geographic atrophy: a histopathological assessment. *JAMA Ophthalmol.* 2014;132(3):338–345. 4. Data on file. Apellis Pharmaceuticals, Inc.

Please see Brief Summary of Prescribing Information for SYFOVRE on the adjacent page.

Apellis

APELLIS®, SYFOVRE® and their respective logos are registered trademarks of Apellis Pharmaceuticals, Inc.  
©2023 Apellis Pharmaceuticals, Inc. 7/23 US-PEGGA-2200051 v2.0

**SYFOVRE® (pegcetacoplan injection), for intravitreal use**  
**BRIEF SUMMARY OF PRESCRIBING INFORMATION**  
Please see SYFOVRE full Prescribing Information for details.

**INDICATIONS AND USAGE**

SYFOVRE is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

**CONTRAINDICATIONS**

**Ocular or Periocular Infections**

SYFOVRE is contraindicated in patients with ocular or periocular infections.

**Active Intraocular Inflammation**

SYFOVRE is contraindicated in patients with active intraocular inflammation.

**WARNINGS AND PRECAUTIONS**

**Endophthalmitis and Retinal Detachments**

Intravitreal injections, including those with SYFOVRE, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering SYFOVRE in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.

**Neovascular AMD**

In clinical trials, use of SYFOVRE was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (12% when administered monthly, 7% when administered every other month and 3% in the control group) by Month 24. Patients receiving SYFOVRE should be monitored for signs of neovascular AMD. In case anti-Vascular Endothelial Growth Factor (anti-VEGF) is required, it should be given separately from SYFOVRE administration.

**Intraocular Inflammation**

In clinical trials, use of SYFOVRE was associated with episodes of intraocular inflammation including: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, and anterior chamber flare. After inflammation resolves patients may resume treatment with SYFOVRE.

**Increased Intraocular Pressure**

Acute increase in IOP may occur within minutes of any intravitreal injection, including with SYFOVRE. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

**ADVERSE REACTIONS**

**Clinical Trials Experience**

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

A total of 839 patients with GA in two Phase 3 studies (OAKS and DERBY) were treated with intravitreal SYFOVRE, 15 mg (0.1 mL of 150 mg/mL solution). Four hundred nineteen (419) of these patients were treated in the affected eye monthly and 420 were treated in the affected eye every other month. Four hundred seventeen (417) patients were assigned to sham. The most common adverse reactions (≥5%) reported in patients receiving SYFOVRE were ocular discomfort, neovascular age-related macular degeneration, vitreous floaters, and conjunctival hemorrhage.

**Table 1: Adverse Reactions in Study Eye Reported in ≥2% of Patients Treated with SYFOVRE Through Month 24 in Studies OAKS and DERBY**

Adverse Reactions	PM (N = 419) %	PEOM (N = 420) %	Sham Pooled (N = 417) %
Ocular discomfort*	13	10	11
Neovascular age-related macular degeneration*	12	7	3
Vitreous floaters	10	7	1
Conjunctival hemorrhage	8	8	4
Vitreous detachment	4	6	3
Retinal hemorrhage	4	5	3
Punctate keratitis*	5	3	<1
Posterior capsule opacification	4	4	3
Intraocular inflammation*	4	2	<1
Intraocular pressure increased	2	3	<1

PM: SYFOVRE monthly; PEOM: SYFOVRE every other month

\*The following reported terms were combined:

**Ocular discomfort** included: eye pain, eye irritation, foreign body sensation in eyes, ocular discomfort, abnormal sensation in eye

**Neovascular age-related macular degeneration** included: exudative age-related macular degeneration, choroidal neovascularization

**Punctate keratitis** included: punctate keratitis, keratitis

**Intraocular inflammation** included: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, anterior chamber flare

Endophthalmitis, retinal detachment, hyphema and retinal tears were reported in less than 1% of patients. Optic ischemic neuropathy was reported in 1.7% of patients treated monthly, 0.2% of patients treated every other month and 0.0% of patients assigned to sham. Deaths were reported in 6.7% of patients treated monthly, 3.6% of patients treated every other month and 3.8% of patients assigned to sham. The rates and causes of death were consistent with the elderly study population.

**USE IN SPECIFIC POPULATIONS**

**Pregnancy**

**Risk Summary**

There are no adequate and well-controlled studies of SYFOVRE administration in pregnant women to inform a drug-associated risk. The use of SYFOVRE may be considered following an assessment of the risks and benefits.

Systemic exposure of SYFOVRE following ocular administration is low. Subcutaneous administration of pegcetacoplan to pregnant monkeys from the mid gestation period through birth resulted in increased incidences of abortions and stillbirths at systemic exposures 1040-fold higher than that observed in humans at the maximum recommended human ophthalmic dose (MRHOD) of SYFOVRE (based on the area under the curve (AUC) systemically measured levels). No adverse maternal or fetal effects were observed in monkeys at systemic exposures approximately 470-fold higher than that observed in humans at the MRHOD.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

**Lactation**

**Risk Summary**

It is not known whether intravitreal administered pegcetacoplan is secreted in human milk or whether there is potential for absorption and harm to the infant. Animal data suggest that the risk of clinically relevant exposure to the infant following maternal intravitreal treatment is minimal. Because many drugs are excreted in human milk, and because the potential for absorption and harm to infant growth and development exists, caution should be exercised when SYFOVRE is administered to a nursing woman.

**Females and Males of Reproductive Potential**

**Contraception**

**Females:** It is recommended that women of childbearing potential use effective contraception methods to prevent pregnancy during treatment with intravitreal pegcetacoplan. Advise female patients of reproductive potential to use effective contraception during treatment with SYFOVRE and for 40 days after the last dose. For women planning to become pregnant, the use of SYFOVRE may be considered following an assessment of the risks and benefits.

**Pediatric Use**

The safety and effectiveness of SYFOVRE in pediatric patients have not been established.

**Geriatric Use**

In clinical studies, approximately 97% (813/839) of patients randomized to treatment with SYFOVRE were ≥ 65 years of age and approximately 72% (607/839) were ≥ 75 years of age. No significant differences in efficacy or safety were seen with increasing age in these studies. No dosage regimen adjustment is recommended based on age.

**PATIENT COUNSELING INFORMATION**

Advise patients that following SYFOVRE administration, patients are at risk of developing neovascular AMD, endophthalmitis, and retinal detachments. If the eye becomes red, sensitive to light, painful, or if a patient develops any change in vision such as flashing lights, blurred vision or metamorphopsia, instruct the patient to seek immediate care from an ophthalmologist.

Patients may experience temporary visual disturbances associated either with the intravitreal injection with SYFOVRE or the eye examination. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

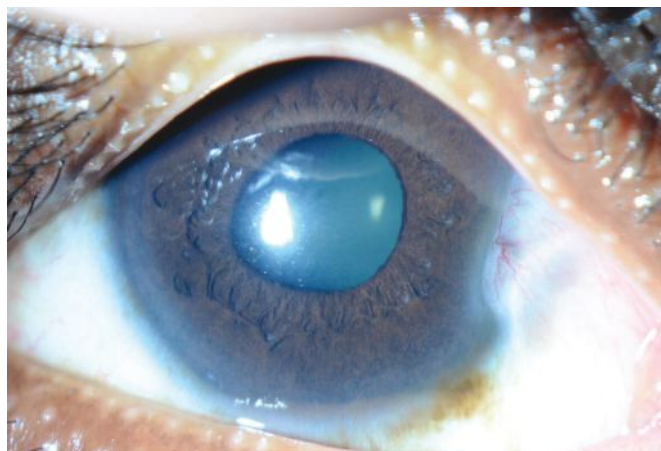
Manufactured for:  
Apellis Pharmaceuticals, Inc.  
100 Fifth Avenue  
Waltham, MA 02451

SYF-PI-17Feb2023-1.0

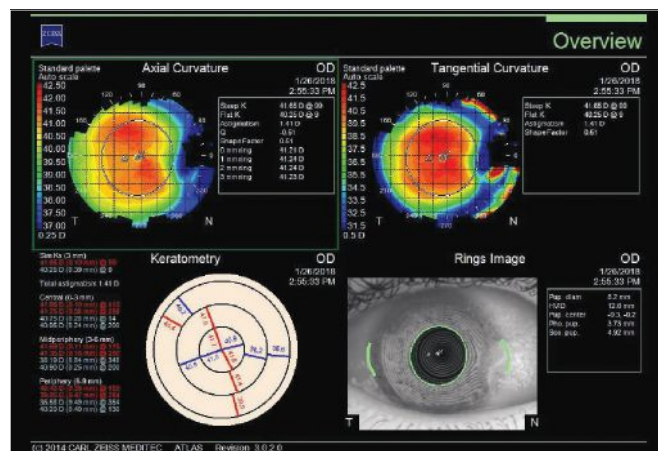
APELLIS®, SYFOVRE® and their respective logos are registered trademarks of Apellis Pharmaceuticals, Inc.  
©2023 Apellis Pharmaceuticals, Inc.

7/23 US-PEGGA-2200163 v3.0





**Slit lamp photograph showing a small- to medium-sized nasal pterygium in the patient's right eye. He has no visual complaints. Even though the pterygium isn't very large, corneal topography of the eye demonstrates some irregular astigmatism beginning to reach the visual axis. For the best results after cataract surgery, one should consider removal of this pterygium prior to cataract surgery.**



Christopher Rapuano, MD

this to heal up properly so we get the proper measurements to pick the best implant for them.”

Patients who've had pterygium removed aren't necessarily limited in their IOL choices, but there are caveats. “It depends on how normal the curvature is after the pterygium surgery,” says Dr. Rapuano. “If the cornea looks beautiful and perfectly smooth, and they have a low chance of recurrence of the pterygium, then you can pretty much use any IOL power you want. But a lot of these patients have some irregularity of the cornea and some corneal scarring after the pterygium is removed, and their vision might be very good after the cataract surgery but not necessarily perfect. For those patients, a multifocal lens is probably not ideal. If they have a lot of astigmatism because their cornea is still somewhat irregular, then they might do well with a hard contact lens after surgery. You probably don't want to use a toric lens in some of those patients either because it's much harder to fit a hard contact lens after a toric IOL. Those would be my main concerns. Again, some patients have a higher chance of recurrence, especially if it's been a recurrent pterygium to begin with, or if there's a lot of scar tissue. If there's a high risk of recurrence, then you may not want to use a multifocal or toric lens because the

recurrence will change the shape of the cornea.”

Cornea experts emphasize the ocular surface and if there are any signs of dry eye. “I do think it's important to address any dry eye with these patients because of the amount of inflammation and solar changes that have led to the pterygium, you may want to be a little more careful in examining their ocular surface to make sure that it's also not going to skew your keratometry, especially if a patient's interested in one of these premium technology lenses,” says Dr. Raju. “Pterygium can also affect the tear film, so if a patient is really considering a premium technology implant, make sure you've done everything you can to ensure nothing is going to affect the tear film, because we know that can cause problems in patients without pterygium if not addressed appropriately.”

### Patient Follow-Up

Moving forward, these patients should be closely followed for any signs of recurrence.

“I say this very often to our residents, it's so important to remove pterygium appropriately the first time,” Dr. Raju says. “When you have to go back, the surgery becomes much more difficult. That initial technique is really important. We have to truly think

about trying to make this a one-and-done type surgery. Not that it's always possible, but that should be our goal.”

She routinely sees her patients monthly for the first four to six months postop. “I look for any increase in redness and help remind them to use their drops, protect their eyes from sun, wind or dryness, which can also exacerbate irritation and makes us more concerned for recurrence,” says Dr. Raju. “Especially in those really thick pterygia, obviously something has elevated inflammation on the surface for some reason so you have to watch those patients very carefully. I always ask them to come back if they're noticing any redness after the initial couple of weeks because I'd expect that to have gone down pretty significantly at that point. We'd possibly increase their topical steroids or sometimes I'll inject steroids subconjunctivally in order to really help target any localized areas of inflammation and hopefully I can prevent it from recurring.”

1. Sharma B, Bajoria SK, Mishra M, Iqbal N. Refractive outcomes of simultaneous pterygium and cataract surgery with fibrin glue. *Cureus* 2021;24:13:11.

### DISCLOSURES

**Drs. Koo and Raju** report no relevant disclosures. **Dr. Rapuano** consults for BioTissue.

# LRIS: STILL A VALUABLE ASSET FOR ASTIGMATISM

Despite advances in toric IOL technology, experienced cataract surgeons say limbal relaxing incisions are still a worthwhile technique to perform.

LIZ HUNTER  
SENIOR EDITOR

Patients undergoing cataract surgery have higher expectations than ever for their visual outcomes. When those patients have astigmatism, the current correction method of choice is toric IOLs; however, there's no toric IOL for the correction of astigmatism <1 D approved in the United States. In this situation, surgeons find themselves turning to long-established intraoperative techniques, such as limbal relaxing incisions, to give patients the best vision possible. Here, experts share their techniques and tips for a successful outcome.

## Why LRIs Still Matter

"In the U.S., the lowest power toric lenses, which are great for addressing astigmatism, only correct about 1 D at the corneal plane," notes Uday Devgan, MD, a refractive and cataract surgeon practicing in Los Angeles. "If the patient has 1 to 2 D of astigmatism in the cornea, by all means put a toric lens in. But what do you do when the patient has 0.5 D of astigmatism or 0.75 D of astigmatism? You don't want to leave them uncorrected."

IOL affordability could also contribute to the decision to perform LRIs. "If you can convince all your patients to have some type of toric lens, you'll never have to do an LRI," says Jeffrey Whitman, MD, chief surgeon at the Key-Whitman Eye Center in Dallas. "However, we have a wide range of patients and perform over 7,000 cataract surgeries in our surgery center each year. We have patients who can't afford premium toric lenses or presbyopia-correcting lenses. We offer financing options as needed, but also remember that there are patients for whom premium lenses just aren't right. There are patients who have bad macular degeneration, so a multifocal lens doesn't make sense. If they choose a monofocal lens, that's not an excuse not to offer them a better quality of vision and fix low amounts of astigmatism. Give them the best visual outcome that they can afford."

## Screening Patients for LRI Candidacy

It's important to recognize who best fits the profile for an LRI.

"Ideal candidates will have regular symmetric astigmatism," says Dr. Devgan. "If it's irregular, it's not worth trying an LRI. The ideal candidate is a patient, who again, in this situation has less than 1 D of astigmatism. If they have more than that, LRIs lose their efficacy above a certain degree. I won't even attempt an LRI for 2 or 3 D of astigmatism. It's just not really feasible, whereas I can put a toric lens to correct 4 D of astigmatism very accurately."

"Candidates to avoid would be those with irregular astigmatism, a high degree of astigmatism or some other irregularity in the cornea," he continues. "If you have a patient with keratoconus, that's asymmetrical astigmatism, and an LRI may further destabilize the cornea."

Thoroughly screening patients will provide further clues about their corneas because some findings may disqualify them as candidates.

"One of my screening questions for keratoconus is to ask the patient whether his eyes itch sometimes," says Anita Nevyas-Wallace, MD, the medical director of Nevyas Eye Associates in the greater Philadelphia

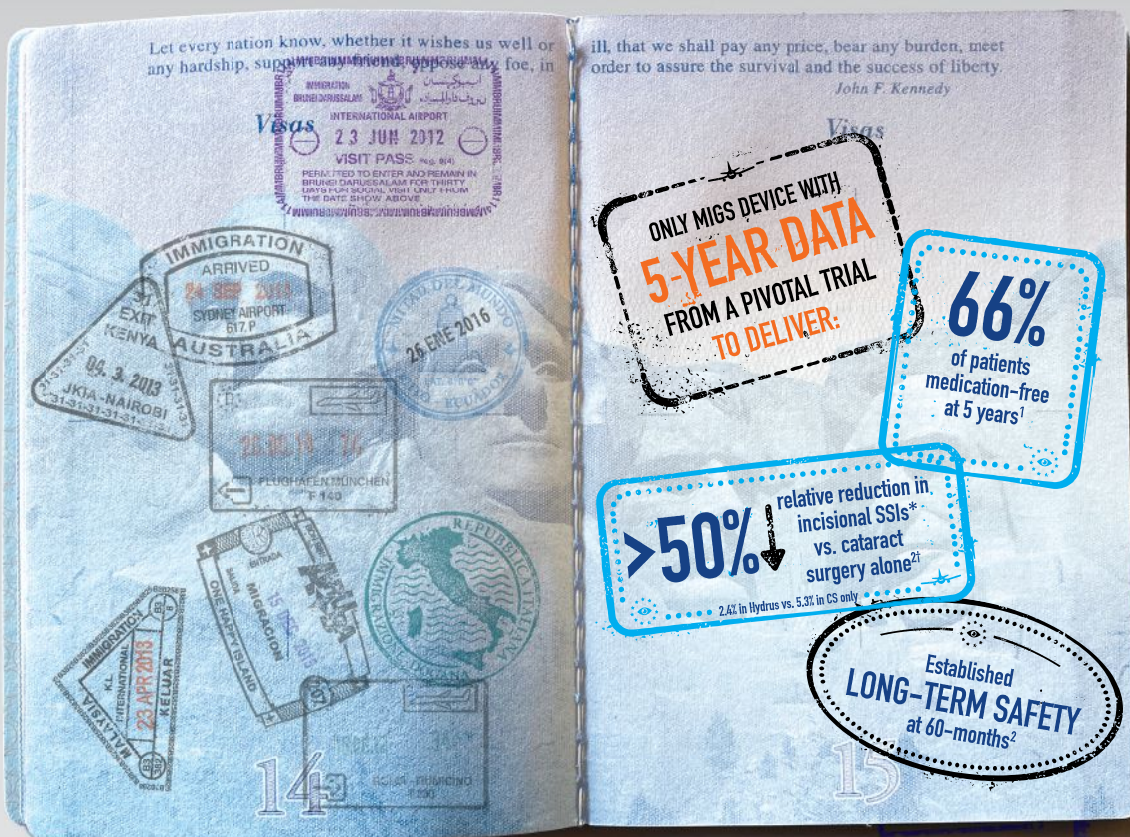
This article has no commercial sponsorship.

Drs. Arbisser, Devgan and Nevyas-Wallace have no relevant disclosures. Dr. Whitman discloses consulting relationships with Alcon, Johnson & Johnson Vision and Bausch + Lomb.



# HYDRUS<sup>®</sup>

MICROSTENT



**YOUR MIGS CHOICE MATTERS**  
 BECAUSE THERE'S SO MUCH MORE TO SEE

Your adult Primary Open-Angle Glaucoma patients have seen tremendous things, and plan to see a whole lot more.

**Choose the MIGS device built to enable life's biggest experiences.**

\*SSI = Secondary Surgical Intervention

† includes trabeculectomy, tube shunt, gel stent, ECP/TSCP, non-penetrating; (9/369 Hydrus and 10/187 CS)



#### IMPORTANT PRODUCT INFORMATION

**CAUTION: Federal law restricts this device to sale by or on the order of a physician.**

**INDICATIONS FOR USE:** The Hydrus Microstent is indicated for use in conjunction with cataract surgery for the reduction of intraocular pressure (IOP) in adult patients with mild to moderate primary open-angle glaucoma (POAG). **CONTRAINDICATIONS:** The Hydrus Microstent is contraindicated under the following circumstances or conditions: (1) In eyes with angle closure glaucoma; and (2) In eyes with traumatic, malignant, uveitic, or neovascular glaucoma or discernible congenital anomalies of the anterior chamber (AC) angle. **WARNINGS:** Clear media for adequate visualization is required. Conditions such as corneal haze, corneal opacity or other conditions may inhibit gonioscopic view of the intended implant location. Gonioscopy should be performed prior to surgery to exclude congenital anomalies of the angle, peripheral anterior synechiae (PAS), angle closure, rubeosis and any other angle abnormalities that could lead to improper placement of the stent and pose a hazard. The surgeon should monitor the patient postoperatively for proper maintenance of intraocular pressure. The surgeon should periodically monitor the status of the microstent with gonioscopy to assess for the development of PAS, obstruction of the inlet, migration, or device-iris or device-cornea touch. The Hydrus Microstent is intended for implantation in conjunction with cataract surgery, which may impact corneal health. Therefore, caution is indicated in eyes with evidence of corneal compromise or with risk factors for corneal compromise following cataract surgery. Prior to implantation, patients with history of allergic reactions to nitinol, nickel or titanium should be counseled on the materials contained in the device, as well as potential for allergy/hypersensitivity to these materials. **PRECAUTIONS:** If excessive resistance is encountered during the insertion of the microstent at any time during the procedure, discontinue use of the device. The safety and effectiveness of use of more than a single Hydrus Microstent has not been established. The safety and effectiveness of the Hydrus Microstent has not been established as an alternative to the primary treatment of glaucoma with medications, in patients 21 years or younger, eyes with significant prior trauma, eyes with abnormal anterior segment, eyes with chronic inflammation, eyes with glaucoma associated with vascular disorders, eyes with preexisting pseudophakia, eyes with pseudoexfoliative or pigmentary glaucoma, and when implantation is without concomitant cataract surgery with IOL implantation. Please see a complete list of Precautions in the Instructions for use. **ADVERSE EVENTS:** The most frequently reported finding in the randomized pivotal trial was peripheral anterior synechiae (PAS), with the cumulative rate at 5 years (14.6% vs 3.7% for cataract surgery alone). Other Hydrus postoperative adverse events reported at 5 years included partial or complete device obstruction (8.4%) and device malposition (1.4%). Additionally, there were no new reports of persistent anterior uveitis (2/369, 0.5% at 2 years) from 2 to 5 years postoperative. There were no reports of explanted Hydrus implants over the 5-year follow-up. For additional adverse event information, please refer to the Instructions for Use. **MRI INFORMATION:** The Hydrus Microstent is MR-Conditional meaning that the device is safe for use in a specified MR environment under specified conditions. **Please see the Instructions for Use for complete product information.**

**References:** 1. Ahmed I, et al; HORIZON Investigators. Long-term Outcomes from the HORIZON Randomized Trial for a Schlemm's Canal Microstent in Combination Cataract and Glaucoma Surgery. [https://www.aaajournal.org/article/S0161-6420\(22\)00160-9/fulltext](https://www.aaajournal.org/article/S0161-6420(22)00160-9/fulltext)  
2. Hydrus Microstent Instructions for Use

# Alcon

## Feature LIMBAL RELAXING INCISIONS

area. “If he says yes, I ask whether he sometimes rubs them. Patients who would never say yes if asked whether they rub their eyes, may admit to it, if the question is phrased as ‘Do you sometimes rub your eyes?’—that, they’ll admit to. And if a patient volunteers that when he rubs his eyes, it feels ‘really, really good,’ that person is probably well on his way to keratoconus, regardless of what other testing shows. Such patients should not have incisional keratotomy, in my view.”

In addition to screening questions, diagnostic exams will complete the picture. “Preoperative corneal tomography provides vital information,” says Dr. Nevyas-Wallace. “At the very least, you need corneal topography. Tomography (such as with the Galilei or Pentacam devices) gives you additional information that’s important, both in assessing whether there’s a tendency to ectasia and also in providing a corneal thickness map.”

Dr. Devgan agrees. “I like to do topography, as well as tomography,” he says. “That will not only tell me the corneal astigmatism pretty accurately, but the tomography will tell us anterior and posterior cornea and also give me thickness (pachymetry). If you have access to it, also measure the pachymetry, if possible.”

The pachymetry reading will help guide the subsequent relaxing incision. “If you’re going to do a 500-micron deep LRI and the patient’s corneas are 550 microns, well that will have more of an effect as opposed to a patient with a 650-micron cornea,” Dr. Devgan says. “Even corneal diameter is a factor. If you have a small eye that’s very hyperopic and the patient is getting a 28-D lens, that same size LRI may have a different effect than in a big myopic eye with a 6-D lens. There’s some experience that you have to take into account. However, the nice part is, even if you just attempt it and even if you undercorrect, patients are still improved.”

No two patients’ tissues will respond the same, he continues. “If you compare a 50-year-old cataract patient to a 90-year-old cataract patient, the same incision in those eyes is going to have a different effect,” he says. “That’s partly due to corneal elasticity. It changes as you get older and becomes less elastic. There’s an age component to how much you’re going to treat their astigmatism.”

LRIs can also be used as a touch-up technique. “One of the advantages of LRIs is that they leave the central cornea untouched, unlike LASIK and PRK,” Dr. Nevyas-Wallace says. “Another advantage is that the very patients who most commonly require LRIs—elderly patients having cataract surgery—are excellent candidates for LRIs and are often not such good candidates for LASIK or PRK. Because we get significantly greater astigmatic effect with an LRI as corneal rigidity increases—and it’s well demonstrated that it increases with age—they actually work better in older patients as well. LRIs of relatively short arc length, performed at the 9- or 10-mm optical zone will correct relatively modest amounts of astigmatism, and are also well-suited to

## Nichamin Nomogram for Clear Corneal Phaco Surgery

### Astigmatic Status: Against the Rule

PREOP CYLINDER (D)		30-40 yo	41-50 yo	51-60 yo	61-70 yo	71-80 yo	81-90 yo	> 90 yo
+0.75 to +1.25	nasal limbal arc only						35°	
	paired limbal arcs on steep axis	55°	50°	45°	40°			
+1.50 to +2.00	paired limbal arcs on steep axis	70°	65°	60°	55°	45°	40°	35°
+2.25 to +2.75	paired limbal arcs on steep axis	90°	80°	70°	60°	50°	45°	40°
+3.00 to +3.75	paired limbal arcs on steep axis	o.z. to 8 mm 90°	o.z. to 8 mm 90°	85°	70°	60°	50°	45°

### Astigmatic Status: With the Rule

PREOP CYLINDER (D)		30-40 yo	41-50 yo	51-60 yo	61-70 yo	71-80 yo	81-90 yo	> 90 yo
+1.00 to +1.50	paired limbal arcs on steep axis	50°	45°	40°	35°	30°		
+1.75 to +2.25	paired limbal arcs on steep axis	60°	55°	50°	45°	40°	35°	30°
+2.50 to +3.00	paired limbal arcs on steep axis	70°	65°	60°	55°	50°	45°	40°
+3.25 to +3.75	paired limbal arcs on steep axis	80°	75°	70°	65°	60°	55°	45°
		Degrees of arc to be incised						

The Nichamin nomogram is widely used for LRIs and accounts for the patient's age in determining the degrees of arc to incise. It assumes the temporal incision is first made by creating a two-plane grooved phaco incision (600 µm depth), which is then extended to the appropriate arc length at the conclusion of surgery. (Courtesy of Uday Devgan, MD)

touching up other procedures, such as toric lens implants.”

### Considerations for the Procedure

Whether it's determining when to perform the LRI or the number of incisions, surgeons must consider the risks and their own skill set.

“My preference is to do the LRI before the cataract procedure so as to avoid placing a side port right where an arcuate incision is planned,” says Dr. Nevyas-Wallace. “Placing an arc over a sideport risks perforation. The corneal marking and the incision are done at the beginning of the case.”

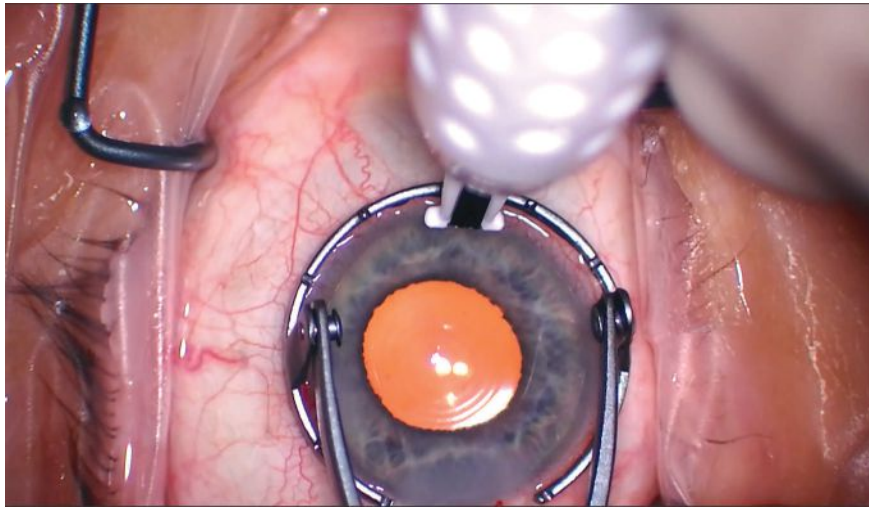
Dr. Devgan says perforation is the worst possible complication of LRIs. “If you need to do an LRI at 500 microns depth and the cornea has a

thickness of 560 microns, that's great; you're not going to perforate,” he says. “But if you end up compressing the corneal tissue or pushing down too hard and the blade goes full thickness and aqueous leaks out, now you've got to put in at least one suture if not multiple sutures to close that to prevent leaking. That's the challenge.” For this reason, Dr. Devgan says he prefers to perform LRIs at the end of a case.

The question of how many incisions are needed depends on the amount of astigmatism, as well as other factors of the surgery itself. “Symmetry is nice, but it can depend on the level of astigmatism. Sometimes a small amount can be taken care of by one incision,” says Lisa Arbisser, MD, an adjunct professor at the University of Utah, Moran Eye Center. “Something

that helped me tremendously was the Mastel keratoscope, which is a simple little ring of lights that goes on to the bottom of the ocular of the microscope. It's so helpful for any astigmatic work including toric because you get a reflex off of the cornea and you also get a reflex off of the lens, which you can then make sure it's 90 degrees apart. And with some practice, you can even pick up 0.75 D or 1 D of astigmatism with that. And that was always reassuring for me, despite any markings or any other equipment, that I was on the correct axis and I could see it change with my LRI/PAK and confirm.”

Surgeons can also pair their phaco incision with an LRI. “If we happen to be operating on the steep meridian, then the surgical incision can



Uday Devgan, MD

**Uday Devgan, MD, performs LRIs manually with the help of a fixation ring marked off in clock hours to guide his incisions.**

be considered one of the astigmatic incisions,” says Dr. Nevyas-Wallace. “A single arcuate incision opposite that gives good effect. Or you can plan the surgery so that the surgical incision is on the steep meridian. That certainly simplifies the vector addition calculations which add the effect of the surgical incision and the astigmatic incisions in order to determine at what axis the astigmatic incision should be placed. Online calculators are helpful, but it’s simplest if the main incision is on the steep axis, which isn’t always possible. It’s hard to make the main incision at 6 o’clock, and if the superior cornea is truncated, it’s hard to make it at 12 o’clock. Location of the cataract incision is determined partly by the corneal anatomy.”

“In general, I tend to do two limbal relaxing incisions, unless I’m pairing it with the phaco incision,” says Dr. Devgan. “If I’m pairing it with a phaco incision, I’ll do one opposite the phaco incision. When you calculate how to do the LRI you have to take into account the effect of your phaco incision. When you’re doing your LRI and the patient’s steep axis is 30 degrees, you can make the phaco incision at 30 degrees and therefore opposite that on the other side I can do another limbal relaxing incision to pair it up with that so I don’t need to have two. As long as I’m placing my

phaco incision on the steep axis then I can just make the LRI opposite. If I’m making my phaco incision somewhere else, then I probably want to do paired LRIs, but I also take into account mathematically what is the effect of my phaco incision on changing the astigmatism.”

### Techniques and Tools For Success

The right technique and the right tools will go a long way for LRIs. One of the first pieces of advice Dr. Nevyas-Wallace offers is regarding fixation of the globe.

“Performing an LRI or AK is significantly safer when the globe is fixated with a surgical instrument. One thing that’s become popular is doing LRIs at the slit lamp,” she says. “In an LRI course I teach, I point out that if you have one hand on the joystick and one hand on the knife, that doesn’t leave you any way to fixate the globe. When performing LRIs at the time of cataract surgery, the surgeon shouldn’t have two hands on the knife, but rather one hand should be fixating the globe. The best way to fixate it is with forceps that grasp limbus-to-limbus, meaning two points 180 degrees apart. But even grasping one point is a lot better than no fixation at all, because without fixation, there’s a risk that the patient suddenly glancing away could

result in disaster.

“That doesn’t mean that you can’t do LRIs in the office,” she continues. “When we do LRIs in the office, we lay the patient down under a surgical microscope so that the surgeon can use one hand to fixate as the other creates the incision.”

Dr. Devgan uses a specially designed fixation ring to hold the eye. “This fixation ring is marked off in clock hours,” he says. “Each clock hour is 30 degrees. If I want to do a 30-degree arc, that’s just one clock hour. I usually put my fixation ring down and you can just trace the blade against that so your arc will be perfect.”

It’s important to accurately mark your steep axis and take cyclorotation into account when the patient is lying down, continues Dr. Devgan. “Surgeons need to have a guarded diamond blade, or at least a guarded blade of some sort—it doesn’t necessarily have to be diamond, but that’s our sharpest option if we can keep it safe and in good condition,” he says. “We need to know what depth to place it, although in general, people will often use 600 microns, which works for just about everyone, however it’s nice to have topography ahead of time to be sure we have regular astigmatism to help us choose our steep axis and to be able to follow that patient afterwards as well.”

LRIs can be made much more predictable by using instrumentation that allows the surgeon to control the incision architecture, says Dr. Nevyas-Wallace. “We used to think that creating uniform depth incisions would solve those problems and give a more regular and predictable effect,” she says. “To some extent, uniform depth incisions are more predictable in that at least the effective axis is what it’s intended to be, but the depth is still an issue. With femtosecond laser corneal relaxing incisions, most nomograms call for an incision depth that’s not really deep enough to get the desired

*(Continued on page 43)*

Help protect their vision from getting worse as they grow.



**MAKE CHILDREN'S SIGHT YOUR FIGHT™.**

ADVERTORIAL

## Educate, Prescribe, Treat: Perceptions About Myopia Management Revealed

Recent survey results indicate the need for intentional, continuous education in the examination room.<sup>1</sup> More ophthalmologists are actively engaged in myopia management and prescribing MiSight® 1 day\* contact lenses for their age-appropriate patients.<sup>2</sup>

By Rupa Wong, MD

**Myopia is a significant public health concern with cases rising across the globe.**<sup>1</sup> As clinicians, we've seen the statistics, which should give us pause. Currently, it's estimated that about 30% of the world's population has myopia, and by the year 2050, that number is expected to grow to 50%.<sup>3</sup>

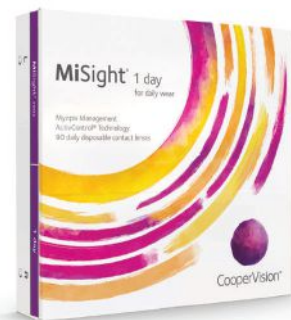
\*Indications for Use: MiSight® (omafilcon A) daily wear single use Soft Contact Lenses are indicated for the correction of myopic ametropia and for slowing the progression of myopia in children with non-diseased eyes, who at the initiation of treatment are 8-12 years of age and have a refraction of -0.75 to -4.00 diopters (spherical equivalent) with  $\leq 0.75$  diopters of astigmatism. The lens is to be discarded after each removal.

1. Luo EL, Wong R. Parental Attitudes Toward Myopia Management. AAPOS 2023 Meeting Poster.

2. AAPOS Myopia Survey. Data on File.

3. Sankaridurg P, Tahhan N, Kandel H, et al. IMI Impact of Myopia. Invest Ophthalmol Vis Sci. 2021 Apr 28;62(5):2.

4. Zhou S, Yang L, Lu B, et al. Association between parents' attitudes and behaviors toward children's visual care and myopia risk in school-aged children. Medicine (Baltimore). 2017 Dec; 96(52): e9270.



American Academy  
of Pediatrics



JULY 2021

DEDICATED TO THE HEALTH OF ALL CHILDREN™

**Statement of Endorsement: Guidance for the Clinician in Rendering Pediatric Care**  
Reducing the Global Burden of Myopia by Delaying the Onset of Myopia and Reducing  
Myopic Progression in Children

A few studies have indicated that early parental awareness of their child's vision is linked to a decreased risk in childhood myopia, however, there's little information available in the literature that sheds light on parents' awareness of and reception to myopia control strategies and treatments.<sup>4</sup>

To gain a greater understanding in this area, I recently surveyed parents with myopia who follow me on social media and have children under 18 about their perceptions of myopia and current treatment options. Based on the results, our study found that, **during the time of their child's visit, almost half of parents were unaware of myopia treatments currently available for their child.**<sup>1</sup>

As a comparison, a separate Harris poll of parents and eye care professionals (ECPs) conducted four years ago found only 33% of parents were familiar with the term "myopia" or how it could affect their child's future vision.<sup>5</sup> In other words, **myopia awareness appears to be growing at a modest pace, but there is still much work to be done.**

### Here are some other findings of my survey<sup>1</sup>:

- Not surprisingly, parents with myopia that was greater than -6.00D were more inclined to be worried or extremely worried about their child's myopia.
- Although 56% of parents believed their child's myopia had worsened over the past year, 49% had never heard of myopia before.
- The top three factors that motivated parents to seek early treatment for their child included rapid progression; threat to their child's overall well-being; and FDA approved treatment with long-term data.
- Of interest, cost did not rise to the top as a treatment barrier for parents. Insurance coverage ranked fourth as a motivating factor to seek earlier treatment, and overall financial cost ranked last for parental justification for not saying yes to myopia intervention.

**What we can glean from these findings is that ongoing outreach is needed to help protect children's eye health.** From my perspective, this encompasses a two-pronged approach. One, ophthalmologists and optometrists should actively embrace myopia management sooner than later, and second, we need to be vigilant in educating parents about myopia management.<sup>1</sup>

## Where Do ECPs Currently Stand on Myopia Management?

A recent survey conducted by the American Association for Pediatric Ophthalmology and Strabismus (AAPOS) garnered responses from 238 pediatric ophthalmologists about their perceptions of myopia and myopia management. A majority of MDs said they partner with three or more optometrists at their practices.<sup>2</sup>

After hearing their recommendation for myopia management treatment, more than 75% of patients pursued it, according to a majority of pediatric ophthalmologists surveyed.<sup>2</sup> Further, a vast majority of our colleagues, over 80%, said they have been practicing myopia management for the past several years, while approximately 87% said they are familiar with soft contact lenses designed for myopia control, and about one-third prescribe MiSight® 1 day\* for age appropriate children. Finally, a majority of doctors surveyed agreed that they would consider fitting children as young as 8 in contact lenses for myopia control.



A separate survey of ODs found **90% of ECPs agreed that they confidently prescribed MiSight® 1 day in their practice,**<sup>6†</sup> and **87% believed myopia management should be a standard of care.**<sup>6∞</sup> Regarding treatment, **ECPs reported 70% of patients purchase MiSight® 1 day following their recommendation.**<sup>6</sup>

\*Indications for Use: MiSight® (omafilcon A) daily wear single use Soft Contact Lenses are indicated for the correction of myopic ametropia and for slowing the progression of myopia in children with non-diseased eyes, who at the initiation of treatment are 8-12 years of age and have a refraction of -0.75 to -4.00 diopters (spherical equivalent) with ≤ 0.75 diopters of astigmatism. The lens is to be discarded after each removal.

† 64% strongly agree, 26% somewhat agree.

∞ 56% strongly agree, 31% somewhat agree.

1. Luo EL, Wong R. Parental Attitudes Toward Myopia Management. AAPOS 2023 Meeting Poster.

2. AAPOS Myopia Survey. Data on File.

5. CooperVision data on file 2019. Myopia Awareness, The Harris Poll online survey 6/27/19 to 7/18/19 of n=1,005 parents (with child age 8-15) in U.S. Number increases to 48% or 52% if parent or child respectively had myopia.

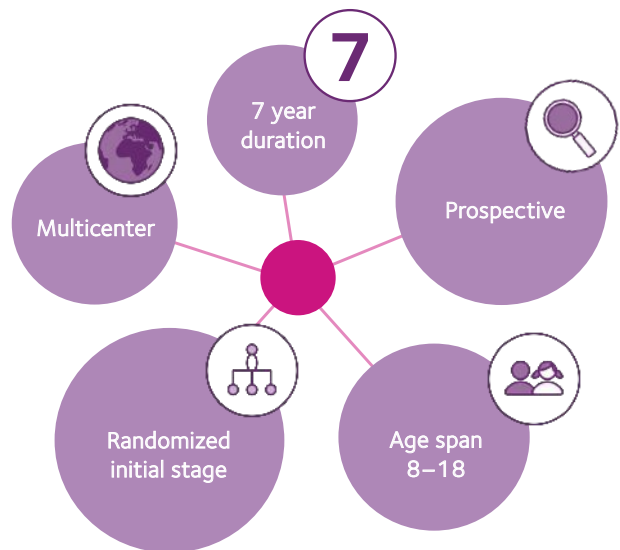
6. CVI data on file 2022. U.S. CooperVision online survey: ECP MiSight® 1 day Perspectives; n=101 ECPs that prescribe MiSight® 1 day.



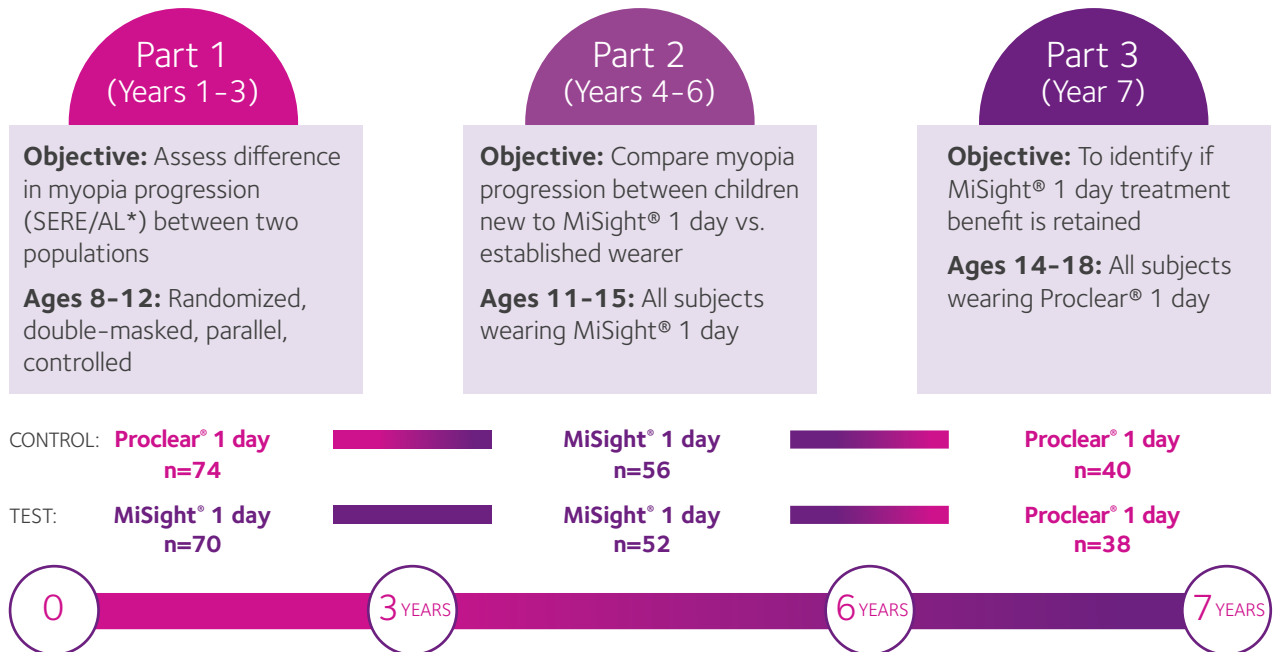
## Put the Facts and Figures into Focus

As a clinician who cares for children’s vision and eye health, it’s heartening to know that many of my colleagues also embrace myopia management, as the need is clearly there and growing.<sup>1</sup> What is also promising is that as recent as March 2020, we now have an FDA-approved treatment to help keep children’s myopia from getting worse so quickly.<sup>7,8</sup> At my practice, I prescribe MiSight® 1 day for my age-appropriate patients based on its strong science and results.<sup>7,8,9\*</sup>

Just consider:  
MiSight® 1 day is the longest continuous soft contact lens study for myopia control.<sup>7</sup>



### MiSight® 1 day clinical trial design



Over a 3-year period, MiSight® 1 day slowed the progression of myopia in children by 59% on average, and 41% of eyes had no progression.<sup>8†</sup>

Additionally, on average, age-appropriate children wearing MiSight® 1 day progressed less than -1.00D over 6 years.<sup>7‡</sup>

\*Indications for Use: MiSight® (omafilcon A) daily wear single use Soft Contact Lenses are indicated for the correction of myopic ametropia and for slowing the progression of myopia in children with non-diseased eyes, who at the initiation of treatment are 8-12 years of age and have a refraction of -0.75 to -4.00 diopters (spherical equivalent) with ≤ 0.75 diopters of astigmatism. The lens is to be discarded after each removal.

† Compared to single vision lens. -0.25D or less of change. Fitted at 8-12 years of age at initiation of treatment.

‡ Fitted at 8-12 years of age at initiation of treatment.

1. Luo EL, Wong R. Parental Attitudes Toward Myopia Management. AAPOS 2023 Meeting Poster.

7. Chamberlain P, Arumugam B, Jones D et al. Myopia Progression in Children wearing Dual-Focus Contact Lenses: 6-year findings. Optom Vis Sci 2020;97(E-abstract): 200038.

8. Chamberlain P, Peixoto-de-Matos SC, Logan NS. A 3-year randomized clinical trial of MiSight lenses for myopia control. Optom Vis Sci. 2019 Aug;96(8):556-567.

9. Chamberlain P, Arumugam B, et al. Myopia progression on cessation of Dual-Focus contact lens wear: MiSight 1 day 7 year findings. Optom Vis Sci 2021;98:E-abstract 210049.

Finally, MiSight® 1 day are **the first and only**<sup>§</sup> **FDA-approved\*** lenses to slow the progression of **myopia** when prescribed for children 8-12 years old at the initiation of treatment.<sup>8</sup>◊

With childhood myopia on the rise,<sup>3</sup> it's paramount that ECPs continue to educate in the examination room, prescribe treatment that not only corrects refractive error but also helps slow myopia progression, and rely on valid, long-term science and clinically meaningful results to guide our treatment decisions.

As ophthalmologists, we owe our youngest patients at least that.



Dr. Rupa Wong is a board-certified pediatric ophthalmologist and the managing partner of Honolulu Eye Clinic. She also serves as Clinical Associate Professor at University of Hawaii School of Medicine.

This article was sponsored by CooperVision, Inc.



**MAKE CHILDREN'S SIGHT YOUR FIGHT™.**



\*Indications for Use: MiSight® (omafilcon A) daily wear single use Soft Contact Lenses are indicated for the correction of myopic ametropia and for slowing the progression of myopia in children with non-diseased eyes, who at the initiation of treatment are 8-12 years of age and have a refraction of -0.75 to -4.00 diopters (spherical equivalent) with ≤ 0.75 diopters of astigmatism. The lens is to be discarded after each removal.

§ Only FDA approved soft contact lens designed for myopia control in the U.S.

◊ Compared to a single vision 1 day lens over a 3 year period.

3. Sankaridurg P, Tahhan N, Kandel H, et al. IMI Impact of Myopia. Invest Ophthalmol Vis Sci. 2021 Apr 28;62(5):2.

8. Chamberlain P, Peixoto-de-Matos SC, Logan NS. A 3-year randomized clinical trial of MiSight lenses for myopia control. Optom Vis Sci. 2019 Aug;96(8):556-567.

(Continued from page 38)

effect. Consequently, the arcs are longer and/or the optical zones smaller than they might ideally be. We know that the longer the arc, especially beyond a certain point, the greater the induced aberration.”

One of the most significant sources of inaccuracy is that the effective portion of a limbal relaxing incision is usually far shorter than the incision length on the surface, explains Dr. Nevyas-Wallace. “Most manual corneal incisions are shallower at each end than they are at the center of the arc. At the slit lamp, blade incisions are shallow at both ends. Only the deep portion has useful astigmatic effect,” she says. “So a 45-degree arc may actually be at the intended depth for only 30 degrees. But here’s the problem: a diamond blade doesn’t reach the micrometer-set depth until it’s been cutting through tissue. Consequently, the portion at the intended depth is not the central 30 degrees of that arc. The effective portion is nearly the terminal 30 degrees, so the effective axis is likely to be way off.”

Dr. Nevyas-Wallace says it’s important to consider the early days of elevation corneal topography to understand how tools have been developed. “In the early days of elevation corneal topography, I noticed that the

arcuate incisions were having more effect at the center of the incision than at the two ends,” she says. “This was leading to induced astigmatism at oblique axes. I’m not the first person to notice that; it’s called keratopyramis because it does look sort of like a pyramid. There was a procedure designed to correct this (described by Canrobert Oliveira, MD, from Brazil), in which a smaller incision was made just peripheral to each end of the AK in order to augment the effect at the ends. And someone else, also from Brazil, suggested placing the smaller incisions just central to LRIs. At least until recently, you could buy markers from Mastel for the ‘Canrobert C Procedure.’ But the problem is that additional incisions can have unexpected effects as well and it seemed to me that if we could only make our incisions uniform depth, that would solve the problem.”

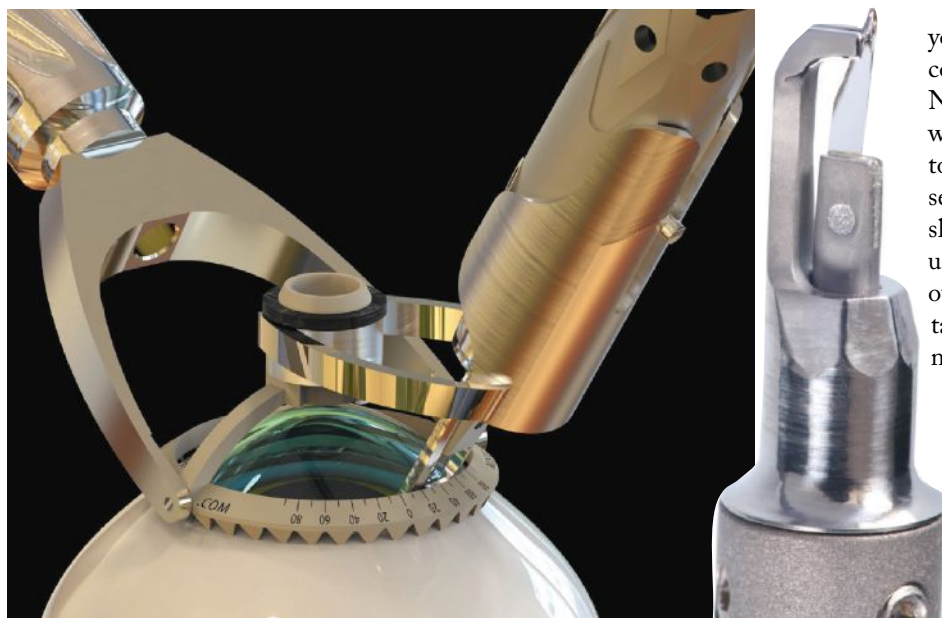
Dr. Nevyas-Wallace says a modification to knives used for radial keratotomy helped improve LRI outcomes. “First, the DuoTrak/Genesis knife didn’t allow the surgeon to visualize the blade cutting an arcuate incision, as it was designed for radial incisions, not arcuate incisions,” she says. “The solution was a diamond knife whose blade was mounted just a little bit in front of the footplates, which

Mastel made for me. But the other issue was that, to my surprise, I found that for a uniform depth incision, the uneven effect of the incision was less pronounced, but it still existed. There continued to be greater effect at the center of the incision. That was when I realized that indeed the center has to be the area of greatest relaxation because each end is stabilized by an intact cornea. Any incision is apt to gape the most at its center. In order to reduce the effect of the arc’s center, I started making the arcuate incisions shallower in the center. That helped, but didn’t solve it completely. I made the arcs more and more shallow at the center until there was no longer an uneven effect. Surprisingly, I was also getting the desired astigmatic effect with shorter incisions.”

While Dr. Nevyas-Wallace continued doing LRIs that way, it occurred to her that a femtosecond laser might be able to control the incision architecture. She says that after working with a team of researchers in Switzerland, they found that her “‘shallower in the center incisions’—which she calls ‘Bridge AK’ (because the shape reminded her of a bridge)—induced a lot less aberration. The modeling also showed that a Bridge AK incision actually gets greater astigmatic effect—15 percent more in that [Swiss] study.

“The next question was how would you know just what that Bridge AK contour should be?” continues Dr. Nevyas-Wallace. “We’re developing a way to make this capability available to surgeons. This will tell the femtosecond laser just what the arc’s shape should be. Creating manual LRIs that use this principle is an improvement over uniform depth incisions and certainly over traditional shallow-ended manual LRIs.”

**Tools such as the Bridge AK knife (right) and the arcuate compass (left), both from Mastel, can improve accuracy of manual LRIs. The compass is used to make an arcuate incision at a lesser depth, then the Bridge AK knife deepens the two ends.**



However, Dr. Nevyas-Wallace says manual LRIs don't need to be done freehand. A helpful tool to consider is an arcuate compass (Mastel), that allows guidance of the manual incision, she says. "Now, that alone doesn't give you a bridge incision or even uniform depth because the diamond, as I mentioned, doesn't achieve the desired depth until it's been moving through tissue. Even then, it achieves full depth only if it's applanating the cornea. Applanating the cornea is counterintuitive. I can't think of anything else we do in cataract surgery or corneal surgery in which you press hard enough to dent anything in. Normally, we pride ourselves on not doing that. And yet in this particular situation, the desired depth is not achieved unless the footplates applanate the cornea," says Dr. Nevyas-Wallace.

The Bridge AK knife has a vertical "enhancement" edge sharp only for the distal 300 microns, she continues. "We use the compass to make an arcuate incision at lesser depth and then use the Bridge AK knife to deepen the two ends. This incision architecture is often detectable at the slit lamp and the results are more predictable," Dr. Nevyas-Wallace says.

Predictability may be improved with the use of nomograms and femtosecond lasers. Dr. Devgan recommends starting with a simple nomogram proposed by Kevin Miller, MD, of UCLA Health. He explains:

- use 1 clock hour of paired incisions for 1 D of corneal astigmatism;
- note that 1 clock hour is 30 degrees;
- vary this with the patient age;
- do a little more in younger patients (<60);
- do a little less in older patients (>80);
- take into account the effect of your phaco incisions;
- if operating temporally, more LRI arc length for WTR, less for ATR.

The Nichamin nomogram (*Figure 1*) is another vetted nomogram, Dr. Devgan adds.

Dr. Whitman recommends speaking with colleagues about their nomogram preference if you're just starting out with LRIs. Using a femtosecond laser has helped him as well.

“**As our diagnostic equipment and technology improve, we'll be able to be even more precise and get even better results.**

— Anita Nevyas-Wallace, MD

"I have my own self-generated nomogram developed over the years, but there are a lot of published nomograms that you can use for accurate, long-lasting astigmatism correction," Dr. Whitman says. "A lot of that has to do with doing adequate depth, which has to be at least 80 percent or more depth because you don't want the effect to go away. In the past people may have avoided doing LRIs thinking the effect goes away too soon. But a lot of people were afraid to go deep, only doing 50 to 60 percent depth. Incisions like that will close up. We always went for 80 to 90 percent depth when we used a diamond blade for manual LRIs, and we would do ultrasound measurements over the area so we could be more accurate.

"We now routinely use the laser for LRIs. It's much easier using modern lasers because they'll take a measurement, and if you tell it to do 80 percent, it's going to do 80 percent," he continues. "It takes all of the guesswork out of it. It can make sure you're doing a consistently deep incision, at a consistent length, in a consistent optical zone because the smaller the optical zone and the longer the incision, the more effect you're going to get."

Dr. Whitman advises that every femtosecond laser is somewhat different. "They don't all measure the depth

in the same manner, so my advice would be to know your laser well so you can get the best performance from your LRIs," he says. "If you don't get enough correction or you overcorrect, it's not the laser's fault. You have to figure out what to do differently."

## Complications

Aside from the aforementioned perforations, surgeons should be aware of other complications involving LRIs.

"People do get concerned with flipping the axis, and we can overcorrect," says Dr. Arbisser. "There are some people who will make it a full thickness, nasal clear corneal incision that they never open as another option for treating against-the-rule astigmatism along with their temporal clear corneal incision that they use for the surgery. That's another route I never chose as that's now through-and-through the incision with a very rare—but potential—risk for endophthalmitis."

Along with overcorrection, Dr. Nevyas-Wallace mentions ectasia. "This can occur either because the incision is longer than that cornea can tolerate or because the patient had undetected subclinical keratoconus," she says.

Dr. Whitman says postop topical antibiotics are important to prescribe. "There are a lot of surgeons who put antibiotics inside the eye at the end of surgery, but don't place the patient on topical antibiotics afterwards," he says. "I think you need them. We learned that the hard way when we were doing dropless surgery for a while and LRIs would sometimes get inflamed. There's always the possibility of bacteria from the eyelid and eyelash junction rubbing over the LRI area, causing an infection or ulcer."

Dr. Nevyas-Wallace expects LRIs will remain an important technique for refractive cataract surgeons. "I think it's very important to be able to do LRIs and to be able to do them safely and precisely," she says. "As our diagnostic equipment and technology improve, we'll be able to be even more precise and get even better results." ◀

YOU'RE THERE *for them.*  
WE'RE HERE *for you.*

Care is everything. Integrated EHR/PM software makes healthcare *better for everyone.*

**BELIEVE IN BETTER®**

[NextGen.com/Better-Oph](https://NextGen.com/Better-Oph)



© 2023 NXGN Management, LLC. All Rights Reserved. NextGen is a registered trademark of NXGN Management, LLC. All other names and marks are the property of their respective owners.



# CROSS-LINKING: BEST PRACTICES

Stabilizing the cornea takes significant work—in and out of the chair. Here, veteran surgeons share their top tips for cross-linking patients.

**CHRISTINE YUE LEONARD**  
SENIOR ASSOCIATE EDITOR

**C**orneal cross-linking brought about a paradigm shift for keratoconus treatment. “Before this procedure was around, we’d have keratoconus patients getting gas-permeable lenses then scleral lenses and then transplants,” recalls Edward Manche, MD, a professor of ophthalmology and director of the cornea and refractive surgery service at Stanford University. “To have this technology that can save people from the need for invasive transplantation procedures is really remarkable. It’s an exciting time for cross-linking, and we’re just at the beginning of the journey.”

We spoke with several experts about the ins-and-outs of the cross-linking procedure. Here, they share their tips and insight on patient selection, protocols and the future.

## Identifying Early Keratoconus

The time to catch keratoconus is before any visible signs of the disease such as obvious coning, iron rings or Vogt striae are seen on physical exam. Posterior corneal elevation changes are some of the first early warning signs of keratoco-

nus, with the classic pattern of inferior steepening. Less common appearances can also include central or superior steepening.

In addition to topography, clinicians use tomography to further analyze the shape of the eye. “Pentacam’s parameters, including the Belin Ambrósio Enhanced Ectasia Display score, help us differentiate between normal and abnormal corneal shape,” says William Trattler, MD, of the Center For Excellence In Eye Care in Miami.

This screening index analyzes both anterior and posterior corneal elevation. Two pachymetry profiles: corneal thickness spatial profile and percentage thickness increase assess how thickness is distributed across the entire cornea and how these changes progress, compared with the normal population.

According to Audrey R. Talley Rostov, MD, a partner at Northwest Eye Surgeons in Seattle, epithelial thickness mapping is an indispensable modality for keratoconus detection and evaluating potential cross-linking candidates. She says that epithelial mapping is a useful adjunct to tomography, particularly in borderline cases, because it can help to confirm irregular astigmatism or inferior steepening that may be unclear on tomography via a corresponding thin area seen on epithelial mapping.

“One of the earliest signs is thinning in the area of steepening,” she says. “The superior epithelium should be thinner than the inferior epithelium, and the inferior epithelium should be thinner than the center epithelium. If the inferior is thinner than the superior, you know that there’s a thin spot there and you want to be very suspicious for keratoconus. On the other hand, if you see thickening in the area of steepening area, then the patient may be an eye rubber or there could be some dry eye that’s looking like a false positive for keratoconus.”

“This often comes up in patients who want refractive surgery,” she continues. “Patients come in for a refractive surgery evaluation, and they’re kind of borderline or their epithelial thickness mapping isn’t definitive or it’s a little iffy. Maybe there’s some asymmetric astigmatism. The first thing I do is treat dry eye. Dry-eye disease can masquerade as some inferior steepening. I have the patient come back and repeat the measurements. For patients with

This article has no commercial sponsorship.

Dr. Rostov consults for Glaukos and Zeiss. Dr. Manche consults for Zeiss. Dr. Trattler consults for Glaukos and has a financial interest in Epion Therapeutics. Dr. Baartman is a consultant and investigator for Glaukos.



# Serum Tears Made Simple.

Give your patients **fast, hassle-free access** to serum tears.

Eye care providers have offered serum tears to patients with ocular surface conditions for over 30 years, but access to these drops has been limited.

With **Vital Tears**, you and your patients now have access to:

- **Rapid serum drop delivery**
- **Convenient blood draw options**
- **Affordable payment options**
- **Superior customer service**



DOWNLOAD OUR  
PHYSICIAN PACKET



**Vital Tears**<sup>™</sup>  
THE LEADER IN SERUM TEARS

[www.vitaltears.org](http://www.vitaltears.org)

good best-corrected vision who aren't interested in refractive surgery and were referred to me for some astigmatism, I'll wait and see them back depending on their age. If it's a younger patient, in the pediatric or adolescent age range, I'll see them back in three or four months to check whether the dry-eye treatment resolved the issue. If it's an older patient, it could be six months. If the patient is interested in refractive surgery and their epithelial thickness mapping looks borderline, I may offer an ICL instead of a laser vision correction treatment."

"Be sure to do tomography and epithelial thickness mapping first before the patient has had drops in their eyes for the exam for the most accurate results," she adds.

One of the newer keratoconus diagnostics available is genetic testing. While it's not typically administered as part of a standard screening, one genetic testing scenario might be when a relative of a keratoconus patient is interested to know whether or not they might have the same condition. "Genetic testing isn't a definitive diagnostic test," cautions Brandon Baartman, MD, of Vance Thompson Vision in Omaha, Nebraska. "We still want to see other signs of keratoconus progression before we offer a cross-linking procedure. But we also know to maybe follow those patients a little closer if they have a positive genetic test and keep them on our radar."

### To Treat or Not to Treat?

When it comes to young keratoconus patients, treating early and immediately is the usual mantra—but how young is too young to cross-link? "This is a great debate among many anterior segment surgeons, particularly corneal surgeons," Dr. Baartman says. "We're asked that all the time, especially in our referral networks when there's a young kid. Doctors see advancing astigmatism and worry about keratoconus. The FDA approval age is 14; however, the earlier the disease is treated, the better. We know that cross-linking is effective and that preventing the development of visually devastating keratoconus is a significant

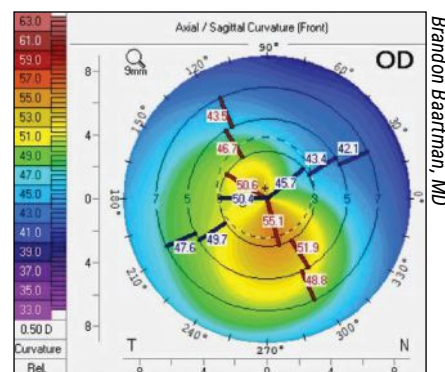
quality of life enhancer. I wouldn't hesitate to treat a patient younger than 14 if there's clear evidence of keratoconus and progression—even if it required, which in some cases it has, bringing a patient to a pediatric hospital and using general anesthesia to perform a bilateral same-day procedure. It's very meaningful to that patient and family."

Likewise, Dr. Rostov says, "If I'm really concerned about progression of disease in a pediatric patient, I wouldn't necessarily wait for them to show a lot of progression, because that could risk vision loss."

Fewer and fewer keratoconus patients today go on to require corneal transplants because of cross-linking. "Now, we're trying to identify these patients at a younger age," says Dr. Manche. "Most patients we end up seeing already have moderate to advanced disease and now need specialty contact lenses. There's been a number of efforts to expand screening to younger people." Dr. Manche is involved in a small company that's developing an app with a phone adapter to help primary care doctors or pediatricians to identify possible keratoconus suspects for subsequent referral. "If we can identify patients earlier, and cross-link them to stabilize the cornea, we can hopefully get them in spectacles or soft contact lenses instead."

Though keratoconus is usually first diagnosed in young and adolescent patients, the disease doesn't limit itself, and neither does the treatment. "A few years back when I reviewed my—at that point about 1,000—cross-linking cases," says Dr. Rostov, "I discovered that about a third of my patients who had cross-linking were over the age of 40. Cross-linking isn't just for younger patients; you can actually get good results with older patients. In fact, despite some of the older myths out there, keratoconus can progress after age 40. I've seen a small spike in cases from the ages of 40 to 50. I've also seen progression, although rarely, in patients at age 50 or even 60. Again, it's more unusual, but it can occur."

"Age isn't a factor," agrees Dr. Trattler, who's successfully treated a 79-year-



**A topographic map from the Pentacam of a 37-year-old patient with increasing refractive cylinder suggesting an irregular astigmatism with asymmetric bow tie and skewed radial axis.**

old keratoconus patient and a patient in their 80s. "We found that in our patients who had a delay from the time they came in to see us to actually having a cross-linking procedure, of those 40 years and older, about 41 percent progressed at a rate of one diopter per year or more. So, just because a patient is 50, 60 or 70 doesn't mean they can't progress. Similarly, just because a patient has been stable for several years, doesn't mean they'll be stable forever. Consistent follow-up is important."

Indeed, despite the much lower odds of keratoconus progression after age 40, the likelihood never reaches zero.<sup>1</sup> In patients over 40, some mild posterior corneal steepening and thinning may occur, independent of normal age-related changes.<sup>2</sup> Follow-up with corneal tomography is advised, as well as counseling to avoid eye rubbing.

While progressive disease is a call for prompt cross-linking, stable disease doesn't warrant treatment in every single case, especially in older patients. Dr. Manche says that many of his older patients assume they need corneal cross-linking simply because they have keratoconus. "But we go back and look at their records, and they've had no change in their prescription or topography," he explains. "Keratoconus can stabilize on its own. You don't want to perform surgery unnecessarily on a patient in their 30s or 40s with long-standing but unchanging keratoconus. The FDA specifically approved cross-linking for

Brandon Baartman, MD



the treatment of progressive, unstable keratoconus, so it's important to make sure you're not treating someone who's already stable and not going to rapidly progress."

## Documentation

"Stabilizing an actively warping cornea is one of the most important things we can do for eye health, but for better or for worse, much of the decision to cross-link is dictated by what we know insurance will deem medically necessary," Dr. Baartman says. "We practice in a climate where there's an expensive procedure to perform and we also need to ensure we remain whole as a business while offering this."

Not all commercial insurance plans cover the FDA-approved epithelium-off corneal cross-linking procedure; those that do usually have progression criteria such as an increase of 1 D in Kmax, astigmatism or myopia over 12 to 24 months.

"Sometimes the prior authorization comes back as a 'no,' and so then our plan is to follow the patient for an additional three months or so, depending on their age," Dr. Baartman says. "If it's a patient in their 40s, we're not as concerned about rapid progression as we would be with a patient in their mid-teens. We bring the youngsters back pretty quickly to repeat those tests, and usually in those scenarios, if it's true keratoconus that's progressing as we suspect, there will be some changes we can notate that will allow us to move into the treatment phase."

"Generally, we look at some of the criteria that insurance deems important, such as a reduction in best-corrected visual acuity that we deem is the result of keratoconus," he continues. "Other criteria might include an increase in corneal steepness or keratometry readings or progression of a refractive error."

"But at the end of the day, we also believe that no one is born with a keratoconic cornea," he says. "We know that if we see one in the clinic, it hasn't always been like that, so at some point it's progressed. While we know cross-linking is medically necessary, the patient's

insurance company wants to see that too. The onus is on us to demonstrate that to them."

Dr. Baartman says that this is one of the main things his practice talks about when asked about how they conduct their keratoconus screenings. "You have to be an investigator when you get a keratoconus referral," he says. "One of most valuable things you can do for that patient, and for your team and the doctor's time, is to gather the patient's prior ocular information, get referral notes, or if there aren't any, call the patient so we know which doctors to call. We want to get as much information as we possibly can so that at the time of the evaluation, we can compare that to our current information. We don't want to have to see them once and then wait a number of months to see them again to make our determination. Sometimes there's a gray area if a patient wasn't measured using the same tool, but I think we all agree that if there's clear keratoconus and even the slightest bit of evidence, it's worth considering that patient's cornea unstable and ready to be cross-linked."

Dr. Baartman notes that insurance coverage of cross-linking is more widespread today than in the past. "I'm spending a lot less time on the phone with insurance companies pleading the case, particularly in young individuals, so I think that probably points to increased awareness of the significance of the condition. But every once in a while, we'll still need to demonstrate further progression to get a patient cross-linked."

## Patient Counseling

Many patients are under the impression that cross-linking is like a laser refractive procedure and that it'll improve their vision, says Dr. Manche. "It's important to emphasize that cross-linking is meant to stop keratoconus progression, not improve vision," he says. "There's typically not much improvement in vision."

"We also have to warn patients of the risks associated with cross-linking," he continues. "Patients may get transient corneal haze. Some will develop infectious keratitis, corneal ulceration, infections or even neurotrophic corneal

neuropathy. That being said, without the treatment, patients are going to have progressive keratoconus. So, if they don't get it treated, it'll invariably worsen and then they'll potentially need some type of corneal transplantation."

Dr. Baartman says that on the day of the procedure, he spends most of the time talking about the disease. "While I don't want to minimize the actual procedure itself, I make sure to talk about the etiology of keratoconus." He says most of those patients are eye-rubbers, so he explains that eye rubbing weakens the cornea and that continuing to do so could compromise the cornea to the point that cross-linking re-treatment might not be enough. "I spend most of the time getting to the why of keratoconus and why stopping eye rubbing is important."

"Eye rubbing can exacerbate the disease at any age, but especially in young patients," Dr. Rostov points out. She adds that eye rubbing probably doesn't cause keratoconus. "Plenty of patients who rub their eyes will have astigmatism but not keratoconus, and there are patients with keratoconus who don't rub their eyes. It's likely there's a genetic predisposition in addition to the environmental eye-rubbing factor that contributes to keratoconus progression."

## Contraindications

Cross-linking isn't advised in certain patients, such as those with insufficient corneal stroma. Those with the following may not be good candidates:

- **Active infections.** "A history of herpes keratitis is concerning because herpes can be reactivated with ultraviolet light," Dr. Manche explains.

- **Corneal scarring.** "You may be able to stabilize the cornea in a patient with dense scarring, but if the scarring is too dense you're not going to gain any benefit from the cross-linking and will need to do a transplant either way," Dr. Manche says.

- **Inability to cooperate.** Patients who aren't able to fixate on the light during the UV irradiation aren't ideal candidates. "Theoretically, you could cross-link a patient under general

anesthesia,” Dr. Manche says. “We don’t do that here at Stanford, but you could certainly do that.”

• **Autoimmune diseases.** “Sjogren’s or rheumatoid arthritis—those are conditions where you can get corneal melts and poor healing,” he says.

Some conditions may predict poorer outcomes with cross-linking. “A patient with advanced keratoconus can get some effect from cross-linking, but they’ll still be left with pretty significant distortion and will need specialty contact lenses,” Dr. Manche notes.

“Another condition that tends not to do as well with cross-linking is pellucid marginal degeneration,” he adds. “Cross-linking isn’t as effective, likely because the thinning is more peripheral and inferior as opposed to central or paracentral. Cross-linking treats the central 9 mm of the cornea, so quite possibly we’re not targeting the main weak areas of the cornea in a patient with pellucid marginal degeneration. There has been some work done with customized cross-linking, where it could be done more inferiorly in these cases, and that might improve efficacy.

“Patients who have corneal ectasia following keratorefractive surgery tend to do slightly less well with cross-linking than those with keratoconus,” Dr. Manche says. “We aren’t sure why cross-linking isn’t as effective in post-LASIKPRK/SMILE ectasia, but in my experience, there isn’t as much flattening of the cornea.”

Patients who rub their eyes after cross-linking are at increased risk for needing a second treatment, Dr. Trattler points out. “In our experience, the need for second treatments is about one to two percent,” he says. “Follow-up after cross-linking is important, every six to 12 months to monitor the shape of the cornea. The good news is retreatments are very safe and effective.”

## The Current Cross-linking Procedure

Cross-linking uses a photosensitizer (such as riboflavin) and an UV-A light source to create a photochemical reaction that strengthens the chemical

bonds of collagen fibrils in the cornea. The cross-linking process also occurs naturally with age, which is why keratoconus is thought to stabilize as patients get older. For both procedural and age-related processes, oxygen availability is key.

The FDA-approved iLink procedure with the KXL System, first involves epithelial debridement under topical anesthesia to approximately 9 mm. One drop of riboflavin (Photrex Viscous, riboflavin 0.146% 5’-phosphate in 20% dextran ophthalmic solution) is then applied topically every two minutes for 30 minutes. The eye is observed for yellow flare. If no flare is detected, one drop of Photrex Viscous is instilled every two minutes for an additional two to three cycles until yellow flare is observed. If corneal thickness is less than 400  $\mu\text{m}$ , hypotonic Photrex (0.146% riboflavin 5’-phosphate ophthalmic solution) is instilled every five to 10 seconds until corneal thickness is at least 400  $\mu\text{m}$ . Finally, the eye is irradiated at 3 mW/cm<sup>2</sup> at a wavelength of 365 nm for 30 minutes, with continued instillation of one drop of Photrex Viscous every two minutes for 30 minutes.

“We use the FDA-approved Glaukos technology to cross-link patients,” says Dr. Trattler. “We do a variation of the continuous 30-minute UV light where we pulse the light, on for 15 seconds and off for 15 seconds. While the amount of energy can’t be changed, the time of the procedure can be. For example, for a patient with thin corneas—let’s say 200  $\mu\text{m}$ —and advanced keratoconus, instead of doing a full 30-minute treatment, you could certainly achieve an effect in 15 or even 10 minutes of UV light exposure because the cornea is so thin that the full 30 minutes aren’t necessary.”

Most surgeons use a 400- $\mu\text{m}$  cutoff for cross-linking but, as Dr. Trattler notes, some thinner corneas can undergo cross-linking as well. “Different doctors use different cutoff points,” Dr. Manche notes. “Intraoperatively, you can swell the cornea using hypotonic saline or hypotonic riboflavin. The cornea soaks it up like a sponge. After epithelium

removal and installation of the riboflavin, check the pachymetry. If it’s less than 400  $\mu\text{m}$ , you want to then swell the cornea. If you’re starting at less than 400  $\mu\text{m}$ , you can run into situations where you can’t swell the cornea enough, and then you might be in a situation where it’s unsafe to perform cross-linking. If the cornea is significantly thinner, such as 370  $\mu\text{m}$  or less, these patients typically won’t be good candidates for epithelium-off cross-linking. They’d benefit from epithelium-on cross-linking. Though it’s not yet FDA approved, there are a number of protocols that have been employed.”

Corneal cross-linking is sometimes performed in advance of refractive surgery to achieve better visual outcomes or in combination with intrastromal corneal ring segments. In the case of the former, Dr. Rostov says, “I always tell patients that the goal of cross-linking is to prevent progression of disease. It’s not to reverse disease that’s already there. Cross-linking often produces some mild flattening of the cornea, which can give patients a better fit for glasses or contact lenses to improve best-corrected vision. Some patients who have keratoconus with mild progression want a topography-guided treatment later on. If they have cross-linking first, we can then potentially do a topography-guided treatment to improve their vision—not in all cases, but in some.”

Intacs were originally approved for treating low myopia. “They were pretty much abandoned once excimer lasers were introduced,” Dr. Manche says. “Now, they’ve been repurposed to try to regularize the corneal curvature, and they can be quite effective in some cases.”

While Intacs help regularize the corneal shape, helping reduce astigmatism and irregularity, they don’t stabilize the cornea. Dr. Manche says, “In our system, what we typically do is perform cross-linking first to allow for corneal remodeling and reshaping, and then, depending on the patient, we’ll insert Intacs ring segments. I don’t think there’s a right or wrong order in which to do the procedures. Some people

# Restore Balance for MGD Patients

with Retaine® MGD® Ophthalmic Emulsion



Retaine® MGD® targets all three layers of the tear film for long-lasting comfort.

- ✓ Preservative-Free
- ✓ Developed for MGD Patients
- ✓ Lipid Active Ingredients
- ✓ Positively Charged Nano-droplets



For more information call (800) 233-5469  
or visit [www.ocusoft.com](http://www.ocusoft.com)

Part of a complete line of Retaine® Brand Products

perform cross-linking after Intacs, and others do combined. The way I look at it is that with cross-linking, you get some flattening—usually 1 to 1.5 D—but occasionally you get quite a bit of flattening, and some shifts in the orientation of steepness or axis of irregular astigmatism. When you place the Intacs, you're using that data not only for the placement of the rings but also for their dimensions."

Dr. Trattler doesn't implant Intacs. "Most of our patients who get cross-linked will get improvement in corneal shape over months and years," he says. "Some doctors feel that Intacs could be additive, but I certainly see patients' improvement over time [with only cross-linking]. We also recommend scleral contact lenses for patients with moderate to advanced keratoconus, and these patients see well. So, if a patient has moderate to advanced keratoconus, you can put Intacs in and they're still going to need scleral contact lenses. Intacs won't change that need. So, we focus on the cross-linking procedure. Our main additional procedure is the ICL for patients who have improvement in corneal shape, a decrease in astigmatism and reasonably good BCVA. We use the ICL to get rid of a lot of myopia."

Dr. Baartman says he used to implant Intacs in certain patients, such as those "who have more mild disease and a shift of the cone where an Intacs ring might be able to centralize some of the aberration profile that developed from inferior steepening." He created the channel for the Intacs ring or rings using a femtosecond laser, placed the rings and then debrided the epithelium and proceeded with cross-linking.

"I've stopped doing that as frequently, largely because of the quality of vision that a lot of patients are getting from scleral lenses," he continues. "A lot of our referral network had made mention of the fact that sometimes after Intacs, it's harder to fit a good scleral lens. So, if somebody was going to be in a scleral lens anyway, it probably didn't make sense for us to be putting in Intacs. On rare occasions, I'll still consider it, but much less

frequently, with the widespread acceptance of scleral lenses and excellent visual acuity patients are getting."

He says scleral lenses are his third stage for a keratoconus visual rehabilitation treatment plan. "The first thing is corneal stabilization," he explains. "A concern could be, 'Well, a patient is already in scleral lenses. Do they need to be cross-linked?' The answer is probably still yes. We want to, in essence, re-strengthen the cornea to a level at which it'll stop progressing, to maintain what the patient has in scleral lenses, even if they're already seeing well in scleral lenses. I think that's the perfect time to cross-link. Once you go through that stage of treatment in both eyes, and the second stage of healing—management of epithelial closure and early pain and vision rehabilitation—then you go to long-term vision rehabilitation with things such as scleral lenses or consideration of topography-guided ablations, in the right corneas."

Dr. Baartman adds that there are a number of protocols that have been developed for simultaneous or staged cross-linking with corneal refractive procedures—mainly PRK since it's more tissue-sparing than LASIK. "My current protocol is to approach stabilization first using cross-linking and ensure that we've demonstrated stability—I like a course of at least nine to 12 months," he says. "Then we can consider vision correction or vision rehabilitation measures like topography-guided ablations, in the scenario where it makes sense: enough corneal tissue and a motivated patient who accepts the need for remaining in glasses or contacts but wants some improvement in the overall correction or quality of vision in that correction. In that scenario, topography-guided ablations can be really beneficial. I don't commonly do simultaneous in my practice, like the Athens protocol, but is something to be considered as cross-linking device technology continues to improve."

## Postop Management

Ensuring rapid healing of the epithelium is the main goal following epi-

thelium-off cross-linking. "A bandage contact lens is used, and patients are placed on antibiotic drops [usually fluoroquinolones] for prophylaxis," explains Dr. Trattler. "Patients receive a topical steroid and can use an NSAID for pain. The eye should heal over a period of about three to five days."

Sometimes there's delayed re-epithelialization due to anatomical issues such as floppy lid syndrome or an external disease. "For whatever reason the patient is taking a long time to heal, sometimes amniotic membrane grafting or a temporary tarsorrhaphy is needed," Dr. Manche says.

## Epi-on Anticipation

Most surgeons agree that a major challenge of the current approved cross-linking procedure is the need for epithelial debridement and subsequent re-epithelialization healing stage. An advantage of epithelium-on cross-linking is much faster healing. While patients will still need to recover from a UV insult to the cornea, Dr. Manche explains, even with a bandage lens, they'll still heal faster than if they'd had epithelial debridement. "Without an epithelial defect, the risk of infectious keratoconus is drastically reduced and the visual rehabilitation is significantly better," he says. "Patients usually get back to work faster and it doesn't have as much impact on their vision. If epithelium-on cross-linking works as well as epithelium-off—that's a bit caveat—I think it'll become the procedure of choice and cut down on the morbidity of the procedure as well as the time required of both the health-care professionals and the patients."

"It's going to change the landscape completely," says Dr. Trattler. "I think that once we start doing epithelium-on cross-linking, we'll never go back to epithelium-off. It'll be standard of care once it's approved." ◀

1. Kollros L, Torres-Netto EA, Rodriguez-Villalobos C, et al. Progressive keratoconus in patients older than 48 years. *Contact Lens and Anterior Eye* 2023;46:2:101792.
2. Hashemi H, Asgari S, Mehravaran S, et al. Keratoconus after 40 years of age: A longitudinal comparative population-based study. *Int Ophthalmol* 2020;40:3:583-589.

# Find qualified ophthalmic technicians fast

Finding a qualified ophthalmic technician for your practice can be difficult. That's why private practices and large employers alike trust Eyes On Eyecare® for specialized job posting and recruiting services.

## SOURCE TALENT MORE EFFICIENTLY WITH OUR:



Large talent pool of active and passive job seekers



Syndication to major job platforms and cross-promotion to our affiliate network



Dedicated recruiting team with years of eyecare experience sourcing talent for specialized positions



*"I had such a wonderful experience using Eyes On Eyecare. It was so easy to post a job and they walk you through the entire process. I recommend them to everyone I know."*

*- Ashley Wojcik*

PROUD PARTNER OF JOBSON OPTICAL GROUP

Learn more at [eyesoneyecare.com/hire-now](https://eyesoneyecare.com/hire-now)

# HOW TO SELECT THE RIGHT MIGS FOR THE JOB

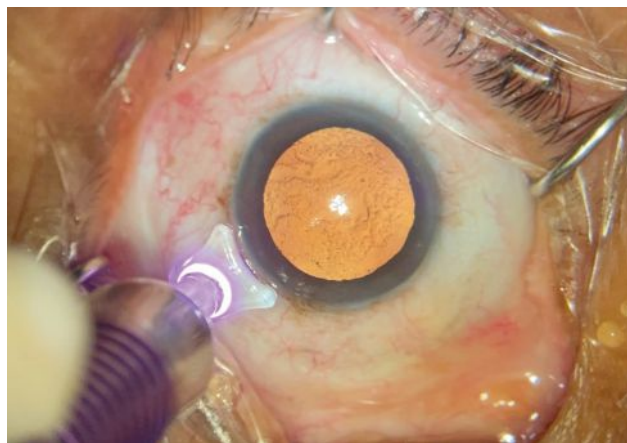
Considerations include severity of glaucoma, IOP and the number of medications the patient is taking.

**MICHELLE STEPHENSON**  
CONTRIBUTING EDITOR

**M**inimally-invasive glaucoma surgery is intended to lower intraocular pressure with less tissue disruption than traditional glaucoma surgeries. Current options include canal-based, subconjunctival and suprachoroidal procedures.

According to Manjool Shah, MD, who's in practice at NYU Langone Health in New York City, nearly all glaucoma patients are potential MIGS candidates, unless they rule themselves out. "The discussion with patients regarding the likelihood of success and expectations will be tailored to the individual and his or her particular disease state," he says. "If the kind of glaucoma that we're dealing with will work really well with canal-based procedures, then we're going to lean in a little bit harder. If not, then the conversation about intervention is going to be about using a tailored, stepwise approach to arrive at the least invasive

surgical solution that optimizes safety and efficacy, recognizing the fact that there is a chance that we would have to return to the operating room and do a bigger procedure. The choice of a more invasive, but more powerful procedure versus smaller stepwise increments is often left up to the patient, with my guidance. Different patients have different goals and we want to optimize different attributes, such as time away from work, number of surgical interventions, comfort of the eye, etc."



**Figure 1. Some surgeons combine Micropulse cyclophotocoagulation with the patient's cataract surgery.**

## The Three Varieties of MIGS Procedures

Most MIGS procedures are Schlemm's canal-based. Stents, goniotomies and canaloplasty all fall into this category. Dr. Shah lists the three versions of canal-based stents currently available to surgeons: iStent Inject (Glaukos); iStent Infinite (Glaukos); and the Hydrus Microstent (Alcon). Goniotomies can be performed with various devices like the Kahook Dual Blade (New World Medical), the SION (SightSciences), and the TrabEx (MicroSurgical Technology), or can simply be performed with a Sinsky hook or a bent needle (bent *ab interno* needle goniotomy, or BANG). Circumferential goniotomies can also be performed using devices like the Omni (Sight Sciences), iTrack or iTrack Advance (Nova Eye Medical), or with suture-based gonioscopy-assisted transluminal trabeculectomy (GATT). Canaloplasty, or viscodilation of Schlemm's canal and distal outflow structures, can be performed with iTrack

All images: James T. Murphy, MD

This article has no commercial sponsorship.

Dr. Shah is a consultant to Glaukos, Elios, Alcon, and Abbvie/Allergan. Dr. Seibold is a consultant for New World Medical and Allergan. Dr. Murphy is a consultant for Sight Sciences and Nova Eye.



## 2ND YEAR OPHTHALMOLOGY RESIDENT

**PROGRAMS AND WET LABS**

## SAVE THE DATE

**DECEMBER 2–3, 2023**

FORT WORTH, TX

**Derek DelMonte, MD**  
 Course Director

REGISTER NOW

**FEBRUARY 10–11, 2024**

FORT WORTH, TX

**Kourtney Houser, MD**  
 Course Director

REGISTER NOW

**FEBRUARY 24–25, 2024**

FORT WORTH, TX

**Jonathan Rubenstein, MD**  
 Course Director

REGISTER NOW

Dear Resident Program Director and Coordinator,

We would like to invite you to review the upcoming 2nd-Year Ophthalmology Resident Wet Lab Programs for the 2023–2024 Residency Year in Fort Worth. These programs offer a unique educational opportunity for second-year residents. To better familiarize beginning ophthalmologists with cataract surgery, these programs will consist of both didactic lectures and a state-of-the-art, hands-on wet lab experience. Technology and technique will be explained and demonstrated and surgeons will leave better prepared to optimize outcomes and manage complications when they arise. The programs also serve as an opportunity for your residents to network with residents from other programs.

After reviewing the material, it is our hope that you will select and encourage your 2nd Year residents to attend one of these educational activities, which are CME accredited to ensure fair balance.

Best regards,

Derek DelMonte, MD, Kourtney Houser, MD, and Jonathan Rubenstein, MD

**Registration Open: [www.ReviewEdu.com/CSE2ndYr2023-24](http://www.ReviewEdu.com/CSE2ndYr2023-24)**

**CME courses are restricted to 2nd-year residents enrolled in an ophthalmology residency program at the time of the course. There is no registration fee for this activity. Air, ground transportation in Fort Worth, shared hotel accommodations, and modest meals will be provided through an educational scholarship for qualified participants.**

**Joint Accreditation Statement**

In support of improving patient care, this activity has been planned and implemented by Amedco LLC and Review Education Group. Amedco LLC 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.

Amedco Joint Accreditation #4008163.

**Physicians (ACCME) Credit Designation**This activity has been approved for **AMA PRA Category 1 Credits™**.

For more information visit the registration site above or  
 email Denette Holmes at [dholmes@postgradhealthed.com](mailto:dholmes@postgradhealthed.com) or call 866-627-0714

Jointly provided by



Supported by an independent  
 medical education grant from **Alcon**

and iTrack Advance or Omni as described above, as well as with iPrime (Glaukos).

“There are also two laser-based trabeculostomy-type procedures currently in clinical trials—femtosecond laser trabeculostomy by ViaLase and excimer laser trabeculostomy (ELT) by Elios,” Dr. Shah adds.

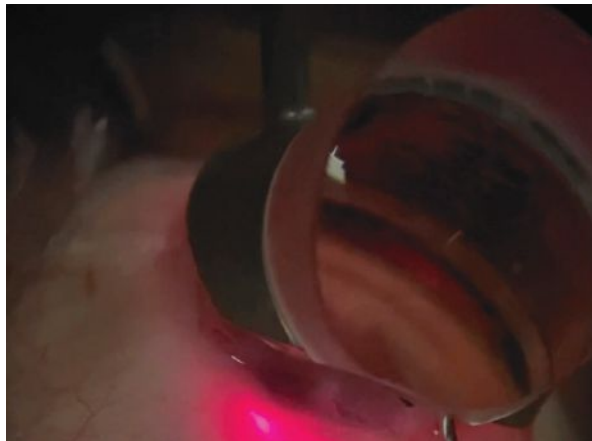
Xen (Allergan) is the only subconjunctival MIGS device approved for use in the United States. “PreserFlo (Glaukos), which some would call MIGS, is available outside the United States,” Dr. Shah explains.

Conventional procedures like trabeculectomy and glaucoma drainage devices also fall into the category of subconjunctival procedures.

Suprachoroidal procedures include the MINIject (iStar Medical) and Allopass (Iantrek), which are currently in clinical trials in the United States.

“I like to think about the three big families [of MIGS] as setting the tone because canal-based procedures may not cut it in some patients. In those situations, U.S. surgeons move to the subconjunctival set of options. Outside of the U.S., surgeons may consider the suprachoroidal option as an intermediary or in patients who aren’t good candidates for subconjunctival outflow procedures,” Dr. Shah says.

“Now that we have all of these tools to manage glaucoma, we need to broaden our definition of success. Pressure reduction isn’t the only marker of success,” Dr. Shah notes. “Reducing medications and achieving steadier IOP in terms of diurnal fluctuations could be an endpoint. Quality of life and patient-reported outcomes are also going to be relevant endpoints, because ultimately our goal as physicians is to help patients lead their best lives. As an example, you could have a patient who’s on two bottles of eyedrops with a pressure of 14 mmHg but, after surgery, he or she is on no medication with a pressure of 15 mmHg. By conventional criteria, that would be a surgical failure, but I



**Figure 2. The iTrack Advance performs 360-degree canaloplasty and doesn’t involve the implantation of a stent.**

would argue that’s a huge win because you took that patient from two bottles to zero bottles of medication. I’m sure that patient would be thrilled.”

“While we definitely incur a little bit more risk as we move up the algorithm from canal surgery to subconjunctival surgery, we have to balance that level of risk tolerance with the likelihood of success based on the individualized success criteria we have for that person, that eye, and that disease state. I am hopeful that, with improvements in big data and AI, we will continue to develop more powerful decision support tools that enable surgeons to make these nuanced surgical choices more confidently,” he explains.

### Matching Patients To Procedures

When choosing a procedure, James T. Murphy, MD, who is in practice in Hamden, Connecticut, says that he considers the severity of the glaucoma, the IOP, corneal thickness/hysteresis, the number of medications that the patient is taking as well as their efficacy, and the patient’s ability to tolerate any side effects of his or her current medications, which affects the likelihood of drop compliance. “Field characteristics are also important,” he says. “Someone with severe glaucoma or a fixation-threatening field deficit is at higher risk of snuff-out and is more likely to require a bleb. For others, the more severe the glaucoma is and the

more eyedrops he or she is on, the more likely I am to combine MIGS procedures synergistically.”

Leonard Seibold, MD, who is in practice in Aurora, Colorado, also considers the target pressure and whether or not the patient has controlled pressure on medications or uncontrolled pressure. “That changes things a little bit,” he says.

He also considers whether the angle is open or closed and whether or not the patient has a cataract. “The severity of a patient’s disease and his or her tolerance for risk are important,” Dr. Seibold adds. “For milder disease, we’re not willing to tolerate a huge risk in the procedure that we choose, whereas for more severe disease, we’re willing to tolerate higher risk to get a more robust reduction in pressure.”

He also assesses any risk factors that a particular patient may have. “For example, if a patient is at risk for blood reflux or bleeding, you may want to shy away from a goniotomy procedure that is more likely to result in a hyphema,” Dr. Seibold says. “If the patient is uveitic or has a history of macular edema, I would steer away from doing a micropulse laser or endoscopic cyclophotocoagulation procedure that would put the patient at higher risk for developing macular edema afterward.”

Patients with open-angle glaucoma have the full range of options available to them. However, having closed-angle glaucoma takes stents off the table. “I like ECP a little bit more in a closed-angle patient, but you can also perform goniosynechialysis using a Kahook Dual Blade and then perform a goniotomy,” he adds.

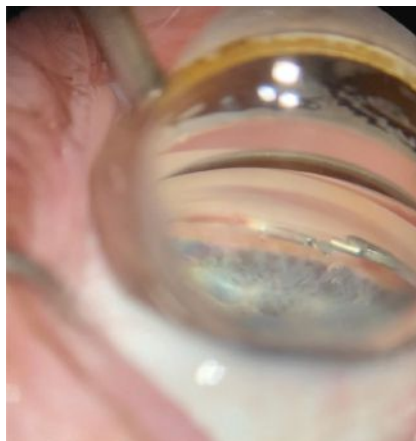
For patients who have very mild disease and who are on one or two medications, Dr. Seibold chooses a procedure that’s less invasive, lower risk and less disruptive to the tissue. “Choices include iStent, Streamline (New World Medical) or even Hydrus,” he says. “Canaloplasty can also be a good



option. But for more moderate disease, I'm turning more toward goniotomy, with the Kahook Dual Blade, with or without canaloplasty. I don't think stents or canaloplasty have as much of a role when you get to severe disease, and I think goniotomy or ECP, or perhaps a combination of the two, can be used—so you combine an inflow and an outflow procedure. Again, when you have more severe disease, you're willing to tolerate more risk, so combining two procedures to really maximize the effect for MIGS is what I'm typically turning to in those scenarios. I'm trying to avoid or push traditional surgery further down the line if possible.”

Dr. Shah says he almost always chooses canal-based surgery as his first attempt, unless he feels like it won't produce the desired result. “Canal-based procedures may not work as well in patients who have severe primary open-angle glaucoma,” he says. “The two-year outcomes from GATT show that the efficacy trails off as the severity of the disease goes up, but that assumption is being challenged a little bit by the most recent iStent infinite data, which show a decent efficacy in reasonably severe patients who have a pretty complicated history. They'd had multiple procedures, pretty severe disease, high pressures, a lot of medications, and they actually did well. This book is being rewritten constantly, but the standard belief is that canal procedures don't work as well in severe primary open-angle glaucoma. This, however, is in contrast to how well they work in secondary open-angle glaucoma.”

He adds that patients with pseudoexfoliative glaucoma, pigmentary glaucoma, uveitic glaucoma and steroid-induced glaucoma do remarkably well with canal-based procedures, often even when they have severe disease. “So, the type of disease, as well as the severity, play a role in whether we would try a canal-based procedure or would move to some of these other options, which are fundamentally not physiologic,” he explains. “So, there's always an appeal to try to tap into physiologic pathways whenever we can, but, again, if that op-



**Figure 3. Some surgeons combine the Hydrus micro-bypass stent with ECP, since the latter leaves the trabecular meshwork intact.**

tion isn't available, then we go subconjunctival.”

Dr. Murphy often combines up to four MIGS procedures. “I will perform either micropulse, traditional transscleral cyclophotocoagulation, and/or ECP when I'm performing cataract surgery, and then I'll subsequently perform either goniotomy or canaloplasty, but often a combination of both,” he says. “Leaving the trabecular meshwork intact in the nasal quadrant as a scaffold allows for placement of one of the trabecular meshwork micro-bypass stents, which I will consider in mild or moderate primary open-angle glaucoma patients, as I'm constrained by insurance coverage in the United States. These are my full-court-press patients.”

He explains that whether you're considering one, two, three or even four MIGS procedures, patient expectations are important. “I like to do dropless surgery if and when possible, as one of the most significant barriers to success is ‘the patient factor,’ meaning the patient's responsibility burden postoperatively,” Dr. Murphy says. “If dropless isn't an option, I default to a 503A compounded postoperative eyedrop. Depending on the patient's glaucoma severity, I will at a minimum streamline the patient's glaucoma medications to one or maybe two, but often I simply perform a washout and add back as needed in the postoperative period.”

He notes that his goal is one or two

drops per day while maintaining target IOP after combined cataract and MIGS procedures. “Let's say you have mild glaucoma, you are on two, three, or four aqueous suppressants, and your pressure is upper teen or low 20s with an average corneal thickness. It's entirely reasonable to reduce that patient's drop burden to one or none while achieving a mid- to low-teens stable IOP for years after their surgery,” he adds.

### What's New?

Dr. Seibold says that Streamline (New World Medical), which came to the market in the past year or two, can be useful. “The device performs goniotomy and canaloplasty at the same time,” he says. “Streamline makes micro-goniotomies that can be widened to a more linear goniotomy. It's effective and safe for mild to moderate patients, but it can also be used to extend to a longer goniotomy if more of an IOP reduction is needed. Then, there's a new version of the Omni called the Omni Ergo (Omni Surgical). It works the same, but has some ergonomic improvements to make the procedure a little smoother. Also, the iTrack device, a lighted catheter which is used to perform a 360-degree canaloplasty, has a new version called iTrack Advance. Previously, the iTrack was a freestanding catheter that had to be fed in using forceps from a separate incision. Now, the catheter is fed through a single handpiece, which ergonomically makes the procedure easier. One fewer incision is required, allowing the procedure to be completed all through your main incision like most other MIGS.”

He believes that MIGS are here to stay and that there may be a few new approaches coming soon. “One would be in the suprachoroidal space,” muses Dr. Seibold. “Currently, some new stents are in clinical trials, and they'll be placed in the suprachoroidal space. In the future, I think we'll also combine MIGS with extended drug release, using a MIGS plus meds approach to maximize outcomes.” ◀

# WHERE PK FITS IN THE TRANSPLANT LANDSCAPE

Since the development of endothelial keratoplasty techniques, penetrating keratoplasty cases began to drop. Cornea specialists weigh in on this trend and where PK fits into their armamentarium.

ANDREW BEERS  
ASSOCIATE EDITOR

**P**rior to the 21st century, penetrating keratoplasty was the only corneal transplantation technique available for Fuchs' dystrophy, endothelial dysfunction and other corneal diseases. When endothelial keratoplasty was first developed, it supplanted PK for many of these diseases. Over time, endothelial keratoplasty procedures such as Descemet's stripping endothelial keratoplasty and Descemet's membrane endothelial keratoplasty began to be more prominent in corneal transplantation. Today, PK procedures are slowly declining, but they still exist. In this article, corneal surgeons will explain how PK is being used and why it's not the foremost procedure for all corneal diseases.

## Endothelial Keratoplasty

There are different procedures under the umbrella of keratoplasty. Historically, PK has been the tried-and-true technique for surgeons,

Involving a full thickness corneal transplantation where a diseased cornea is removed and replaced with a healthy donor cornea.<sup>1</sup> Then, in the early 2000s, EK took off.

"Most surgeons doing a lot of corneal transplants converted around '03, '04 and '05 because most of the transplants we were doing were for endothelial dysfunction," says Sadeer Hannush, MD, an ophthalmologist at Wills Eye Hospital in Philadelphia. "For all who've trained in the '80s and '90s, we were longing for a procedure that wouldn't replace the entire cornea when the abnormality was only in the endothelium."

DSEK was the first procedure to make waves in corneal transplantation surgery. This technique was developed in 2004 by Dutch surgeon Gerrit Melles, MD, PhD. For this procedure, a smooth surface is created for graft application and the source of disease is removed, all while sparing posterior stroma.<sup>2</sup>

"When it first came on the scene 25 years ago, it was the easiest way to address Fuchs' dystrophy or endothelial dysfunction because the

previous procedure that had been used always was PK," says William Culbertson IV, MD, of the Bascom Palmer Eye Institute in Miami. "The advantages of DSEK are that it requires a small incision, the eye isn't exposed openly [during surgery] and the patient often has recovery of good vision without any significant induced astigmatism within a couple of months, rather than a year or two [with PK]."

"Also, the eye is much more secure because the incision is four or five millimeters in diameter as compared to a 360-degree full-thickness incision," Dr. Culbertson continues. "The other advantage is that if the graft fails, it could be easily replaced with the same outcome of good vision."

DMEK, which was developed years after DSEK, is a more delicate procedure than other EK techniques. Interestingly, Dr. Melles was behind the development of DMEK in 2008 as well. Both DSEK and DMEK target Descemet's membrane, but DSEK removes a part of the posterior stroma, while DMEK does not.<sup>3</sup> The graft for DMEK is

This article has no commercial sponsorship.

Dr. Kenyon is a consultant for Beaver-Visitec International. Dr. Syed is a consultant for BioTissue. Drs. Hannush and Culbertson have no financial interests to disclose.

# PAASS

## 3RD YEAR RESIDENT

## PROGRAM ON ADVANCED ANTERIOR SEGMENT SURGERY PROGRAM & WET LAB

**PROGRAM DATES**  
**JANUARY 19–20, 2024**  
(FRIDAY & SATURDAY)

### Didactic sessions

Pleasanton Marriott  
11950 Dublin Canyon Road  
Pleasanton, California 94588

### Wet Labs

Zeiss Innovation Center  
5300 Central Pkwy  
Dublin, California 94568

**Yousuf Khalifa, MD**  
**Madeline Yung, MD**

Course Co-Directors

### Program Highlights Include

- Intimate meeting (limited to the first 28 residents registered)
- Hands-on wet lab
- Refractive Surgery (LASIK, PRK (refract lenticule extraction)
- MIGs
- Yamane technique
- Capsular Tension Segments
- Complex/dense cataract mgmt

Dear Resident Program Director and Coordinator,

We are excited to announce the upcoming CME Accredited Resident Wet Lab Program on Advanced Anterior Segment Surgery (PAASS). PAASS is an intimate meeting (limited to the first 28 residents registered maximum) designed to help prepare third-year ophthalmology residents to transition successfully into a private practice setting in ophthalmology or their chosen fellowship program, or into an educational environment. The 3rd Year PAASS & Wet Lab will be approved for AMA PRA Category 1 Credits™ and will have an emphasis on successful outcomes by concentrating on building diagnostic, medical and advanced surgical skills in the wet lab (including Yamane, Capsular Tension Segments, MIGs, etc). The course directors and the faculty create a “safe” environment, so the third-year residents feel comfortable discussing questions, new technology, and complications in an atmosphere that strongly encourages interactive participation. **We are capping the number of residents to 28 so that the residents are fully immersed in the learning environment along with a one-to-one (faculty-to-resident) ratio in the wet lab to maximize learning curve with the advanced surgical skills wet lab.**

Ophthalmology residencies in the United States strive to introduce their residents to advanced surgical techniques and technologies in an environment characterized by rapid innovation. Due to continuously evolving technological developments, best practices are constantly changing. As such, there are too few opportunities to gain hands-on training. This meeting will concentrate on advanced techniques and technologies geared towards residents approaching the end of their 3rd Year (PGY4) residency. The meeting will cover topics specifically in the areas of refractive surgery, minimally invasive glaucoma surgery, management of aphakia, new technologies for dense cataract management, intraocular lens selection technologies, heads-up displays, and progression tracking software.

This 2-day course will include one day of didactic and one day of hands-on wet lab experience. The meeting will be led by a faculty comprised of renowned key opinion leaders and specialized surgeons with a background in resident education. The wet lab will feature nationally recognized leaders with one-on-one wet lab mentorship.

We believe this program offers a unique opportunity for residents to gain hands-on experience on advanced anterior segment surgery techniques. We hope that you will select and encourage your 3rd-year residents (PGY-4) to attend this CME accredited program.

Sincerely,

Yousuf M. Khalifa, MD, and Madeline Yung, MD

**REGISTRATION IS OPEN NOW at [www.ReviewEdu.com/PAASS2024](http://www.ReviewEdu.com/PAASS2024)**



JOINTLY ACCREDITED PROVIDER™  
INTERPROFESSIONAL CONTINUING EDUCATION

**Joint Accreditation Statement** – In support of improving patient care, this activity has been planned and implemented by Amedco LLC and Review Education Group. Amedco LLC 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. Amedco Joint Accreditation #4008163.

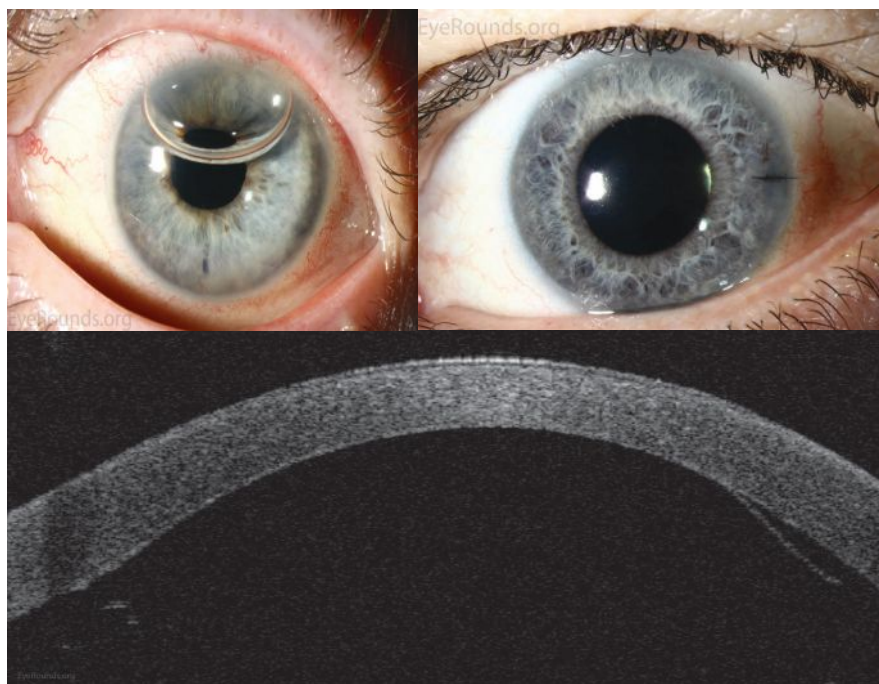
**Physicians (ACCME) Credit Designation** – This activity has been approved for **AMA PRA Category 1 Credits™**

For more information visit the registration site above or email Denette Holmes  
at [dholmes@postgradhealthed.com](mailto:dholmes@postgradhealthed.com) or call 866-627-0714

Supported by an independent  
medical education grant from  
Carl Zeiss Meditec

Jointly provided by





Antoinette Venokus, CRA

**(Top Left)** Postoperative appearance of patient who underwent DMEK for Fuchs' endothelial corneal dystrophy at one week post-operatively with residual anterior chamber gas bubbles. **(Top Right)** Postoperative appearance of patient who underwent DMEK for Fuchs' endothelial corneal dystrophy at two weeks postoperatively with complete resorption of the gas. **(Bottom)** Anterior segment optical coherence tomography demonstrating a limited, peripheral graft-edge lift one week after DMEK surgery (right side of image). The attached portion of the graft mimics normal anatomy due to the precise one-to-one replacement of tissue with DMEK. *Ophthalmic Atlas Images by EyeRounds.org, The University of Iowa are licensed under <https://creativecommons.org/licenses/by-nc-nd/3.0/deed.en>. No changes were made.*

around 10 to 15  $\mu\text{m}$  in thickness,<sup>2</sup> while graft thickness for DSEK can be nanothin (15 to 49  $\mu\text{m}$ ) all the way up to a conventional size (150 to 250  $\mu\text{m}$ ).<sup>4</sup>

Out of all keratoplasty procedures, DMEK results in the most positive outcomes for endothelial disease cases. In 2019, researchers compared long-term graft survival outcomes and complications of patients who underwent DMEK, DSEK and PK for Fuchs' dystrophy and bullous keratopathy. One hundred twenty-one eyes underwent DMEK, 423 eyes underwent DSEK, and 405 eyes underwent PK. Patients who received DMEK had the best overall graft survival of 97.4 percent, compared to DSEK (78.4 percent) and PK (54.6 percent).<sup>5</sup> Additionally, DMEK had the lowest rate of graft rejection of

1.7 percent, compared to DSEK (5 percent) and PK (14.1 percent).<sup>5</sup>

What makes DMEK a far more advanced EK procedure is its effective recovery time. "In terms of stability and anatomical recovery time, it would most certainly be DMEK because when it's done properly, the ability of the new endothelial cells to pump the cornea clear and compact and have improved vision is over within a matter of a couple of weeks," says Kenneth Kenyon, MD, of Eye Health Vision Center in Dartmouth, Massachusetts.

"As the field of cornea has grown more advanced, we've learned how to replace the specific layers of the cornea that are diseased," explains Zeba Syed, MD, Director of the Cornea Fellowship Program at Wills Eye Hospital. "So, instead of

replacing the entire cornea regardless of the layers involving disease, we can now do a layer-specific transplantation. The evolution over time reflects (1) newer surgeries, (2) people getting more comfortable with the newer surgeries and (3) improvement of techniques overall.

"People are increasingly performing EK procedures because eye banks have become very good at pre-stripping, pre-loading, pre-staining, and pre-cutting the tissue, so it makes it very easy to complete," Dr. Syed continues.

Experts explain the differences between DMEK and DSEK: "To get the tissue to stick, we have to inject the transplant into the eye and then we put a bubble underneath it, because we're just replacing the back layer of the cornea," says Dr. Syed. "We either use air or gas and we inject it under the transplant, and we have the patient lay flat for several days face up depending on what kind of transplant: DSEK I usually do two days, and for DMEK I usually do three to five days of lying flat.

"There's always a conversation about when we should do a DMEK versus a DSEK," Dr. Syed adds. They both are EKs, they both treat endothelial disease, but they're different in their technique. The tissues are different in thickness, and in general a DSEK is easier to perform because it's a thicker tissue so it's easier to handle, DMEK is the one with the steeper learning curve because it's really thin tissue and harder to maneuver intraoperatively."

Dr. Hannush adds that DSEKs aren't always favored over DMEKs. "In Germany, for example, 98 percent of the endothelial grafts are DMEK," he says. "Now you may say, 'Are they better surgeons?' What people don't know in America is that in Germany all DMEKs are done in the hospital and are admitted for six to nine days. We're lucky to keep our patients in the

surgery center for five hours. So, they go home, they don't follow any instructions, they're not lying flat on their back, and so on and so forth." Basically, German surgeons can opt for DMEK, which provides a better visual outcome over other procedures, because they have more control over the postoperative outcome than American surgeons.

According to the 2022 Eye Banking Statistical Report from the Eye Bank Association of America (EBAA), 15,544 DSEK, DSAEK or DLEK procedures were performed and 15,248 DMEK or DMAEK procedures were performed last year in the United States. In 2019, prior to the pandemic, 17,428 DSEK, DSAEK or DLEK procedures were performed and 13,215 DMEK or DMAEK procedures were performed. Today, PK shares a third of corneal transplantation cases along with EK procedures.

In 2019, 17,409 PK procedures were performed; then in 2022, this number dropped to 15,835. The total number of corneal grafts in 2019, including PK, EK, LK and other keratoplasty procedures, was 85,601. In 2022, the total number dropped to 79,126, due to the pandemic in 2020 affecting donor populations.<sup>6</sup>

"During the pandemic, there was a dip in surgery, but that was very short-lived," says Dr. Hannush. "The dip wasn't because people were too busy. It's because there wasn't any tissue to give everyone. The Eye Bank Association of America created some very strict rules on which tissues we can be used from donors who may have had COVID, so there was less availability of donor tissue for our patients who needed it." According to EBAA, only 66,278 corneal grafts were performed in 2020. In the United

States, the usage of keratoplasty tissue dropped 20 percent due to the pandemic. Now, eye banks are recovering and usage rates in 2022 are only down by 5 percent compared to pre-COVID levels.<sup>6</sup>

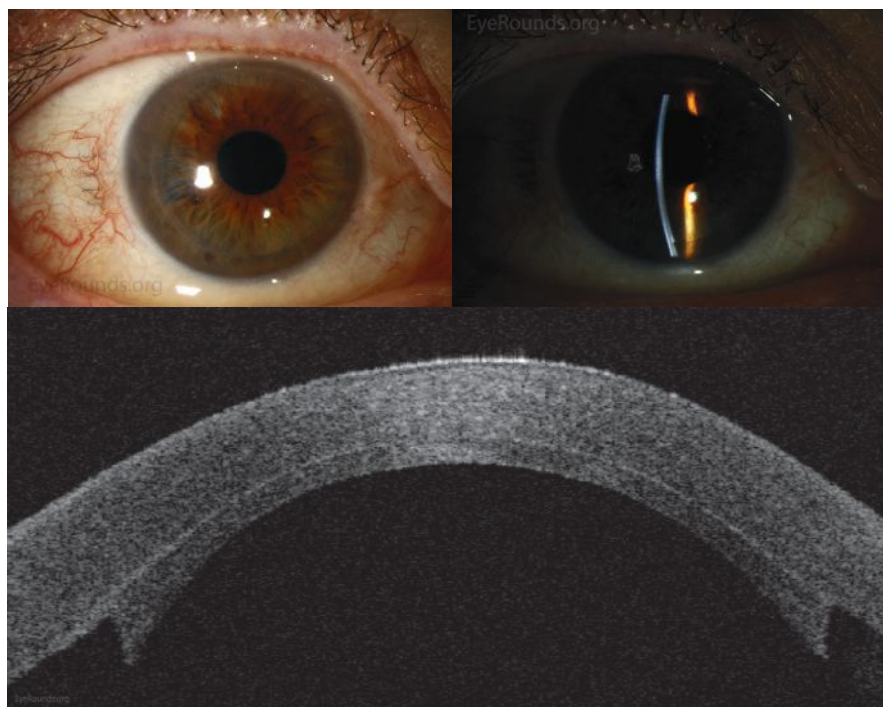
## Penetrating Keratoplasty

There's still a place for PK in corneal transplantation, but nowadays it has to do with more severe cases, experts say. "It's for patients who have full-thickness corneal opacities, full-thickness thinning or even perforation," says Dr. Culbertson. "We do a lot of our penetrating keratoplasties to excise infections and/or seal the perforation from an infection."

Dr. Syed adds, "When someone has an infected cornea, like corneal ulcers for example, and the ulcer is eating through their cornea and it perforates, then we do a full thickness transplant. The goal in that case is a therapeutic PK. We're trying to cut out the infection and those are almost always full thickness transplants."

There are times when a graft fails from a PK and a surgeon must decide whether to redo a full thickness transplant or try another method. "Doctors have a choice for patients who had previous successful penetrating keratoplasty and saw well until the graft failed," says Dr. Hannush. "You can do an endothelial graft, DSEK or DMEK, behind the full thickness transplant, or you can simply repeat the transplant depending on your level of comfort."

Dr. Hannush provides another example on when to employ PK. "If I feel that the stroma of the cornea is involved, not just through edema but through scarring, then I know they need the stroma to be replaced," he says. "If I think they have endothelial dysfunction, then I know that the entire cornea needs to be replaced. For example: herpes simplex keratitis. A patient has had multiple episodes and developed



Stefani Karakas, CRA

**(Top Left)** The DSAEK grafts can be visualized as a subtle ring in diffuse illumination. **(Top Right)** The DSAEK grafts can be seen protruding posteriorly from the cornea in the inferior aspect of the slit beam. **(Bottom)** Anterior segment optical coherence tomography demonstrating an attached DSAEK graft one day after surgery. *Ophthalmic Atlas Images by EyeRounds.org, The University of Iowa are licensed under <https://creativecommons.org/licenses/by-nc-nd/3.0/deed.en>. No changes were made.*

scarring in the cornea. We know at the very least they need 96 percent of the anterior cornea to be replaced, but for that you only need DALK. But when I'm able to image the endothelium to discover that the endothelial cell count is very low, then I know the patient needs a full thickness transplant for visual rehabilitation. Corneal scarring will remain the main indication for penetrating keratoplasty. It will decrease over time, but it will never go away."

### Other Keratoplasties

The scope of corneal transplantation surgery doesn't stop at PK, DSEK and DMEK. There are lamellar keratoplasty procedures and keratoprosthetics that have been developed over the years that are useful in practice. DALK is the most widely used lamellar keratoplasty.

"DALK is a procedure that replaces 96 percent of the cornea, leaving the endothelium and Descemet's membrane behind and, usually, leaving behind the pre-Descemet's layer, also known as Dua's layer," says Dr. Hannush. "The main indication for DALK is keratoconus. However, the total number of grafts done, whether they're DALK or penetrating keratoplasty for keratoconus, have decreased with the advent of scleral lenses to manage these patients and improve their vision and the approval of collagen cross-linking in the United States."

If there's no sign of endothelial dysfunction or dystrophy, then employing a DALK has its benefits. "DALK is terrific if one can master it because it has that great advantage of retaining one's own corneal endothelium," says Dr. Kenyon. "If you proceed with a DALK, you can essentially give the patient lifelong normal vision, because that tissue won't reject to any degree of concern, whereas a penetrating keratoplasty has lifelong risks of rejection and some other

significant complications and failure risks."

There is some leeway with DALK. "Anytime we do a DALK, we have to be prepared that the DALK in our hands may not work and we will just convert it to a full-thickness corneal transplant," says Dr. Hannush.

“  
**Corneal scarring will remain the main indication for penetrating keratoplasty. It will decrease over time, but it will never go away.**

— Sadeer Hannush, MD

On the other side of the corneal transplant spectrum is the Boston Keratoprosthesis, or KPro, the most widely used artificial cornea. It's not employed in practice as much as keratoplasty, since PK, DSEK and DMEK can restore the eye's vision without the need for an artificial cornea. "The Boston keratoprosthesis is performed in cases where the patient is not a candidate for any of the above," says Dr. Syed. "It is usually reserved for severely sick eyes in which any other form of corneal transplant would fail. If a patient has failed three or four transplants, then a subsequent transplant will typically do worse than the previous one. So, if I'm referred a patient who failed three PKs over their lifetime, I'm generally not putting a fourth PK in their eye. In those cases, I'll do the Boston keratoprosthesis if the patient is a candidate."

"A small fraction of keratoplasty procedures, about 3 to 4 percent, are procedures like anterior lamellar keratoplasty, keratoprosthetics,

and other techniques," says Dr. Culbertson. In the United States EEBA reported 476 DALK procedures in 2022, which is much lower than pre-COVID levels. In 2019, 745 DALK procedures were performed. KPro procedures across the country held steady numbers until the pandemic. In 2019, 251 KPro surgeries were performed versus 122 in 2022.<sup>6</sup>

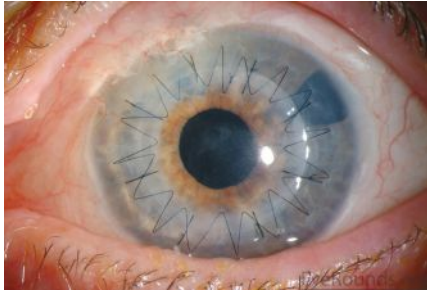
### Future of PK

Surgeons were asked if they believe PK will become obsolete in the future as the number of EK procedures continue to grow. They all showed optimism towards PK and its place in their armamentarium. Dr. Hannush stated previously that corneal scarring will remain the main indication for PK, and while cases will decrease over time, the procedure will never go away. Dr. Syed adds, "There will always be a role for penetrating keratoplasty in our field because of infections, and advanced keratoconus."

EK procedures may decline since surgeons have exhausted the advancements of the procedures. "I think we're getting to the point where we sort of maxed the refinement of DSEK and DMEK as compared to their original iterations," says Dr. Culbertson. "There are improvements that can be made in technique and other things, but I think that's kind of reached a plateau where any advancements will be minimal compared to what we have now and the results we see."

"The reimbursement for this work is so low in America," adds Dr. Hannush. "EK is such an undervalued procedure. For a surgeon to invest time in the procedure—when he or she could be doing cataracts—and then also have to deal with the potential complications is going to affect the growth of these procedures."

The future advancements in keratoplasty currently look to involve less-invasive endothelial



Stefani Karakas, CRA

**Combination of running sutures and interrupted sutures.** *Ophthalmic Atlas Images by EyeRounds.org, The University of Iowa are licensed under <https://creativecommons.org/licenses/by-nc-nd/3.0/deed.en>. No changes were made.*

transplantation such as that pioneered by Shigeru Kinoshita, MD, in Japan, which involves the injection of a patient’s own cultured endothelial cells. “Endothelial keratoplasty may at some point become much less frequent, because cultured injected endothelial cells are on the horizon,” says Dr. Syed. “Instead of having to surgically

implant them, you can inject them similar to how our retina colleagues inject patients who have macular degeneration or macular edema. This approach will theoretically replace endothelial keratoplasty if it ends up being successful.”

In 2020, Dr. Kinoshita and a team of researchers followed up on a five-year study of 11 eyes of 11 patients who underwent corneal endothelial cell injections to treat some form of endothelial failure. After five years, 10 of the 11 eyes were restored to normal corneal endothelial function.<sup>7</sup> BCVA was improved significantly in the 10 eyes. Prior to the injections, the mean VA was 0.876 logMAR in patients, then after the injections, the mean VA was 0.046 logMAR.<sup>7</sup> Researchers reported no major adverse reactions directly related to the endothelial injections.<sup>7</sup>

In the next decade, who knows where corneal transplantations will

stand? “What we’re working on in the next 10 years won’t address corneal scarring through genetic research or cell-based therapy,” says Dr. Hannush. In the end, then, it appears PK is here to stay. ◀

- Gurnani B, Kaur K. Penetrating keratoplasty. StatPearls 2023. <https://www.ncbi.nlm.nih.gov/books/NBK592388/>.
- Moshirfar M, Thomas AC, Ronquillo Y. Corneal endothelial transplantation. StatPearls 2023. <https://www.ncbi.nlm.nih.gov/books/NBK562265/>.
- Fernandez MM, Afshari NA. Endothelial keratoplasty: From DLEK to DMEK. Middle East Afr J Ophthalmol 2010;17:1:5-8.
- Tourabaly M, Chetrit Y, Provost J, Georgeon C, Kallel S, Temstet C, Bouheraoua N, Borderie V. Influence of graft thickness and regularity on vision recovery after endothelial keratoplasty. Br J Ophthalmol 2020;104:9:1317-1323.
- Woo JH, Ang M, Htoon HM, Tan D. Descemet membrane endothelial keratoplasty versus Descemet stripping automated endothelial keratoplasty and penetrating keratoplasty. Am J Ophthalmol 2019;207:288-303.
- 2022 Eye banking statistical report. Eye Bank Association of America; 2023.
- Numa K, Imai K, Ueno M, Kitazawa K, Tanaka H, Bush JD, Teramukai S, Okumura N, Koizumi N, Hamuro J, Sotozono C, Kinoshita S. Five-year follow-up of first 11 patients undergoing injection of cultured corneal endothelial cells for corneal endothelial failure. Ophthalmology 2021;128:4:504-514.

## ADVERTISER INDEX

*This advertiser index is published as a convenience and not as part of the advertising contract. Every care will be taken to index correctly. No allowance will be made for errors due to spelling, incorrect page number, or failure to insert.*

Alcon .....	15, 16
..... <a href="http://www.myalcon.com/professional/cataract-surgery/iols/clareon-panoptix">www.myalcon.com/professional/cataract-surgery/iols/clareon-panoptix</a>	
Apellis .....	30-32
..... <a href="http://www.apellis.com">www.apellis.com</a>	
Bausch + Lomb .....	5
..... (800) 323-0000	
..... <a href="http://www.bausch.com">www.bausch.com</a>	
CooperVision .....	39-42
..... (800) 341-2020	
..... <a href="http://www.coopervision.com">www.coopervision.com</a>	
Dompe .....	25, 26
..... <a href="http://www.oxervate.com/HCP">www.oxervate.com/HCP</a>	
Genentech .....	Cover Tip
..... <a href="http://www.gene.com">www.gene.com</a>	
Glaukos .....	Cover 4
..... (800) 452-8567	
..... <a href="http://www.glaukos.com">www.glaukos.com</a>	

Harrow .....	23
..... <a href="http://www.harrow.com">www.harrow.com</a>	
Icare USA .....	8
..... (888) 422-7313	
..... <a href="mailto:infoUSA@icare-world.com">infoUSA@icare-world.com</a>	
..... <a href="http://www.icare-world.com/USA">www.icare-world.com/USA</a>	
Iveric Bio .....	18-20
..... <a href="http://www.IvericBio.com">www.IvericBio.com</a>	
Iveric Bio .....	13
..... <a href="http://www.IvericBio.com">www.IvericBio.com</a>	
Nextgen .....	45
..... <a href="http://www.nextgen.com/1-ophth">www.nextgen.com/1-ophth</a>	
OcuSoft .....	51
..... (800) 233-5469	
..... <a href="http://www.ocusoft.com">www.ocusoft.com</a>	
Reichert Technologies .....	Cover 2, 3
..... (888) 849-8955	
..... <a href="http://www.reichert.com">www.reichert.com</a>	
Tarsus .....	11, 12
..... <a href="http://www.tarsusrx.com">www.tarsusrx.com</a>	
Thea Pharma .....	74, Cover 3
..... <a href="http://www.ivizia.com/ecp">www.ivizia.com/ecp</a>	
Vital Tears .....	47
..... <a href="http://www.vitaltears.org">www.vitaltears.org</a>	



EDITED BY CARL REGILLO, MD,  
AND YOSHIHIRO YONEKAWA, MD

**RETINAL INSIDER**

# Neurodegenerative Diseases and OCTA

*Peering into the retina may yield prognostic clues on diseases such as Alzheimer's.*

**JOSHUA WOO, BA, SEJAL PATEL, SHARON FEKRAT, MD, FASRS, AND DILRAJ S. GREWAL, MD, FASRS**  
DURHAM, N.C.

**N**eurodegenerative diseases are the leading cause of disability around the world, and this burden is expected to increase exponentially over the next several decades.<sup>1</sup> Alzheimer's disease (AD), accounting for 60 to 80 percent of dementia cases, remains plagued by underdetection due to diagnostic barriers.<sup>2</sup> Currently, brain tissue histopathology at autopsy remains the only definitive diagnosis of AD, and alternate diagnostic tools such as positron emission tomography scans and cerebrospinal fluid testing remain underutilized due to cost, invasiveness and lack of widespread availability.<sup>3,4</sup> Identification of more widely applicable biomarkers to diagnose and monitor neurodegenerative diseases, especially preclinically when lifestyle changes may delay onset, remains an unmet need.

Retinal imaging provides a noninvasive and low-recurring-cost opportunity to capture structural changes to the neurosensory retina and its microvasculature, both of which may serve as biomarkers for cognitive impairment and neurodegenerative disease.<sup>5,6</sup> Here, we describe the evolution and limitations of OCTA as a potential

diagnostic tool for neurodegenerative disease, along with its utility as an input into machine-learning algorithms.



**Mild cognitive impairment (MCI) is often a transitional state before the development of Alzheimer's disease, making an early diagnosis imperative.**



## OCTA's Potential

Optical coherence tomography angiography offers a 3-dimensional image of the retinal and choroidal structure and vasculature, allowing for the observation of vascular density and thickness of the different layers. Because OCTA essentially captures motion-contrast images, it may allow detection of retinal vessel density (VD) and perfusion density (Pfd) at high resolution, and this microvasculature may demonstrate abnormalities earlier than larger retinal vessels visualized on retinal photographs.

Before exploring OCTA's applications, it's important to define the terms used for characterizing the

microvasculature using OCTA: VD and Pfd. Their structural definition varies to some extent with different OCTA platforms such as the Spectralis (Heidelberg), Solix (Visionix), Xephilio (Canon Medical Systems), and Angioscan (Nidek). On the Zeiss Cirrus HD-5000 Angioplex OCTA platform (Carl Zeiss Meditec), VD is defined as the total length of perfused vasculature per unit area within the region of measurement ( $\text{mm}/\text{mm}^2$ ). Perfusion density is defined as the total area of perfused vasculature per unit area in the region of measurement (percentage). For the 3x3-mm scans, VD and Pfd are measured in the Early Treatment Diabetic Retinopathy Study (EDTRS) 3-mm circle and ring. For 6x6-mm scans, the VD and Pfd are measured in the ETDRS 6-mm circle, inner ring and outer ring.

Our initial work at the Duke Eye Multimodal Imaging in Neurodegenerative Disease (iMIND) research study group reported a relationship between both reduced VD and enlarged foveal avascular zone (FAZ) area and AD using an OCTA-based comparative assessment.<sup>7</sup> Early studies used OCTA to visualize VD in AD, as well as to find significant correlations between Mini Mental State Examination scores and FAZ area.<sup>8</sup> Such findings have been the foundation to current literature highlighting OCTA as a potential clinical tool to identify biomarkers of AD.<sup>7,9</sup> Of note, those carrying the apolipoprotein  $\epsilon 4$  gene, a known risk factor for AD, showed variations in retinal layer thickness over time, highlighting potential early biomarkers of asymptomatic patients at higher risk of AD.<sup>10</sup>

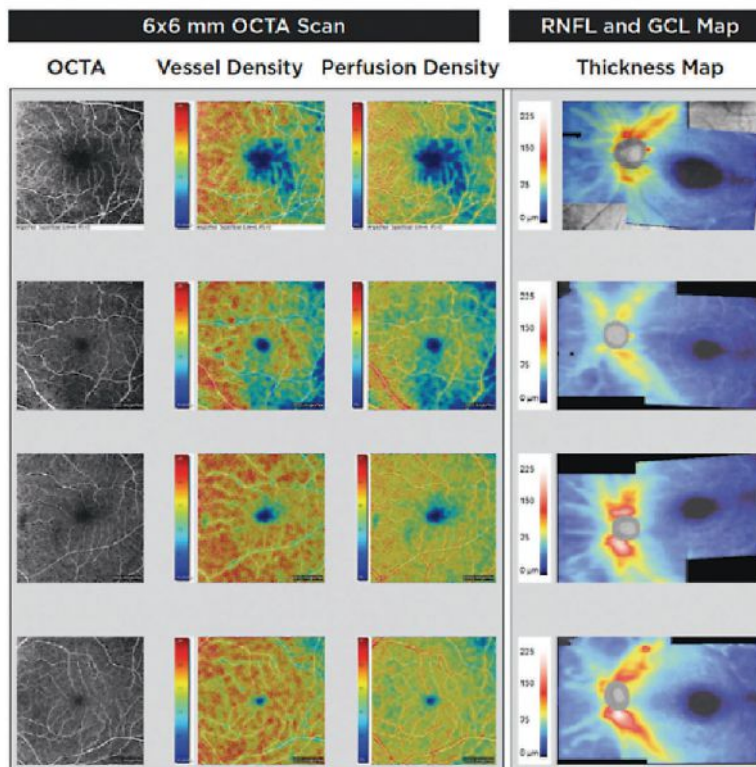
Mild cognitive impairment (MCI) is often a transitional state before the development of AD, making an early

**This article has no commercial sponsorship.**

**Dr. Regillo** is the director of the Retina Service of Wills Eye Hospital, a professor of ophthalmology at Thomas Jefferson University School of Medicine and the principle investigator for numerous major international clinical trials.

**Dr. Yonekawa** is an assistant professor of ophthalmology at Sidney Kimmel Medical College at Thomas Jefferson University. He serves on the Education Committee of the American Society of Retina Specialists and on the Executive Committee for the Vit Buckle Society, where he is also the vice president for academic programming.





**Figure 1. OCTA images showing differences in the retinal microvasculature among individuals with Alzheimer's disease, Parkinson's disease, mild cognitive impairment and age-matched controls. OCT images showing corresponding retinal nerve fiber layer (RNFL) and ganglion cell-inner plexiform layer (GC-IPL) thickness findings are included on the right. Adapted from Grewal et al. (2022).<sup>11</sup>**

diagnosis imperative. Thus, OCTA has previously been used as a tool to identify significant microvascular loss among those with MCI.<sup>12</sup> Among those with amnesic MCI, which is more likely to progress to clinical AD, PfD was significantly lower compared to non-amnesic MCI patients and controls.<sup>13</sup>

Several cross-sectional studies have also shown the utility of OCTA in identifying biomarkers of Parkinson's disease.<sup>11,14,15</sup> We previously demonstrated structural choroidal changes, as well as decreased VD and PfD, among those with PD characterized by OCTA (Figure 1). However, because PD has an average disease course of more than 14 years, the use of OCTA to study retinal alterations over time provides additional vital insights into the pathophysiology and progression of PD and how it may differ from normal age-related changes in OCTA and OCT metrics. Duke Univer-

sity's Anita Kundu and co-workers used OCTA to examine longitudinal retinal structural and microvasculature changes among patients with PD and found a significantly faster rate of decline in VD, PfD and ganglion cell-inner plexiform layer (GC-IPL) thickness among those with PD, compared to the age-related decline seen in controls. PD patients with more advanced disease displayed faster rates of VD decline.<sup>16</sup>

In addition to AD and PD, OCTA imaging continues to show promise in biomarker identification for other neurodegenerative diseases including Traumatic Brain Injury (TBI) and Huntington's Disease. Traumatic brain injury has been established as one of the strongest epigenetic risk factors for development of dementia. Among TBI patients, OCTA can be used to identify secondary structural changes in the retina in the absence of visual symptoms.<sup>17</sup> Elahe Amini, MD, of

the Iran University of Medical Sciences and her co-authors demonstrated reduced macular thickness and peripapillary retinal nerve fiber layer, and a paper authored by Duke's Alice Haystead observed decreased VD, GC-IPL thickness and FAZ area among those with Huntington's Disease.<sup>18,19</sup> While such relationships should be confirmed with larger studies, it demonstrates the utility of OCT/OCTA across a spectrum of neurodegenerative diseases.

### OCTA and AI as Diagnostic Tools

Machine learning models have recently been used to provide clinical diagnoses of AD and MCI with brain MRI and PET images.<sup>20</sup> Retinal images may also be used as quantitative inputs to machine learning models, with lower costs and easier access. Jing Tian and co-workers at the Alzheimer's Disease Research Center used publicly available UK Biobank data to train a modular machine

learning model that accurately classified patients with AD 82 percent of the time.<sup>21</sup>

Recent work by the Duke iMIND Study Group has used OCTA images as an input into neural network models to determine the probability of neurodegenerative disease.<sup>22</sup> A data set of 154 eyes from 80 patients with MCI were fed into the convolutional neural network (CNN) model, with 30 eyes used for testing (remaining 124 used for training and validation), and a probability score was produced, indicating likelihood that a patient would carry a clinical diagnosis of MCI. OCTA images were used as quantitative inputs to capture potential vascular features, while GC-IPL images were used in conjunction to capture potential structural features, yielding an 80.9 percent probability score. Using these combined inputs, the best performing model achieved

sensitivity of 79 percent and specificity of 83 percent, performing comparably to a previous CNN differentiating control and AD patients using OCTA multimodal inputs.<sup>23</sup> The combined CNN model yielded an area under the curve (AUC) of 0.836 while the model using only imaging inputs yielded an AUC of 0.829. Thus, the results suggest that the feasibility of creating a predictive risk model using only OCTA images as inputs. The model showed higher rates of specificity when given quantitative and demographical inputs. This suggests that a machine learning model may provide predictive capacity a significant amount of time prior to clinical symptom onset.

### Congruence Between OCTA and Brain Imaging

Considering the proximity and shared embryological origin of the retina and brain, the use of OCTA images to reflect—and even predict—neurological changes would make sense; however, literature examining correlations between retinal and brain imaging is limited. Our group has demonstrated a negative correlation between lateral ventricle volume and OCTA VD, suggesting a relationship between OCTA imaging and cerebral biomarkers.<sup>24</sup> Such findings are consistent with earlier associations between retinal thinning and medial temporal lobe atrophy.<sup>25</sup> Other studies, although limited in sample size, have shown associations between OCTA parameters and fewer white matter hyperintensities (WMH), a precursor to cognitive decline and AD.<sup>26</sup> These relationships between OCTA-identified biomarkers and neurological biomarkers in neurodegenerative disease, however warrant further investigation with longitudinal follow-up, and larger, more diverse and heterogenous populations.

### Limitations of OCTA in Clinical Settings

Despite the growth of OCTA as a tool for identifying biomarkers in neurodegenerative diseases, there

remain several unsolved challenges. First, characteristics measured by OCTA can be heterogenous across individuals, making it difficult to apply them broadly to diverse cohorts. As additional studies with larger and more diverse datasets become available, such limitations may be reduced. Longitudinal studies, such as that of Kundu et al., also provide a unique opportunity to examine relationships between OCTA and neurodegenerative disease over time and may confer a unique opportunity to assess the impact of disease-modifying therapies.<sup>16</sup>



Another limitation is inaccurate information from optical coherence tomography angiography analysis due to image quality issues and resulting artifacts.



The existence of confounding ocular diseases such as glaucoma, diabetic retinopathy, and age-related macular degeneration need to be accounted for when using OCTA in clinical settings. This is particularly relevant given the prevalence of glaucoma and AMD in the elderly population vulnerable to neurodegenerative diseases. The majority of neural network models to date have been built on otherwise healthy patients with no known confounding ocular or systemic diseases. Differentiating patterns of change between ocular diseases and preclinical and clinical neurodegenerative disease will be a key step to increase the generalizability of OCT- and OCTA-based retinal imaging models.

Another limitation is inaccurate information from OCTA analysis due to image quality issues and resulting artifacts. Good image quality is an essential prerequisite for accurate characterization of retinal

and choroidal changes. For example, neurodegenerative disease patients with impaired motor function or head tremor may yield less reliable and repeatable OCTA scans. Towards this end, a paper from Duke's Justin Ma demonstrated that the OCTA repeatability—measured by intraclass correlation coefficients—was good to excellent among those with AD, MCI and PD. The researchers also noted that interocular asymmetry in peripapillary OCTA wasn't significant, indicating that single-eye imaging may present an option for future studies.<sup>27</sup> Facilitating a shorter image acquisition time could minimize the limitation of motion artifacts. It's critical to screen images carefully for quality control prior to using them for analysis. Our group recently created a neural network model that could help automate the time-consuming and resource-intensive task of assessing image quality for OCT and OCTA images. The model assessing OCTA image quality achieved an AUC of 0.83 while the combined model assessing both OCTA and GC-IPL images reached an AUC of 0.99.<sup>28</sup> These results show that neural networks can be trained to sort through good-quality and poor-quality retinal images with accuracy, as well as integrate with existing automated model pipelines to help classify neurodegenerative diseases.

Also, it's important to consider the varying OCTA platforms and scan types used. A previous comparison of five OCTA systems found poor agreement between systems, highlighting the variability that can occur when using OCTA across different imaging platforms.<sup>29</sup> Differences in VD, PfD and FAZ aren't cross-applicable across OCTA systems. Such barriers highlight the challenges of standardizing OCT, particularly OCTA images. One study found that while OCTA can identify biomarkers of AD, there remained significant heterogeneity across studies, largely attributable to different retinal layer segmentation algorithms and different definitions and

# 2023 YEAR IN REVIEW

As practicing ophthalmologists, our readers have numerous demands on their time: patient exams; surgery; postop visits; and practice management duties, just to name a few. With so much going on, it's tough for busy physicians to keep up with every article we publish, or even to remember in which issue an interesting article appeared.

That's where our *2023 Year in Review* issue comes in. This digital-only 13th edition will include articles that run the gamut of ophthalmology topics, ranging from practical, how-to cataract surgery articles and tips for dry-eye management to expert takes on glaucoma, retina, pediatric ophthalmology and oculoplastics. After perusing our *Year in Review*, ophthalmologists can feel confident that they didn't miss out on anything important from 2023.



## DETAILS:

- Digital-only 13th edition
- More than 100 pages of editorial content
- Launches mid-December 2023
- Flipbook and downloadable PDF versions



## VISIBILITY:

- Promoted in social media every day from mid-December to mid-January.
- House ads in December, January and February print issues.
- Link from [reviewofophthalmology.com](http://reviewofophthalmology.com) home page to digital edition.
- Several digital edition driver e-blasts to Review mailing list with direct link.



## OPPORTUNITIES:

- Display ads within article layouts—digital flipbook and downloadable PDF
- Digital edition banner ads—digital flipbook only
- Digital edition driver banner e-blast

For ad rates, call your  
*Review* sales rep today!

**MICHAEL HOSTER**

mhoster@jobson.com • 610-492-1028

**MICHELE BARRETT**

mbarrett@jobson.com • 215-519-1414

**JONATHAN DARDINE**

jdardine@jobson.com • 610-492-1030

After a highly successful launch with our 2022 edition (at right), we'll now accept ad placements when 2023's edition publishes this December.

**REVIEW**  
of OPTHALMOLOGY

thresholding algorithms for metrics like VD and PfD.<sup>30</sup> Recommendations to standardize OCTA inputs across platforms have been put forward, and efforts to establish consensus among researchers, industry and regulators are critical to improve the clinical applicability across settings.

As the field of artificial intelligence flourishes, emerging machine learning architectures provide great promise in simplifying diagnostic efforts for neurodegenerative diseases. Improvements in our databases and AI technology would help overcome some of the limitations of current neural networks. These include techniques to reduce the risk of overfitting with small datasets, wherein the model associates images with certain outputs rather than learning why particular inputs are predictive of certain outputs. As the training population and different imaging platforms used for data collection grow, the generalizability to other populations and imaging platforms should also increase.

In conclusion, the role of OCT and OCTA-based retinal imaging in neurodegenerative diseases is rapidly expanding. A growing body of literature now shows the potential of OCTA detecting microvascular biomarkers for MCI, AD, PD and other neurodegenerative diseases, including TBI. While additional studies are needed to overcome the heterogeneity across OCTA platforms, we've made significant progress in evaluating OCT- and OCTA-based retinal biomarkers in the diagnosis and progression of neurodegenerative disease, and this is just the beginning. With advances in imaging technologies, analytics and data processing, OCTA is anticipated to have a greater role in the diagnosis and potential management of neurodegenerative diseases. ◀

1. Feigin VL, Vos T, Nichols E, et al. The global burden of neurological disorders: Translating evidence into policy. *Lancet Neurology* 2020;19:3:255-265.
2. Alzheimer's Association. 2020 Alzheimer's disease facts and figures. *Alzheimer's & Dementia* 2020;16:391-460.
3. Liao H, Zhu Z, Peng Y. Potential utility of retinal imag-

- ing for Alzheimer's disease: A review. *Frontiers in Aging Neuroscience* 2018;10:188.
4. Kim JC, Goldman S, Racke MK, Clarke NJ. PS-136 – A new LC-MS/MS assay for the quantification of Ab40 and Ab42 in plasma: Validation and clinical performance. Presented at: Alzheimer's Association International Conference. San Diego, 2022.
5. Chan VTT, Sun Z, Tang S, et al. Spectral-domain OCT measurements in Alzheimer's disease: A systematic review and meta-analysis. *Ophthalmology* 2019;126:4:497-510.
6. Lad EM, Mukherjee D, Stinnett SS, et al. Evaluation of inner retinal layers as biomarkers in mild cognitive impairment to moderate Alzheimer's disease. *PLoS One* 2018;13:2:e0192646.
7. Grewal DS, Polascik BW, Hoffmeyer GC, Fekrat S. Assessment of differences in retinal microvasculature using oct angiography in Alzheimer's disease: A twin discordance report. *Ophthalmic Surgery, Lasers and Imaging Retina* 2018;49:6:440-444.
8. Bulut M, Kurtuluş F, Gözkaya O, et al. Evaluation of optical coherence tomography angiographic findings in Alzheimer's type dementia. *British Journal of Ophthalmology* 2018;102:2:233-237.
9. Robbins CB, Grewal DS, Stinnett SS, et al. Assessing the retinal microvasculature in individuals with early and late-onset Alzheimer's disease. *Ophthalmic Surgery, Lasers and Imaging Retina* 2021;52:6:336-344.
10. Ma JP, Robbins CB, Lee JM. Longitudinal analysis of the retina and choroid in cognitively normal individuals at higher genetic risk of Alzheimer's disease. *Ophthalmology Retina* 2022;6:7:607-619.
11. Grewal DS, Sadda SR, Fekrat S. Understanding the role of the retina specialist in systemic diagnoses. *Retina Times* 2022;40:2:94.
12. Yoon SP, Grewal DS, Thompson AC, et al. Retinal microvascular and neurodegenerative changes in Alzheimer's disease and mild cognitive impairment compared with control participants. *Ophthalmology Retina* 2019;3:6:489-499.
13. Grewal DS, Fekrat S. Assessment of retinal microvascular alterations in individuals with amnesic and non-amnesic mild cognitive impairment using optical coherence tomography angiography. *RETINA* 2022;42:1338-1346.
14. Robbins CB, Thompson AC, Bhullar PK, et al. Characterization of retinal microvascular and choroidal structural changes in Parkinson's disease. *JAMA Ophthalmology* 2021;139:2:182-188.
15. Zou J, Liu K, Li F, et al. Combination of optical coherence tomography (OCT) and OCT angiography increases diagnostic efficacy of Parkinson's disease. *Quantitative Imaging in Medicine and Surgery* 2020;10:10:1930-1939.
16. Kundu A, Ma JP, Robbins CB, et al. Longitudinal analysis of retinal microvascular and choroidal imaging parameters in Parkinson's disease compared to controls. *Ophthalmology Science* 2023;100393.
17. Justin GA, Winslow L, Robbins CB, et al. Evaluating the retinal architecture and microvasculature in traumatic brain injury using optical coherence tomography angiography. Presented at The Retina Society. Pasadena, 2022.
18. Amini E, Moghaddasi M, Habibi SAH, et al. Huntington's disease and neurovascular structure of retina. *Neurological Sciences* 2022;43:5933-5941.
19. Haystead A, Joseph S, Allen A, et al. Characterizing

the retina structure and microvasculature in Huntington's disease. ARVO, 2023.

20. Liu M, Cheng D, Wang K, et al. Multi-modality cascaded convolutional neural networks for Alzheimer's disease diagnosis. *Neuroinformatics* 2018;16:3-4:295-308.
21. Tian J, Smith G, Guo H, et al. Modular machine learning for Alzheimer's disease classification from retinal vasculature. *Scientific Reports* 2021;11:238.
22. Wisely CE, Richardson A, Henao R, et al. A convolutional neural network using multimodal retinal imaging for differentiation of mild cognitive impairment from normal cognition. *Ophthalmology Science* 2023;100355.
23. Wisely CE, Wang D, Henao R, et al. Convolutional neural network to identify symptomatic Alzheimer's disease using multimodal retinal imaging. *British Journal of Ophthalmology* 2022;106:3:388-395.
24. Grewal DS, Fine HF, Fekrat S. Is OCT angiography useful in neurodegenerative diseases? *Ophthalmic Surgery, Lasers and Imaging Retina* 2019;50:5:269-273.
25. Casaleto KB, Ward ME, Baker NS, et al. Retinal thinning is uniquely associated with medial temporal lobe atrophy in neurologically normal older adults. *Neurobiology of Aging* 2017;51:141-147.
26. Zhang JF, Wiseman S, Valdés-Hernández MC, et al. The application of optical coherence tomography angiography in cerebral small vessel disease, ischemic stroke, and dementia: A systematic review. *Frontiers in Neurology* 2020;11:1009.
27. Ma JP, Robbins CB, Stinnett SS. Repeatability of peripapillary OCT angiography in neurodegenerative disease. *Ophthalmology Science* 2021;1:4:100075.
28. Lee T, Rivera A, Brune M, et al. Convolutional neural network-based automated quality assessment of OCT and OCT angiography image maps in individuals with neurodegenerative disease. *Translational Vision Science & Technology* 2023;12:6:30.
29. Li XX, Wu W, Zhou H, et al. A quantitative comparison of five optical coherence tomography angiography systems in clinical performance. *International Journal of Ophthalmology* 2018;11:11:1784-1795.
30. Rifai OM, McGrory S, Robbins CB, et al. The application of optical coherence tomography angiography in Alzheimer's disease: A systematic review. *Alzheimer's & Dementia* 2021;13:1:e12149.

ABOUT THE AUTHORS



**Joshua Woo** is a first year medical student at the Duke University School of Medicine (DUSOM) in Durham. **Sejal Patel** is a second-year undergraduate student at Duke University in the Trinity College of Arts and Sciences studying Neuroscience.



They both currently work with Duke's iMIND (Eye Multimodal Imaging in Neurodegenerative Disease) Research Group.



**Dr. Fekrat** is a professor of ophthalmology, associate professor in the Department of Surgery and professor of neurology at Duke. She's also director of the iMIND Research Group.



**Dr. Grewal** is an associate professor of ophthalmology and neurology at Duke. None of the authors have a financial interest in the material presented.

Direct correspondence to Dr. Grewal at 2351 Erwin Road, Durham, NC 27710. dilraj.grewal@duke.edu. (919) 684-8111

# Complications of Cataract Surgery in Wet AMD

Scientists compared the rate of intraoperative complications and visual outcomes in patients with neovascular age-related macular degeneration and control eyes without nAMD undergoing phacoemulsification.

As part of the multicenter retrospective, non-randomized comparative study, investigators classified eyes based on the presence or absence of a nAMD diagnosis. The main outcomes were: the rate of intraoperative complications; the logMAR visual acuity at four to 12 weeks postoperatively in both groups; and the reinjection rate of intravitreal anti-VEGF after phacoemulsification.

Here are some of the findings:

- Preoperative VA was worse in the nAMD group (0.9 +0.5) vs. the reference group (0.6 +0.5).
- No difference was reported in the rates of posterior capsule rupture (PCR) (2.90 vs. 2.77 percent;  $p=0.889$ ), dropped lens fragments (0.46 vs. 0.29 percent;  $p=0.618$ ) or zonular dialysis (0.46 vs. 0.58 percent;  $p=0.749$ ) between the two groups.
- Receiving  $\geq 10$  intravitreal injections before cataract surgery predicted the likelihood of PCR with an odds ratio of 2.86 ( $p=0.027$ ).
- The proportion of eyes achieving a visual gain of  $\geq 0.3$  logMAR ( $\sim 3$  Snellen lines equivalent) was lower in nAMD eyes (39.2 vs. 63.7 percent;  $p<0.0001$ ).
- A total of 203 eyes (73 percent) in the active treatment group and 139 eyes (36 percent) in the inac-

tive treatment group received more than one intravitreal injection after phacoemulsification ( $p<0.0001$ ).

Scientists reported that the risk of posterior capsule rupture was higher for eyes receiving  $\geq 10$  intravitreal injections before phacoemulsification. Only 39 percent of eyes with neovascular age-related macular degeneration had visual improvement by  $\geq 3$  Snellen lines.

*J Cataract Refract Surg 2023; Sep 26. [Epub ahead of print].*  
Siddiqui M, Elhusseiny A, Soliman M, et al.

## Conversion of Drusen to MNV

Investigators analyzed imaging features preceding the occurrence of type 3 (T3) macular neovascularization using tracked spectral-domain optical coherence tomography.

From a cohort of eyes with T3 MNV and  $\geq 12$  months of prior tracked SD-OCT, T3 lesions that developed above soft drusen were selected for OCT analysis. Retinal imaging findings at the location where type T3 MNV occurred were analyzed at each follow-up until the onset of T3 MNV. The following OCT parameters were assessed: drusen size (height and width); outer nuclear layer (ONL)/Henle fiber layer (HFL) thickness at the drusen apex; the presence of intraretinal hyperreflective foci (HRF), retinal pigment epithelium (RPE) disruption, incomplete RPE and outer retina atrophy (iRORA); and complete RORA (cRORA).

Here are some of the findings:

- From a cohort of 31 eyes with

T3 MNV, T3 lesions developed above soft drusen in 20 eyes (64.5 percent).

- Drusen showed progressive growth ( $p<0.001$ ) associated with ONL/HFL ( $p<0.001$ ) thinning prior to T3 MNV.

- The following OCT features were identified preceding the occurrence of T3 MNV, typically at the apex of the drusenoid lesion: disruption of the external limiting membrane (ELM)/ellipsoid zone (EZ) and/or the RPE; HRF; and iRORA/cRORA.

Investigators found specific anatomic alterations preceding the occurrence of type 3 macular neovascularization that commonly originate above soft drusen, including drusen growth, reduced outer nuclear layer/Henle fiber layer thickness and RPE atrophy at the drusen apex. They suggested that identifying these features should warrant close monitoring for identification of type 3 macular neovascularization, which can benefit from prompt intravitreal anti-VEGF therapy.

*Retina 2023; Sep 19. [Epub ahead of print].*  
Bousquet E, Santina A, Corradetti G, et al.

## Corneal Ulcers in Ocular Graft vs. Host Disease

Scientists evaluated the incidence, clinical characteristics, microbiological profile and therapeutic outcomes of corneal ulcers in individuals with chronic ocular graft-vs-host disease.

The retrospective clinical cohort study involved a review of individuals diagnosed with graft-vs-host disease following hematopoietic stem cell transplantation (HSCT) seen at the Bascom Palmer Eye Institute between May 2010 and November 2021. Baseline demographics, clinical characteristics, microbiological profile, risk factors

for corneal ulceration and treatment outcomes were studied. Etiology was deemed infectious in individuals with a positive culture or appropriate clinical scenario (presence of stromal infiltrate or hypopyon); otherwise, ulcers were presumed to be non-infectious. Treatment success was defined as re-epithelialization with infiltrate resolution, and treatment failure was defined as progression to corneal perforation or keratoplasty. Kaplan-Meier survival analysis was used to estimate the incidence of ulceration while Cox regression analyses helped evaluate demographic and risk factors. Infectious and non-infectious ulcer groups were compared using two-way independent T tests, one-way analysis of variances (ANOVAs) and chi-squared tests.

A total of 173 individuals were included (53.7 ±14.4 years old; 59 percent male). Here are some of the findings:

- Thirty-three individuals developed an ulcer 74.5 ±54.3 months after HSCT, with estimated five- and 10-year incidences of 14 and 30 percent, respectively.

- Twenty-two ulcers (66.6 percent) were deemed infectious (15 confirmed microbiologically, seven clinically) and 11 (33.3 percent) were deemed non-infectious.

- Risk factors for corneal ulceration included: black race (HR: 2.89; CI, 1.30 to 6.42;  $p<0.01$ ); previous ocular surgery (HR: 9.16; CI, 3.86 to 21.72;  $p<0.01$ ); lid margin abnormalities (HR: 3.44; CI, 1.69 to 6.99;  $p<0.01$ ); and topical steroid use (HR: 2.74; CI, 1.33 to 5.62;  $p<0.01$ ).

- Contact lens use reduced the risk of corneal ulceration (HR: 0.29;

CI, 0.13 to 0.66;  $p<0.01$ ).

- Infectious ulcers had a significantly higher frequency of treatment failure than non-infectious ulcers (57.1 vs. 20.0 percent;  $p=0.04$ ).

Scientists determined that corneal ulceration is a potential complication of graft-vs-host disease, with several clinical features identified as risk factors. They added that infectious ulcers had worse outcomes than non-infectious ulcers.

*Am J Ophthalmol* 2023; Sep 27.

[Epub ahead of print].

Sepulveda-Beltran PA, Carletti P, Banda V, et al.

### Anti-VEGF Treatment Response in CSCR

Researchers identified baseline predictors of anti-VEGF treatment response at three years in patients affected by choroidal neovascularization secondary to central serous chorioretinopathy.



In the retrospective longitudinal study, medical records of patients diagnosed with choroidal neovascularization secondary to central serous chorioretinopathy and treated using anti-VEGF injections between April 2015 and May 2020, were reviewed. The study's researchers identified or measured the potential qualita-

tive and quantitative predictors of treatment response based on baseline multimodal imaging exams available, including structural optical coherence tomography, fluorescein angiography, indocyanine green angiography and OCT-angiography. Univariate and multivariate analyses were performed.

Twenty-nine eyes from 29 patients affected by CNV complicating CSCR were included. Here are some of the findings:

- At the end of the three-year follow-up, the mean BCVA was 20/50 Snellen equivalent (0.38 ±0.36 logMAR), and no significant difference was found from baseline BCVA (0.37 ±0.29 logMAR) ( $p=0.9$ ).

- Twenty out of 29 eyes (69 percent) had active lesions at the end of the follow-up.

- At multivariate analysis, no included features were independently associated with three-year BCVA outcomes.

- Pigment epithelium detachment height ( $\beta=0.017$ ;  $p=0.028$ ) and outer limiting membrane preservation at the fovea ( $\beta=-5.637$ ;  $p=0.026$ ) were independently associated with choroidal neovascularization activity at three years.

Researchers found that pigment epithelium detachment height and outer limiting membrane obliteration at the fovea might be considered baseline predictors of lesion

activity at three-year follow-up in patients with choroidal neovascularization secondary to central serous chorioretinopathy treated with anti-VEGF therapy. ◀

*Graefes Arch Clin Exp Ophthalmol* 2023; Sep 29. [Epub ahead of print]  
Cozzupoli GM, Sacconi R, Tombolini B, et al.



EDITED BY COLLIN ROZANSKI, MD

## WILLS EYE RESIDENT CASE REPORT

# A 78-year-old man is referred to Wills Eye Hospital for an ominous limbal mass.

BAILEY M. HARRISON, MD, RALPH C. EAGLE JR., MD, AND ZEBA A. SYED, MD  
PHILADELPHIA

### Presentation

A 78-year-old male first noticed a growth on the surface of his left eye in the fall of 2022, which increased in size over several months and began to cause blurred vision. He presented to his primary ophthalmologist in May 2023 for an annual exam. His ophthalmologist noted a concerning ocular surface mass and referred the patient to Wills Eye Hospital for a consultation with a cornea specialist.

### History

The patient had a history of type 2 diabetes and moderate to severe non-proliferative diabetic retinopathy for which he was followed yearly by his general ophthalmologist. He had a known stable choroidal nevus in the right eye which was monitored with annual dilated exams and fundus photos. His surgical history was notable for cataract extraction with intraocular lens implantation in both eyes seven years previously.

### Examination

At presentation, best-corrected visual acuity was 20/25 in his right eye and 20/100 in his left eye. His pupils were round and reactive in both eyes without an afferent pupillary defect in either eye. Intraocular pressures were 16 mmHg in the right eye and 15 mmHg in the left eye. Extraocular motility and confrontation visual fields were full bilaterally.

Anterior segment examination of the left eye disclosed a papillomatous limbal lesion located between 12 and 6 o'clock. The lesion extended

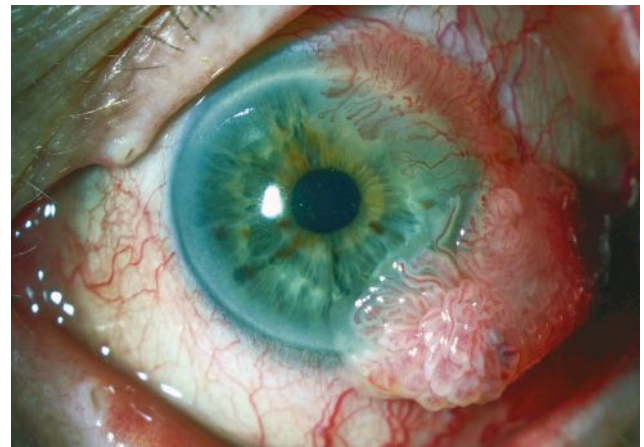


Figure 1. A limbal mass composed of multiple fronds of epithelium with vascular cores. Feeder vessels are present.

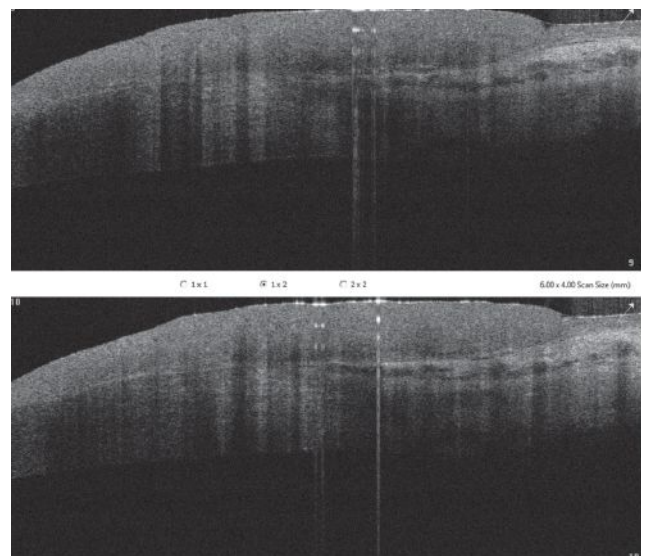


Figure 2. AS-OCT of the limbal mass photographed in Figure 1.

about 2.5 mm onto the cornea. Between 12 and 3 o'clock, it was relatively flat. Between 3 and 6 o'clock, it was elevated, with large feeder vessels (*Figure 1*). Anterior segment optical coherence tomography revealed an abrupt transition between the healthy and the thickened diseased epithelium (*Figure 2*).

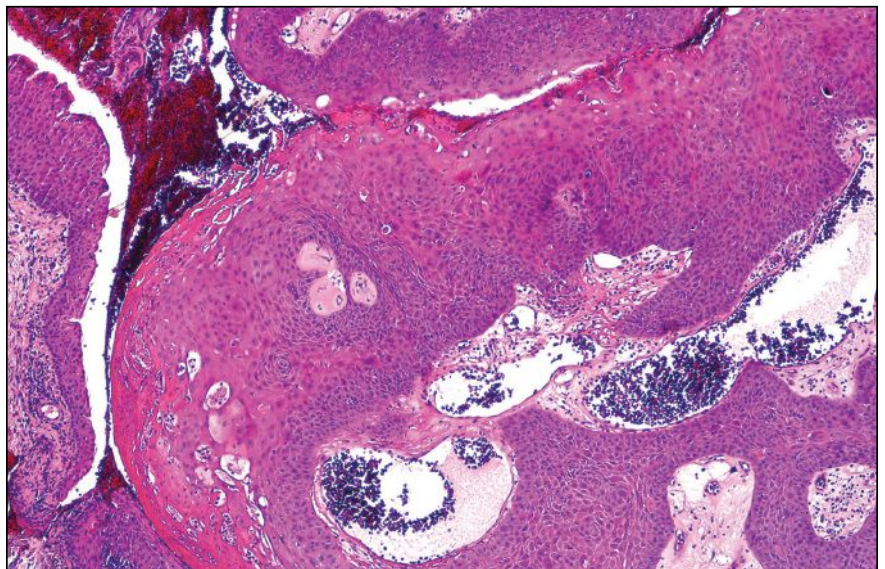
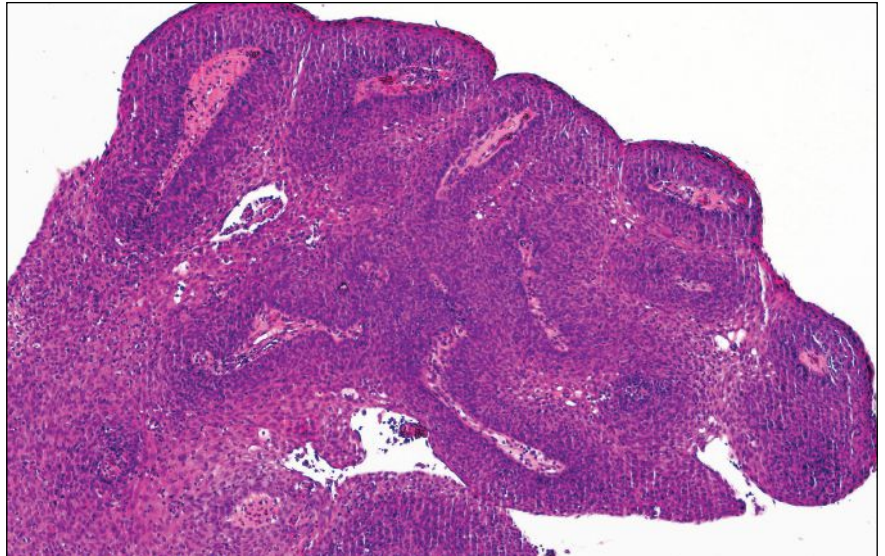
Other notable findings included mild meibomian gland dysfunction bilaterally and posterior chamber intraocular lenses in good position in both eyes. Eversion of both upper eyelids revealed no significant findings. The posterior segments of the right eye and the left eye were unremarkable.

**What's your diagnosis? What work-up would you pursue? The diagnosis appears below.**

### Work-up, Diagnosis and Treatment

The conjunctival mass was excised with cryotherapy of the limbus and margins, followed by amniotic membrane transplantation (AMT) in June 2023. Histopathology disclosed a papillomatous lesion composed of fronds of thickened dysplastic epithelium surrounding cores of inflamed fibrovascular tissue (*Figure 3*). The entire thickness of the epithelium was replaced by severely dysplastic epithelial cells, consistent with a diagnosis of papillary squamous cell carcinoma in situ. Severely dysplastic epithelium was present at the limbal and corneal tissue margins.

Because the lesion was large and was incompletely excised, the patient was treated postoperatively with two cycles of adjuvant topical 5-fluorouracil (four times daily for a week, with three weeks off). Six weeks postoperatively, there was no evidence of recurrence.



**Figure 3. Epithelium is totally replaced by atypical squamous cells consistent with squamous cell carcinoma in situ. Hematoxylin & eosin. Top x25, lower x100.**

### Discussion

The term ocular surface squamous neoplasia (OSSN) refers to a neoplastic spectrum that involves the squamous cells of the conjunctival and corneal epithelium. Most of the

disease entities included in OSSN are rare, with incidences ranging from 0.1 to 35 cases per 1,000,000 people.<sup>1</sup> Risk factors for developing OSSN include ultraviolet light and/or sun exposure, vitamin A deficiency, xeroderma pigmen-



tosum, human immunodeficiency virus (HIV) and human papilloma virus (HPV).<sup>2-4</sup> There is also a higher incidence among Caucasian populations and individuals with lighter colored irides.<sup>2,4</sup>

OSSN includes conjunctival intraepithelial neoplasia (CIN), corneal epithelial dysmaturation and dysplasia, and in situ and invasive squamous cell carcinoma (SCC).<sup>5</sup> OSSN encompasses histologic features ranging from CIN to SCC. These features include varying degrees of epithelial dysplasia, such as CIN, which can progress to SCC in situ neoplasia, and finally invade through the epithelial basement membrane into the substantia propria as invasive SCC.<sup>6</sup> Papillary SCC, as diagnosed in this patient, is a variant of SCC of the ocular surface. It's diagnosed via clinical features as well as excisional biopsy and histopathological examination. This entity typically presents clinically as a unilateral mass at the intrapalpebral limbus that is vascularized and elevated, creating a papillary variant of OSSN. The mass can present with tortuous feeder vessels as well, as in this patient.<sup>6</sup>

AS-OCT, which was obtained for this patient, can be a helpful *in vivo* tool to assess and diagnose an ocular surface mass. A characteristic AS-OCT feature of OSSN is an abrupt transition between normal and neoplastic tissue, as shown in this case. AS-OCT also can demonstrate a thickened and hyperreflective epithelium and be helpful in evaluating for invasion. It can be helpful in cases where the clinical diagnosis isn't abundantly clear, and also can help to assess progress after treatment.<sup>7</sup>

Excisional biopsy is a common treatment modality as it provides immediate resolution and allows for direct histopathological examination of the neoplastic tissue, although biopsy isn't critical for a diagnosis of OSSN.<sup>8</sup> Topical treatment modalities for OSSN include interferon-alpha2b, 5-fluorouracil, and/or mitomycin C. Topical therapy can be used to treat the entire ocular surface, which can be favorable in larger tumors, and can be used to avoid surgical complications. However, topical modalities require patient compliance with several months of therapy.<sup>9</sup>

Recurrence rates of OSSN range between 24 percent and 50 percent in the literature for surgical therapy alone,<sup>10</sup> with recurrence rates reported higher at 56 to 69 percent when there are positive surgical margins.<sup>11</sup> Topical pharmacotherapy has had lower reported recurrence rates ranging from 5 to 11 percent, although follow-up data may be limited.<sup>12</sup> A meta-analysis demonstrated similar recurrence rates among topical therapy and surgical excision.<sup>12</sup> Recurrence typically occurs within two years after surgery, and is highly dependent upon the surgical margins and use of adjuvant therapy.

Cryotherapy is an important step of surgical management, as was performed in this patient. This treatment, when used immediately following tumor excision, causes thermal destruction of tumor cells and their vasculature, and can target residual tumor cells and therefore prevent recurrence.<sup>9</sup> Recurrence rates of combined surgical excision and cryotherapy have been reported as low as 0 to 12.3 percent.<sup>13</sup>

This patient opted for surgical excision for immediate resolution, and we decided to initiate adjuvant topical therapy given the size of the lesion as well as positive tissue margins at both the corneal surface and the conjunctival portion of the tumor. This treatment addresses residual tumor cells and may reduce the risk of recurrence. AMT aided in the reconstruction of the ocular surface after the tumor was resected.

In conclusion, OSSN and particularly SCC can present with characteristic growths on the ocular surface with associated feeder vessels. AS-OCT and histopathologic examination are critical tools in the diagnosis of this entity. There are several treatment options available, including surgical and topical therapies. Ultimately, the treatment approach should be tailored to each patient's individual goals of care. ◀

“AS-OCT, which was obtained for this patient, can be a helpful *in vivo* tool to assess and diagnose an ocular surface mass.”

1. Shields CL, Demirci H, Karatza E, Shields JA. Clinical survey of 1643 melanocytic and nonmelanocytic conjunctival tumors. *Ophthalmology* 2004;111:1747-1754.
2. Napora C, Cohen EJ, Genvert GI, Presson AC, Arentsen JJ, Eagle RC, Laibson PR. Factors associated with conjunctival intraepithelial neoplasia: A case control study. *Ophthalmic Surg* 1990;21:27-30.
3. Porges Y, Groisman GM. Prevalence of HIV with conjunctival squamous cell neoplasia in an African provincial hospital. *Cornea* 2003;22:1-4.
4. Scott IU, Karp CL, Nuovo GJ. Human papillomavirus 16 and 18 expression in conjunctival intraepithelial neoplasia. *Ophthalmology* 2002;109:542-547.
5. Basti S, Macsai MS. Ocular surface squamous neoplasia: A review. *Cornea* 2003;22:687-704.
6. Shields CL, Chien JL, Surakiatchanukul T, Sioufi, K, Lally, SE, Shields, JA. Conjunctival tumors: Review of clinical features, risks, biomarkers, and outcomes—The 2017 J. Donald M. Gass Lecture. *Asia-Pacific Journal of Ophthalmology* 2017;6:2:109-120.
7. Stevens SM, Reyes-Capo DP, Patel U, Choudhary A, Khzam RA, Tang V, Galor A, Karp CL, Dubovy S. Clinical and optical coherence tomography comparison between ocular surface squamous neoplasia and squamous metaplasia. *Cornea* 2023;42:4:429-434.
8. Polski A, Sibug Saber M, Kim JW, Berry JL. Extending far and wide: The role of biopsy and staging in the management of ocular surface squamous neoplasia. *Clin Exp Ophthalmol* 2019;47:2:193-200.
9. Höllhumer R, Williams S, Michelow P. Ocular surface squamous neoplasia: Management and outcomes. *Eye (Lond)* 2021;35:6:1562-1573.
10. Tunc M, Char DH, Crawford B, Miller T. Intraepithelial and invasive squamous cell carcinoma of the conjunctiva: Analysis of 60 cases. *Br. J. Ophthalmol* 1999;83:98-103.
11. Tabin G, Levin S, Snibson G, et al. Late recurrences and the necessity for long-term follow-up in corneal and conjunctival intraepithelial neoplasia. *Ophthalmology* 1997;104:485-492.
12. Kozma K, Dömötör ZR, Csutak A, Szabó L, Hegyi P, Erőss B, Helyes Z, Molnár Z, Dembrovsky F, Szalai E. Topical pharmacotherapy for ocular surface squamous neoplasia: Systematic review and meta-analysis. *Sci Rep* 2022;12:1:14221.
13. Peksayar G, Altan-Yaycioglu R, Onal S. Excision and cryosurgery in the treatment of conjunctival malignant epithelial tumours. *Eye* 2003;17:228-232.

IYUZEH™ (latanoprost ophthalmic solution) 0.005% is the first and only preservative-free latanoprost for patients with primary open-angle glaucoma (POAG) and ocular hypertension (OHT).



# Transform how you lower IOP. POWER WITHOUT PRESERVATIVES.

## INDICATIONS AND USAGE

IYUZEH™ is a prostaglandin analogue indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

## IMPORTANT SAFETY INFORMATION

### CONTRAINDICATIONS

Known hypersensitivity to latanoprost or any other ingredients in this product.

### WARNINGS AND PRECAUTIONS

**Pigmentation:** Topical latanoprost ophthalmic products, including IYUZEH™ have been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periorbital tissue (eyelid), and eyelashes. Pigmentation is expected to increase as long as latanoprost is administered.

The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes.

After discontinuation of latanoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. The long-term effects of increased pigmentation are not known.

Iris color change may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. While treatment with IYUZEH™ can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

**Eyelash Changes:** Latanoprost ophthalmic products, including IYUZEH™ may gradually change eyelashes and vellus hair in the treated eye; these changes include increased length, thickness, pigmentation, the number of lashes or hairs, and misdirected growth of eyelashes. Eyelash changes are usually reversible upon discontinuation of treatment.

## IYUZEH<sup>TM</sup> HAD SIMILAR MEAN IOP REDUCTION WHEN COMPARED WITH XALATAN<sup>®</sup>

IN PHASE III TRIALS, REDUCED IOP WITH PROVEN EFFICACY

**IYUZEH  
LOWERED IOP  
by 3-8 mmHg (n=165)  
vs  
4-8 mmHg (n=169)  
for XALATAN<sup>1</sup>**

NDC 82584-003-30  
**IYUZEH<sup>TM</sup>**  
(latanoprost ophthalmic  
solution)  
**0.005%**  
30 single-dose containers  
(0.2 mL each)  
For Topical Ophthalmic Use - Rx only

IYUZEH<sup>TM</sup> contains no preservatives

“

*We owe it to our patients with elevated intraocular pressure, with open-angle glaucoma or ocular hypertension to provide a new evidence-based best practice. It is an extremely exciting time to prescribe IYUZEH for my patients.*

”

**Monique M. Barbour  
MD, MHA, FAAO**

*Dr. Barbour is a paid consultant of Thea Pharma Inc.*



**Intraocular Inflammation:** IYUZEH<sup>TM</sup> should be used with caution in patients with a history of intraocular inflammation (iritis/uveitis) and should generally not be used in patients with active intraocular inflammation because inflammation may be exacerbated.

**Macular Edema:** Macular edema, including cystoid macular edema, has been reported during treatment with latanoprost ophthalmic products, including IYUZEH<sup>TM</sup>. IYUZEH<sup>TM</sup> should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

**Herpetic Keratitis:** Reactivation of herpes simplex keratitis has been reported during treatment with latanoprost. IYUZEH<sup>TM</sup> should be used with caution in patients with a history of herpetic keratitis. IYUZEH<sup>TM</sup> should be avoided in cases of active herpes simplex keratitis because inflammation may be exacerbated.

**Contact Lens Use:** Contact lenses should be removed prior to the administration of IYUZEH<sup>TM</sup> and may be reinserted 15 minutes after administration.

### ADVERSE REACTIONS

The following adverse reactions have been reported with the use of topical latanoprost products: iris pigmentation changes, eyelid skin darkening, eyelash changes (increased length, thickness, pigmentation, and number of lashes), intraocular inflammation (iritis/uveitis), and macular edema, including cystoid macular edema.

### DRUG INTERACTIONS

The combined use of two or more prostaglandins, or prostaglandin analogs including IYUZEH<sup>TM</sup> is not recommended. It has been shown that administration of these prostaglandin drug products more than once daily may decrease the IOP lowering effect or cause paradoxical elevations in IOP.

**Please see full Prescribing Information at [www.iyuzeh.com](http://www.iyuzeh.com) and Brief Summary on the next page.**

Explore the power of preservative-free latanoprost at [iyuzeh.com](http://iyuzeh.com)





iStent  
infinite



Go with the Flow

Give patients with glaucoma who have failed prior medical and surgical intervention a powerful new direction with iStent infinite®—a first-of-its-kind **standalone** implantable alternative designed to deliver **up to 8 clock hours (240°)** of outflow coverage while minimizing tissue disruption.<sup>1</sup>

**The interventional glaucoma revolution is here.**

**REFERENCE:**

1. Sarkisian SR Jr, Grover DS, Gallardo M, et al; iStent infinite Study Group. Effectiveness and safety of iStent infinite trabecular micro-bypass for uncontrolled glaucoma. *J Glaucoma*. 2023;32(1):9-18.

**iStent infinite® IMPORTANT SAFETY INFORMATION**

**INDICATION FOR USE.** The iStent infinite® Trabecular Micro-Bypass System Model IS3 is an implantable device intended to reduce the intraocular pressure (IOP) of the eye. It is indicated for use in adult patients with primary open-angle glaucoma in whom previous medical and surgical treatment has failed. **CONTRAINDICATIONS.** The iStent infinite is contraindicated in eyes with angle-closure glaucoma where the angle has not been surgically opened, acute traumatic, malignant, active uveitic, or active neovascular glaucoma, discernible congenital anomalies of the anterior chamber (AC) angle, retrolubar tumor, thyroid eye disease, or Sturge-Weber Syndrome or any other type of condition that may cause elevated episcleral venous pressure. **WARNINGS.** Gonioscopy should be performed prior to surgery to exclude congenital anomalies of the angle, PAS, rubeosis, or conditions that would prohibit adequate visualization that could lead to improper placement of the stent and pose a hazard. **MRI INFORMATION.** The iStent infinite is MR-Conditional, i.e., the device is safe for use in a specified MR environment under specified conditions; please see Directions for Use (DFU) label for details. **PRECAUTIONS.** The surgeon should monitor the patient postoperatively for proper maintenance of IOP. Three out of 61 participants (4.9%) in the pivotal clinical trial were phakic. Therefore, there is insufficient evidence to determine whether the clinical performance of the device may be different in those who are phakic versus in those who are pseudophakic. **ADVERSE EVENTS.** The most common postoperative adverse events reported in the iStent infinite pivotal trial included IOP increase  $\geq 10$  mmHg vs. baseline IOP (8.2%), loss of BSCVA  $\geq 2$  lines (11.5%), ocular surface disease (11.5%), perioperative inflammation (6.6%) and visual field loss  $\geq 2.5$  dB (6.6%). **CAUTION:** Federal law restricts this device to sale by, or on the order of, a physician. Please see DFU for a complete list of contraindications, warnings, precautions, and adverse events.

©2023 Glaukos Corporation. All rights reserved. iStent infinite is a registered trademark of Glaukos Corporation.