The Wide World of CORNEAL PROCEDURES

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Tono-Pen AVIA® Tonometer
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.
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. 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
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.1 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.2 Most redness relievers are α1- or α1/α2-adrenergic receptor agonists; α1-adrenergic receptor agonism constricts corneal arterioles, hindering oxygen delivery to the cornea, which causes rebound redness. Brimonidine tartrate, by contrast, is selective for the α2-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.3

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.4 It had a favorable safety profile and, consistent with its mechanism of action, a low incidence of rebound redness (1.2%).4,5,6 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%).7

Opportunity for ECPs to Step In

Market research indicates that patients report use of redness relievers an average of 3 days per week.7 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 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.

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

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

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

“Those 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.


**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 Qlosi (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 Qlosi’s lower concentration, clinicians 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

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You know us for tonometry.

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

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Cross-linking: Best Practices
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INDICATIONS AND USAGE

XDEMVY (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: XDEMVY contains potassium sorbate, which may discolor soft contact lenses. Contact lenses should be removed prior to instillation of XDEMVY and may be reinserted 15 minutes following its administration.

ADVERSE REACTIONS: The most common adverse reaction with XDEMVY 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.

FDA-APPROVED TREATMENT FOR DEMODEX BLEPHARITIS (DB)

44% and 55% of patients taking XDEMVY 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.


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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. 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)
Join us for a collaborative discussion on how IZERVAY™ may benefit your patients

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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, FAAO
Consultative Optometrist
Eye Centers of South Florida
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Priya Vakharia MD
Retina Specialist
Retina Vitreous Associates of Florida
Tampa, FL

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

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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.4*

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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

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* Defined as modified Miyata grade 0, <25μm/mm² 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.

‖ 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® Vivity® Extended Vision Hydrophobic Posterior Chamber IOL and Clareon® Vivity® 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® Vivity® 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 Vivity® 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® Vivity® IOL, most patients implanted with the Vivity® 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® Vivity® 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 Vivity® IOL clinical study, 1% to 2% of AcrySof® IQ Vivity® 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:


(Continued from p. 12)
Cyclodialysis Clefts With MIGS

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

Cyclodialysis clefts occur when the longitudinal ciliary muscle fibers separate from the scleral spur, forming a pathway from the anterior chamber to the suprachoroidal 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.

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 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

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.
GEOGRAPHIC ATROPHY (GA) CAN PROGRESS FASTER THAN YOU THINK

Baseline  | Month 3  | Month 6


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.
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 ≥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.
IZERVAY™ (avacincaptad pegol intravitreal solution)  
Rx only

**Brief Summary:** This information is not comprehensive. Visit IZERVAYscp.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.

2.3 Injection Procedure
Only 0.1 mL (2 mg) should be administered to deliver a single dose. Any excess volume should be discarded.

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 antibiotic 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.

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
- 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>
<thead>
<tr>
<th>Adverse Drug Reactions</th>
<th>IZERVAY N = 292</th>
<th>Sham N = 332</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjunctival hemorrhage</td>
<td>13%</td>
<td>9%</td>
</tr>
<tr>
<td>Increased IOP</td>
<td>9%</td>
<td>1%</td>
</tr>
<tr>
<td>Choroidal neovascularization</td>
<td>7%</td>
<td>4%</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>8%</td>
<td>5%</td>
</tr>
<tr>
<td>Eye pain</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Vitreous floaters</td>
<td>2%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Blepharitis</td>
<td>2%</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>

* 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 5.2 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 0.02, 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.

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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-
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-µm 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.

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. 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. 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
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:

<table>
<thead>
<tr>
<th>NEW!</th>
<th>Tobramycin 1% and Vancomycin 2.5% Ophthalmic Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current</td>
<td>Tobramycin 1.5% and Vancomycin 5% Ophthalmic Solution</td>
</tr>
<tr>
<td>COMING SOON!</td>
<td>Vancomycin 2.5% Ophthalmic Solution</td>
</tr>
<tr>
<td>COMING SOON!</td>
<td>Vancomycin 5% Ophthalmic Solution</td>
</tr>
</tbody>
</table>

- 100% Replacement Guarantee on Expired Product**
- Same-Day Shipping and Easy Ordering***
- Refrigerated; Never Frozen†,1,2
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**Replacement guarantee applies to product that expires before providing to patient.
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††Every batch is tested for potency and sterility at our FDA-registered laboratory.
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 with viscoelastic opposite the scleral groove and fill the anterior chamber with viscoelastic. You can then tie the sutures with the knots buried under the scleral flaps to prevent erosion. 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 correctopia 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.

Bring the needle out through the sclera. Repeat this process with the second needle of the double-armed Prolene suture through the scleral groove. Tie the suture and bury the knot.

• **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. Suture is passed through the scleral flap and across the tissue posterior to the defect and tied, closing the defect. 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.

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4. 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.

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### 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.
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.1-3
† 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%.2,3

**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 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**
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® (cenegermin-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.

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

**References:**

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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).

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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—issues 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.
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. 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 often times 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.”
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...
INDICATION
SYFOVRE® (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, iris, and anterior chamber flare. After inflammation resolves, patients may resume treatment with SYFOVRE.

GA unravels so much
Save retinal tissue by slowing progression
1-3
SYFOVRE achieved continuous reductions in mean lesion growth rate* (mm²) vs sham pooled from baseline to Month 24

**Monthly**

- **OAKS**
  - 3.11 vs 3.98 (22% reduction)

- **DERBY**
  - 3.28 vs 4.00 (18% reduction)

**Every Other Month (EOM)**

- **OAKS**
  - 3.26 vs 3.98 (18% reduction)

- **DERBY**
  - 3.31 vs 4.00 (17% reduction)

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.

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 18.1

GA=geographic atrophy; SE=standard error.

**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 (mm²) was measured by fundus autofluorescence (FAF).1,4


Please see Brief Summary of Prescribing Information for SYFOVRE on the adjacent page.
A total of 839 patients with GA in two Phase 3 studies (OAKS and DERBY) were treated with SYFOVRE. In clinical trials, use of SYFOVRE was associated with increased rates of neovascular age-related macular degeneration (AMD). In a study conducted in diabetic patients, use of SYFOVRE was associated with a 6% increase in rates of neovascular AMD compared to the control group. The most common adverse reactions (≥5%) reported in patients receiving SYFOVRE were conjunctival hemorrhage, ocular discomfort, neovascular age-related macular degeneration, vitreous floaters, and 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 compared directly 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 ninety-one (491) 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.

#### 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.

#### PATIENT COUNSELING INFORMATION

Advise patients that following SYFOVRE administration, patients are at risk of developing endophthalmitis, retinal detachments, hyphema, and retinal tears. 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 operate machinery until visual function has recovered sufficiently.

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 aboritions 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.

### INDICATIONS AND USAGE

#### Contraindications

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 detachment. 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 compared directly 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 ninety-one (491) 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

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>PM (N = 419)</th>
<th>PEOM (N = 420)</th>
<th>Sham Pooled (N = 417)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular discomfort†</td>
<td>13</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Neovascular age-related macular degeneration†</td>
<td>12</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Vitreous floaters</td>
<td>10</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Conjunctival hemorrhage</td>
<td>8</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Vitreous detachment</td>
<td>4</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Retinal hemorrhage</td>
<td>4</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Punctate keratitis†</td>
<td>5</td>
<td>3</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Posterior capsule opacification</td>
<td>4</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Intraocular inflammation†</td>
<td>4</td>
<td>2</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Intraocular pressure increased</td>
<td>2</td>
<td>3</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

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

**SYFOVRE** (pegcetacoplan injection), for intravitreal use

SYFOVRE Through Month 24 in Studies OAKS and DERBY

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

Please see SYFOVRE full Prescribing Information for details.
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.”


DISCLOSURES

Drs. Koo and Raju report no relevant disclosures. Dr. Rapuano consults for BioTissue.
Despite advances in toric IOL technology, experienced cataract surgeons say limbal relaxing incisions are still a worthwhile technique to perform.

**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.”

“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 area.
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)
IOL implantation. Please see a complete list of conditions.

If excessive resistance is encountered during the insertion of the microstent at any time during surgery for the reduction of intraocular pressure (IOP) in adult patients with mild to moderate primary open-angle glaucoma (POAG). WARNING: 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, rubecosis 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 following cataract surgery. Prior to implantation, patients with history of allergic reactions to nickel, 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 pseudophakic or pigmented 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.


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
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.

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

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)

<table>
<thead>
<tr>
<th>Nichamin Nomogram for Clear Corneal Phaco Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Astigmatic Status: Against the Rule</strong></td>
</tr>
<tr>
<td><strong>PREOP CYLINDER (D) 30-40 yo 41-50 yo 51-60 yo 61-70 yo 71-80 yo 81-90 yo &gt; 90 yo</strong></td>
</tr>
<tr>
<td>+0.75 to +1.25</td>
</tr>
<tr>
<td>+1.50 to +2.00</td>
</tr>
<tr>
<td>+2.25 to +2.75</td>
</tr>
<tr>
<td>+3.00 to +3.75</td>
</tr>
</tbody>
</table>

| **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° |

The degrees of arc to incise are determined by the patient’s age and the preoperative cylinder. The nomogram 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.
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
Educate, Prescribe, Treat: Perceptions About Myopia Management Revealed

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

By Rupa Wong, MD

*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.

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.¹

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.⁵ 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 survey¹:

• 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.¹

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.²

After hearing their recommendation for myopia management treatment, more than 75% of patients pursued it, according to a majority of pediatric ophthalmologists surveyed.² 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.

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

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‡ 64% strongly agree, 26% somewhat agree.

∞ 56% strongly agree, 31% somewhat agree.

3. 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.
4. 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.¹ What is also promising is that recent as March 2020, we now have an FDA-approved treatment to help keep children’s myopia from getting worse so quickly.⁷,⁸ At my practice, I prescribe MiSight® 1 day for my age-appropriate patients based on its strong science and results.⁷,⁸,⁹

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

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.⁸†

Additionally, on average, age-appropriate children wearing MiSight® 1 day progressed less than -1.00D over 6 years.⁷±

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† 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.

Finally, MiSight® 1 day are the first and only§ FDA-approved* lenses to slow the progression of myopia when prescribed for children 8-12 years old at the initiation of treatment.80

With childhood myopia on the rise,3 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.
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.”
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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.

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 keratoconus, 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
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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 question 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—not 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-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. In patients over 40, some mild posterior corneal steepening and thinning may occur, independent of normal age-related changes. 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
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 note 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
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 µm, hypotonic Photrex (0.146% riboflavin 5’-phosphate ophthalmic solution) is instilled every five to 10 seconds until corneal thickness is at least 400 µm. Finally, the eye is irradiated at 3 mW/cm² 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 µm—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-µm 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 epithelial removal and installation of the riboflavin, check the pachymetry. If it’s less than 400 µm, you want to then swell the cornea. If you’re starting at less than 400 µm, 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 µm or less, these patients typically won’t be good candidates for epithelial-off cross-linking. They’d benefit from epithelial-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...
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perform cross-linking after Intacs, and others do combine. The way I look at it is that when 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 epithelium-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 healthcare 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.”

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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

Minimally-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.”

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 Sinskey 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 transliminal trabeculectomy (GATT). Canaloplasty, or viscodilation of Schlemm’s canal and distal outflow structures, can be performed with iTrack.

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

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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 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 goniodynechialysis 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 option 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 eyelid. 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 goniometry 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.

**Prior 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. 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.

“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. The graft for DMEK is...
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


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REVIEW

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around 10 to 15 μm in thickness, while graft thickness for DSEK can be nanothin (15 to 49 μm) all the way up to a conventional size (150 to 250 μm).

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’ endothelial corneal dystrophy at two weeks postoperatively with complete resorption of the gas. (Top Right) Postoperative appearance of patient who underwent DMEK for Fuchs’ endothelial corneal dystrophy at one week post-operatively with residual anterior chamber gas bubbles. (Top Left) 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.

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.

“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.

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
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.

**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
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. 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. Researchers reported no major adverse reactions directly related to the endothelial injections.

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.
Neurodegenerative Diseases and OCTA

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

Neurodegenerative diseases are the leading cause of disability around the world, and this burden is expected to increase exponentially over the next several decades. Alzheimer's disease (AD), accounting for 60 to 80 percent of dementia cases, remains plagued by underdetection due to diagnostic barriers. 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. 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. 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 (mm/mm²). 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 (MiD) 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. 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. Such findings have been the foundation to current literature highlighting OCTA as a potential clinical tool to identify biomarkers of AD. Of note, those carrying the apolipoprotein ε4 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.

Mild cognitive impairment (MCI) is often a transitional state before the development of AD, making an early diagnosis imperative.
diagnosis imperative. Thus, OCTA has previously been used as a tool to identify significant microvascular loss among those with MCI. Among those with amnestic MCI, which is more likely to progress to clinical AD, PfD was significantly lower compared to non-amnestic MCI patients and controls. Several cross-sectional studies have also shown the utility of OCTA in identifying biomarkers of Parkinson’s disease. 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.

Several cross-sectional studies have also shown the utility of OCTA in identifying biomarkers of Parkinson’s disease. 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 University’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. 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. 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. 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. 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. 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. 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.\textsuperscript{25} 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 and neurodegenerative disease over time and may confer a unique opportunity to assess the impact of disease-modifying therapies.\textsuperscript{16}

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.\textsuperscript{27} 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.\textsuperscript{28} 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.\textsuperscript{29} 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...
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.
thresholding algorithms for metrics like VD and PrD. 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. 

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 (\( \geq 3 \) 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 inactive 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.

 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 intra-retinal 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.

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

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...
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. Risk factors for developing OSSN include ultraviolet light and/or sun exposure, vitamin A deficiency, xeroderma pigmento-
OSSN includes conjunctival intraepithelial neoplasia (CIN), corneal epithelial dysmaturation and dysplasia, and in situ and invasive squamous cell carcinoma (SCC). 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. 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.

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.

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. 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.

Recurrence rates of OSSN range between 24 percent and 50 percent in the literature for surgical therapy alone, with recurrence rates reported higher at 56 to 69 percent when there are positive surgical margins. Topical pharmacotherapy has had lower reported recurrence rates ranging from 5 to 11 percent, although follow-up data may be limited. A meta-analysis demonstrated similar recurrence rates among topical therapy and surgical excision. 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. Recurrence rates of combined surgical excision and cryotherapy have been reported as low as 0 to 12.3 percent.

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.

References:

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.

Reference: 1. IYUZEH™ (latanoprost ophthalmic solution) 0.005%. Prescribing information. Thea Pharma Inc; 2022.
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.

IYUZEH™ had similar mean IOP reduction when compared with XALATAN®

In Phase III trials, reduced IOP with proven efficacy

Intraocular Inflammation: IYUZEH™ 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™. IYUZEH™ 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™ should be used with caution in patients with a history of herpetic keratitis. IYUZEH™ 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™ 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™ 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 and Brief Summary on the next page.
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.¹

The interventional glaucoma revolution is here.

REFERENCE:

iStent Infinite® IMPORTANT SAFETY INFORMATION

INDICATION FOR USE. The iStent Infinite® Trabecular Micro-Bypass System Model (S3) 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 uveitis, or active neovascular glaucoma, discourse congenital anomalies of the anterior chamber (AC), vascular 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, neovascular, 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 MRI Conditional, i.e., the device is safe for use in a specified MRI 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 6 participants (4.1%) in this 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 those who are pseudophakic. ADVERSE EVENTS. The most common postoperative adverse events reported in the iStent infinite pivotal trial included IOP increase >10 mm Hg, baseline IOP >21 mm Hg, loss of BCVA <2 lines (11.5%), cataract disease (11.3%), perioperative inflammation (6.4%), and visual field loss ≥2.5 dB (6.4%). 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.

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