Wills Eye Resident Series: A patient presents with bilateral choroidal nevi, *p. 63*

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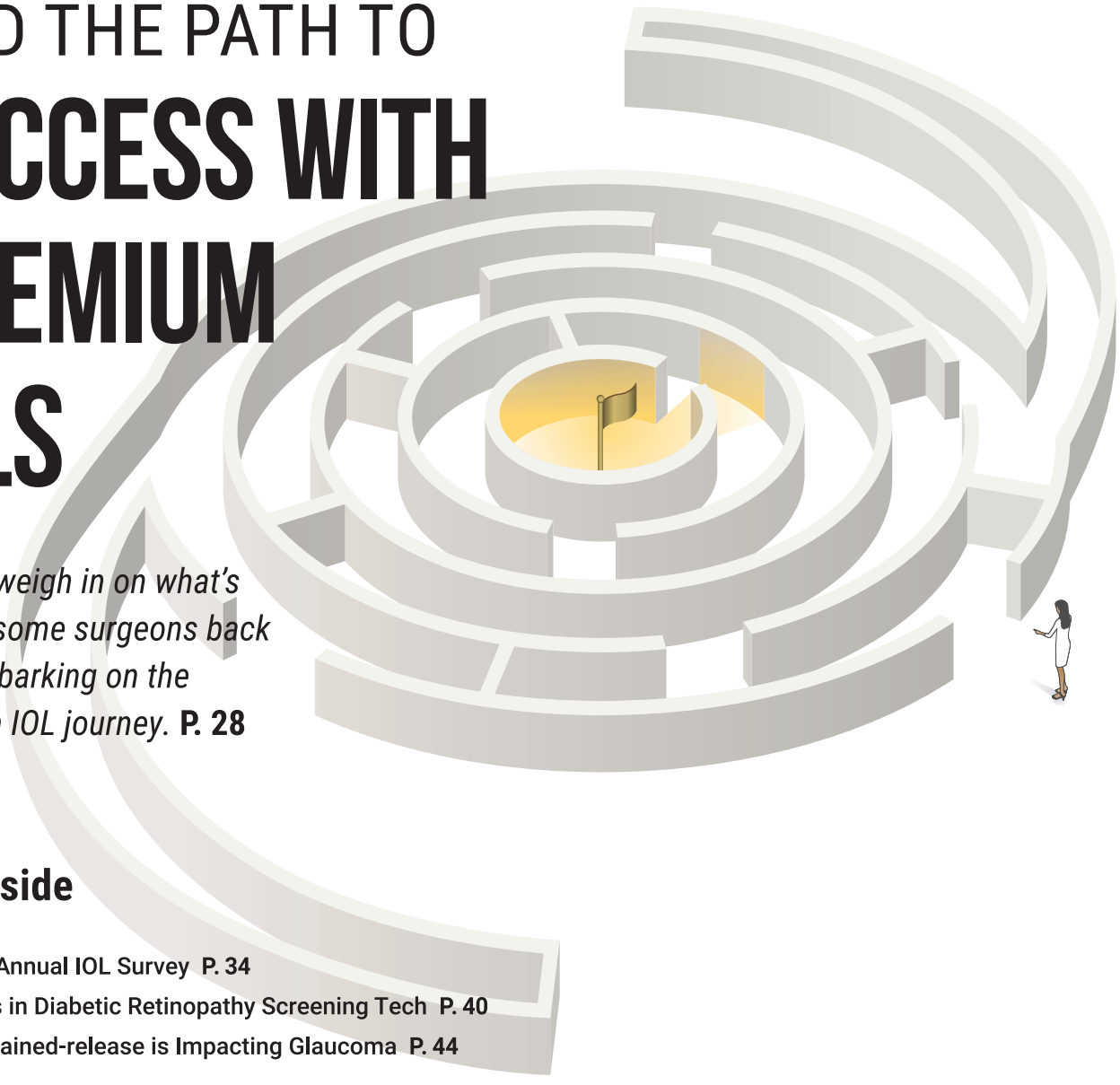

Experts weigh in on what's holding some surgeons back from embarking on the premium IOL journey. **P. 28**

Also inside

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Important Safety Information

The most common adverse reaction reported in 82% of patients was sneezing. Events that were reported in 5-16% of patients were cough, throat irritation, and instillation-site (nose) irritation.

Please see Brief Summary of Prescribing Information on the next page and the full Prescribing Information at Tyrvaya-pro.com.

Reference: 1. Tyrvaya. Prescribing Information. Oyster Point Pharma.

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tyrvaya®
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BRIEF SUMMARY: Consult the full Prescribing Information for complete product information available at www.tyrvaya-pro.com.

INDICATIONS AND USAGE

TYRVAYA® (varenicline solution) nasal spray is a cholinergic agonist indicated for the treatment of the signs and symptoms of dry eye disease.

ADVERSE REACTIONS

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

In three clinical trials of dry eye disease conducted with varenicline solution nasal spray, 349 patients received at least 1 dose of TYRVAYA. The majority of patients had 31 days of treatment exposure, with a maximum exposure of 105 days.

The most common adverse reactions reported in 82% of TYRVAYA treated patients was sneezing. Other common adverse reactions that were reported in >5% of patients include cough (16%), throat irritation (13%), and instillation-site (nose) irritation (8%).

USE IN SPECIFIC POPULATIONS

Pregnancy: Risk Summary: There are no available data on TYRVAYA use in pregnant women to inform any drug associated risks. In animal reproduction studies, varenicline did not produce malformations at clinically relevant doses.

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data: *Animal Data*: Pregnant rats and rabbits received varenicline succinate during organogenesis at oral doses up to 15 and 30 mg/kg/day, respectively. While no fetal structural abnormalities occurred in either species, maternal toxicity, characterized by reduced body weight gain, and reduced fetal weights occurred in rabbits at the highest dose (4864 times the MRHD on a mg/m^2 basis).

In a pre- and postnatal development study, pregnant rats received up to 15 mg/kg/day of oral varenicline succinate from organogenesis through lactation. Maternal toxicity, characterized by a decrease in body weight gain, was observed at 15 mg/kg/day (1216 times the MRHD on a mg/m^2 basis). Decreased fertility and increased auditory startle response occurred in offspring at the highest maternal dose of 15 mg/kg/day.

Lactation: Risk summary: There are no data on the presence of varenicline in human milk, the effects on the breastfed infant, or the effects on milk production. In animal studies varenicline was present in milk of lactating rats. However, due to species-specific differences in lactation physiology, animal data may not reliably predict drug levels in human milk.

The lack of clinical data during lactation precludes a clear determination of the risk of TYRVAYA to an infant during lactation; however, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TYRVAYA and any potential adverse effects on the breastfed child from TYRVAYA.

Pediatric Use: Safety and efficacy of TYRVAYA in pediatric patients have not been established.

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

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VOLUME XXXII • NO. 1

JANUARY 2025

Rapid Visual Field Loss Found in Some Patients in the OHTS

More than 20 years ago, the first participants were enrolled in the Ocular Hypertension Treatment Study. This multicenter, randomized prospective trial sponsored by the National Eye Institute was designed to determine if lowering IOP can delay or prevent the development of primary open angle glaucoma. The cohort ultimately included 1,636 individuals who were followed closely through three stages of the trial through August 2022. Results of their rate of visual field loss before and after the diagnosis of POAG were revealed in a study recently published in the *American Journal of Ophthalmology*, showing rapid rates of VF loss in one or both eyes, despite the fact that they were involved in a clinical study.[1]

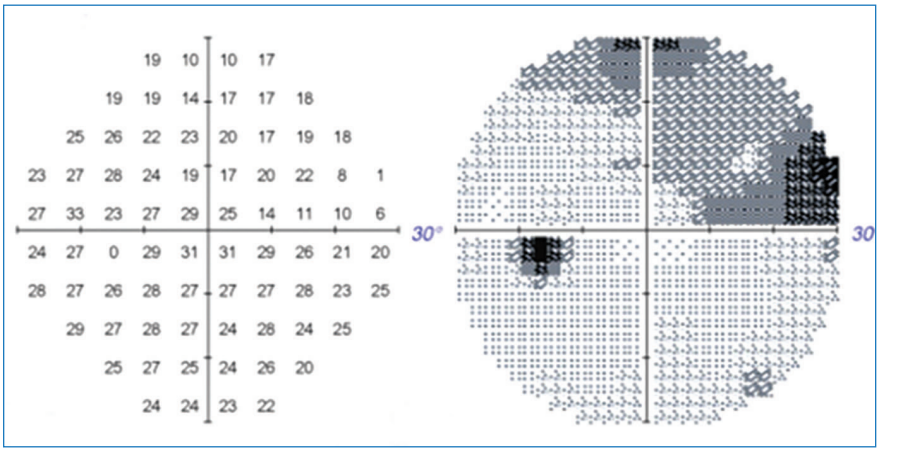
VF tests were performed every six months and stereoscopic optic disc photos were taken every 12 months during OHTS 1 and 2. These tests were repeated in OHTS 3. Slopes of mean deviation (MD) were calculated by linear regression for all eyes in OHTS 1 and 2: eyes that did not develop POAG, eyes that developed optic disc POAG only, and eyes that developed VF POAG with/without optic disc POAG. According to the results, 1,109 participants (n=2,204 eyes) did not develop POAG in either eye. The inception cohort of participants who developed POAG consists of 280 participants (369 eyes): 155 eyes of 103 participants developed only optic disc POAG and 214 eyes of 179 participants developed VF POAG with or without disc POAG.

The mean age at diagnosis of POAG was 66.4 (n= 282 participants), 56 percent were male, 61 percent were white non-Hispanic and 32 percent were black non-Hispanic by self-report. The post-POAG slope was -0.40 ±0.64 dB/year for all POAG eyes (n=280 eyes), -0.19 ±0.4 dB/year for optic disc POAG only eyes (n=112 eyes), and -0.54 ±0.7 dB/year for VF POAG eyes with or without optic disc POAG (n=168 eyes). Among the VF POAG eyes, 69 (41 percent) had post-POAG MD slopes worse than or equal to -0.5 dB/year, 35 (21 percent) had slopes worse than or equal to -1.0 dB/year, and nine (5.4 percent) had slopes worse than or equal to -2.0 dB/year.

The study authors say the marked differences in rates of progression occurred despite all participants being volunteers in a clinical study who were examined every six months. Thirty-five eyes (21 percent) had post VF POAG slopes worse than or equal to -1.0 dB/year, which is considered rapid, noted the authors. Although six-month testing intervals has previously been considered optimal for detecting progression in high-risk ocular hypertensive patients, shorter testing intervals may be warranted in some patients, they speculated.

Study co-author Michael Kass, MD, a glaucoma specialist and professor at Washington University School of Medicine in St. Louis, says the result of this particular study was surprising.

"It's important to put it into context," he says. "Only 25 percent of the patients in OHTS developed visual field loss in one or both eyes after 20 years. However, there was a number of people in



Despite being young, healthy volunteers who were being studied in a prospective fashion, a portion of patients in the well-known OHTS still developed primary open-angle glaucoma that progressed at a very rapid rate.

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Nilson, Robert 10.18.2024

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whom this wasn't true. They developed rapid field loss in one or both eyes; what made it a little surprising is that these are volunteers in a long-term study being closely monitored, yet some of them developed fairly rapid field loss."

Dr. Kass speculates that there are several possible reasons for this.

"When we started the study, we wanted a 20-percent reduction in IOP, since the original reason for the study was to test whether medication affected the outcome in patients," he says. "Though it seems strange now, there was no proof of [medication's effect] then. We wanted to do a big enough study using all the current drugs, which gives you a lot more options, rather than just depending on one drug, and to then see if early treatment mattered—and it did.

"While the 20-percent reduction in pressure was probably a good choice to test the hypothesis," he continues, "it may not have been sufficient to treat people who had progressive disease ... I wonder if the initial choice of 20 percent may have somehow influenced the outcome, but we really don't know."

Drug adherence may be another possibility. "It's possible that perhaps some people didn't take the drops, and that affected their prognosis," Dr. Kass says. "We know that some people don't take medications as prescribed. It could be because of cost, side effects or other reasons.

"Third, intraocular pressure is only one potential mechanism for causing glaucoma," he continues. "There may be inflammatory or vascular factors. It's very hard to address those and there are no good treatments for those right now.

"The fourth possibility is there may be some people who are very susceptible to this damage—to pressure," he concludes. "Maybe they have some properties of their eye that render them very susceptible, even at what we would consider good levels of pressure control."

In eyes that developed optic disc POAG in OHTS 1 and 2 but never developed VF POAG through their last VF test, researchers reported a similar mean MD slope prior to POAG diagnosis as the eyes that never developed POAG. "However, after diagnosis of optic disc POAG, the mean slope of MD, (-0.19 dB/year) was worse than the non POAG eyes (-0.05 dB/year) but less than the VF POAG eyes (-0.54 dB/year)," they wrote.

Dr. Kass says this result may have to do with the eye's structure. "It may be that most people have a reserve function—they have more optic nerve fibers than they need to have a normal result on the test we use [in OHTS] before you see a visual field defect," he says. "Some have estimated that you can lose 25, 30 even 40 percent of the optic nerve fiber layer before you get a visual field defect. This depends on the sensitivity of the test. So, you might see the structural changes in the optic nerve head but you won't see it in the visual field test. Then, at some point, if the structural changes continue long enough they'll show up as a functional defect."

The strengths of this study include its large and diverse inception cohort, as well as standardized testing, diagnostic criteria, use of reading centers with masked readers and use of a masked Endpoint Committee. Authors also noted limitations, including a loss to follow up and death of participants over 20 years. This created missing data especially during OHTS 2 and 3. Change in VF was analyzed by MD only, they said. "MD is a global measure of VF sensitivity and may miss focal changes of POAG that are clinically relevant," they wrote in the study.

Researchers say the rapid and severe VF loss in one or both eyes of participants indicated that ocular hypertensive patients require careful follow-up to detect early signs of glaucomatous damage.

"Remember that these were people with ocular hypertension who were followed for a long time," Dr. Kass says. "As volunteers, they're typically younger, healthier, better educated and likely to do well for a number of reasons. Most of them do well. But, despite all of these things, some will have much more rapid progression, so it's important to try to detect these people. The rate of progression is important. There's a range of rates; some seem to move at a very slow pace and may never develop a visual disability in their lifetimes, while others develop more rapidly. It's important to try to detect these people and then see them more often, test them more often and accelerate treatment as needed."

1. Gordon MO et al. Visual Field Progression in the Ocular Hypertension Treatment Study. American Journal of Ophthalmology. December 6, 2024. [Epub ahead of print].

Current Data on Infectious Hypothesis in AMD Unclear

The pathophysiology of age-related macular degeneration is complex, and the underlying mechanisms are not yet fully understood. In recent years, an infectious hypothesis in the pathogenesis of AMD has emerged, suggesting a link between various infectious agents and AMD. Findings from a group of French researchers, which were published in *Ophthalmology Science*, determined that the currently available data don't clearly speak in favor of or against the implication of infectious agents in AMD.[1] All types of study design, infectious agents, AMD diagnostic methods and AMD stages were considered. Articles dealing with the oral and gut microbiota were not included. Two investigators independently screened the 868 articles obtained by the researchers' algorithm and the reference lists of selected studies. In total, 40 articles were included, among which 30 were on human data, nine were animal studies, six were *in vitro* experiments and one was a hypothesis paper (sometimes

(Continued on p. 12)

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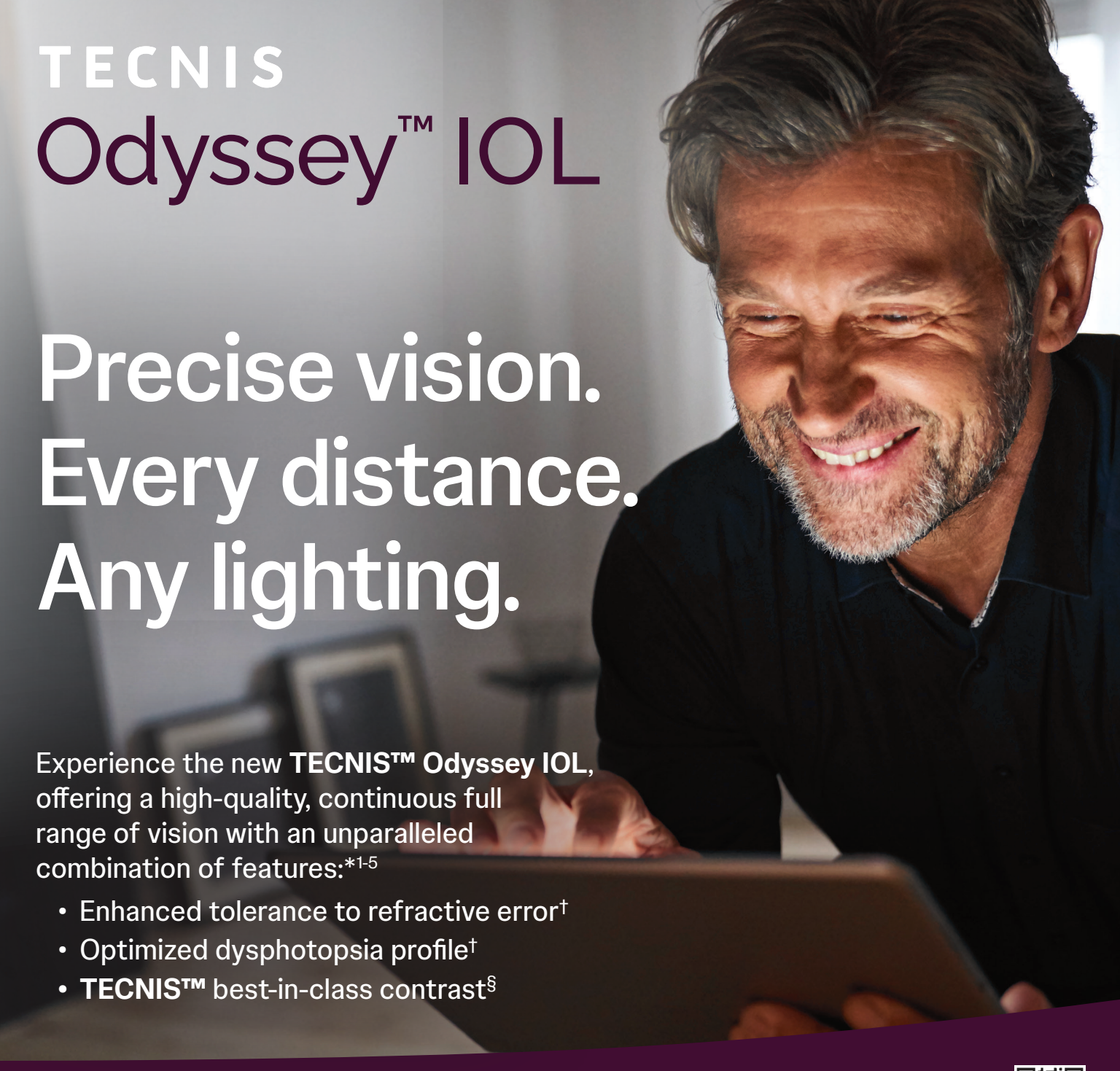

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References:
1. Data on File. DOF2023CT4023
2. Data on File. 2024DOF4003
3. Data on File. 2024DOF4005
4. Data on File. DOF2023CT4007
5. Data on File. 2024DOF4033

INDICATIONS AND IMPORTANT SAFETY INFORMATION

Rx only. The TECNIS Odyssey™ IOL is indicated for primary implantation for the visual correction of aphakia in adult patients, with less than 1 diopter of pre-existing corneal astigmatism, in whom a cataractous lens has been removed. Patients should be informed of possible visual effects, which may be expected in nighttime or poor visibility conditions. Confirmation of refraction with maximum plus manifest refraction technique is strongly recommended. Patients with a predicted postoperative astigmatism greater than 1.0 D may not be suitable candidates for implantation with the TECNIS Odyssey™ IOLs and some patients may still require glasses. The lens is intended for capsular bag placement only. Please reference the Directions for Use for a complete listing of Indications and Important Safety Information.

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FEATURES

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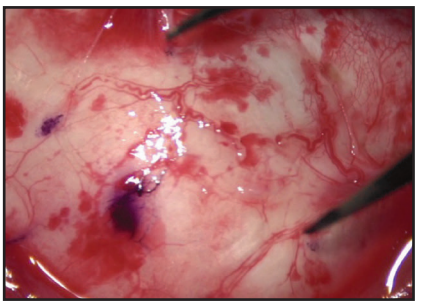
DEPARTMENTS

January 2025



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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).*

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.

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

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

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

tarsus

(Continued from p. 6)

with several data types in the same article). Of these, 27 studies were published after 2010, which highlighted a growing interest in recent years.

A wide range of infectious agents has been investigated, including various microbiota (nasal, pharyngeal), eight bacteria, six viral species and one yeast. Among them, most have been investigated anecdotally.

The researchers found that only *Chlamydia pneumoniae*, cytomegalovirus and hepatitis B virus received more attention, with 17, six and four studies, respectively. Numerous potential pathophysiological mechanisms have been discussed, including 1) an indirect role of infectious agents (i.e., a role of infections located distant from the eye, mainly through their interactions with the immune system) and 2) a direct role of some infectious agents implying potential infection of various cell types within AMD-related tissues.

"Despite these numerous hypotheses, the level of evidence remains low even for the three most studied pathogens," the study authors wrote in their paper.

The team suggested that future studies combining human, animal and in vitro experiments for the same pathogen are needed to improve our understanding. "Experimental studies will be decisive to decipher potential underlying mechanisms and could help to guide the choice of AMD stage to investigate for each suspected pathogen," they noted. "Overall, an intensification of research efforts on the infectious hypothesis and AMD seems essential given the potential repercussions in terms of diagnosis, prevention and treatment."

1. Larsen PP, Dinet V, Delcourt C, et al. Could infectious agents play a role in the onset of age-related macular degeneration? A scoping review. Ophthalmol Sci. November 30, 2024. [Epub ahead of print].

Efficacy of Antimicrobial Agents Studied

New research found low *in vitro* efficacy of common antimicrobial agents used to treat methicillin-resistant or sensitive *Staphylococcus aureus* (MRSA and MSSA) infections of the lacrimal system.[1] Many of the antibiotics examined—mainly β-lactams and fluoroquinolones—demonstrated high rates of resistance, much greater than those of trimethoprim/sulfamethoxazole (TMP/SXT) and gentamicin, prompting the study authors to recommend the latter approach for systemic and topical single-agent treatments.

The study, conducted over 10 years at the Bascom Palmer Eye Institute at the University of Miami, assessed the microbial characteristics and management of *Staphylococcus aureus* by retrospectively reviewing culture-positive *S. aureus* isolates from lacrimal system samples. Other clinical characteristics analyzed included recent history of ocular surgery, presence

of lacrimal biomaterial implant and antimicrobial regimen.

A total of 116 *S. aureus* isolates were identified in 116 patients. Of these, 31 patients (27.4 percent) had recently undergone ocular procedures, while 22 (19.5 percent) had received lacrimal intubation. The first line of treatment for 50 patients (44.2 percent) involved a combination of oral and topical antibiotics, the most frequently prescribed being β-lactams (38.9 percent) and polymyxin B/trimethoprim (31.0 percent).

In roughly one in five patients (20.5 percent), the antibiotic regimen was modified at least once due to a lack of effectiveness. For patients with positive cultures from the lacrimal system, 37.3 percent required surgical intervention as part of their treatment.

Among all identified isolates, 44.8 percent were classified as MRSA. Regarding fluoroquinolone resistance, ciprofloxacin and moxifloxacin exhibited rates of 38.8 percent and 30.4 percent, respectively, with significantly higher resistance observed in MRSA strains. Conversely, resistance rates were much lower for TMP/SXT (8.6 percent) and gentamicin (3.4 percent).

Considering these findings, the study authors stated in their paper that "single-agent therapy with these antibiotics should be avoided." As an alternative, they noted, "We recommend using TMP/SXT and doxycycline for systemic treatment, along with gentamicin for topical application."

Additionally, the authors point out that most patients with MRSA didn't have classical risk factors for the infection, and only 11.1 percent had lacrimal biomaterials. Conversely, patients with MSSA had significantly higher rates of ocular surgery history and lacrimal intubation.

"Given the lack of evident risk factors for MRSA infection in some patients," the authors concluded, "ophthalmologists should always consider MRSA as an etiology for lacrimal apparatus infections, even in the absence of any risk factors."

1. Bineshfar N, Clauss KD, Lee WW, Miller D. Microbiology and management of ***Staphylococcus aureus*** lacrimal system infections: A 10-year retrospective study. PLoS One 2024;19:11:e03143661.

The Benefits of Exercise on Kids' Vasculature System

It's important that kids maintain a level of physical activity, as it improves cardiovascular health, which can be carried into adulthood. Inactivity, conversely, can lead to a child becoming overweight or obese, both of which are linked to cardiovascular disease. What's more, obese kids are five times more likely to also be obese as adults, increasing risk for cardiovascular complications. Researchers from China studied the effects of physical activity vs. inactivity on the microvasculature in children to glean just how pertinent its effects are at a younger age.[1]

All 11,959 participants were taken from the Hong Kong Children Study, which is a population-based and cross-sectional study of kids aged six to eight. All received a comprehensive ophthalmic exam and retinal photography, with demographics and record of physical activity and inactivity taken from validated questionnaires. The retinal photos were used to determine measures known as central retinal arteriolar equivalent (CRAE) and central retinal venular equivalent (CRVE), which estimate the widths of retinal arteries and veins, respectively.

Of all participants, 52.2 percent were boys and the average age was 7.6 years old. An increased ratio of physical activity to inactivity was associated with wider CRAE (β=1.03) and narrower CRVE (β=-2.08). Upon subgroup analysis, boys with an increased ratio of activity vs. nonactivity also had wider CRAE (β=1.36) and narrower CRVE (β=-2.56). For the subgroup analysis of girls, increased ratio of activity to nonactivity was only associated with narrower CRVE (β=-1.76) and not wider CRAE.

Since retinal photography is noninvasive and relatively accessible, it's been frequently used to investigate cardiovascular disease monitoring, screening and prevention in adults. This has yielded findings that adults with narrower arterioles are more at risk of hypertension, incident stroke, coronary heart disease and cardiovascular mortality. Changes in retinal vasculature should have important clinical implications in children, too, since these changes can be tracked to long-term end-organ damage and mortality via cardiovascular disease.

Changes incited in microvasculature by inactivity in kids may be reversed with treatment, suggesting retinal vasculature can be used to monitor disease and treatment response. As well, these changes may occur early in cardiovascular and metabolic disease development, thus the vasculature being used to predict risk. The study authors note in their discussion that CRAE and CRVE changes could be incorporated into existing prediction scores or used separately to predict cardiovascular disease. Thus, a similar prediction score may be implemented for kids, too.

The authors also note that many techniques have already been applied to investigate the microvasculature, as the microvasculature shares similar anatomic and physiological characteristics with systemic circulation. Previous studies have suggested microvasculature may be a potential marker of systemic vascular health and can implicate cardiovascular, respiratory, renovascular and neurovascular diseases.

The researchers wrote that "our study contributes to the growing evidence that physical activity positively influences vascular health from a young age. Therefore, this study also underscores the potential of using the retinal vasculature as a biomarker of cardiovascular health."

1. Zhang XJ, Yuen VL, Zhang Y, et al. Effects of physical activity and inactivity in microvasculature in children: The Hong Kong Children Eye Study. Invest Ophthalmol Vis Sci 2024;65:14:7.

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WALTER C. BETHKE, EDITOR IN CHIEF

EDITOR'S PAGE

As Long as We're Cutting Reimbursements ...

The word is already out about the imminent 2.83-percent cut to Medicare's physician reimbursement in 2025. However, maybe this cut wouldn't even be necessary if the government could cut wasteful spending in other areas. Unfortunately, our country spends all of its taxpayers' funds efficiently, and there's literally nowhere that money is spent needlessly.

Oh, wait, what was I thinking? No it isn't!

Courtesy of Rand Paul (R, Ky.), here are some standouts from his annual report on government waste, both for your entertainment and consternation:

As Sen. Paul points out, while some Americans struggle to pay rent, the government continues to pay for unused office space. And this isn't just a couple offices here and there; we spend a stunning $2 billion on maintenance costs alone for these offices, and $5 billion on leases.

In Las Vegas, the Department of the Interior spent $12 million on the sport that's taking retirees by storm: pickleball. The money went to build a pickleball complex, even though nearby residents fought it due to noise complaints and an anticipated decrease in their overall quality of life when the 30 courts are constructed.

If there's one thing I've learned after perusing this Waste Report each year, is that the government loves spending millions of dollars on redundant research that reaches the same conclusion as research that it funded previously. Along those lines, the Department of Health and Human Services spent $2 million dollars to hook sophisticated eye tracking technology on teenagers to find out what numerous other studies already proved: Snack ads (this time on Facebook) induce teens to eat snacks. You're no doubt picking your jaw off the floor (and maybe filling it with Doritos).

Sen. Paul points out that even though a majority of Americans say they prefer their gas-powered vehicles over electric cars for a variety of reasons, the government still gave $15.5 billion to EV manufacturers to push production of the cars people don't want. Taking care of the environment is admirable, but spending more than $15 billion on this program was excessive.

Staying in the vehicle realm, the government loaned $700 million through the CARES loan program to a trucking company that had been failing since 2008. The money apparently did nothing to help its fortunes, and it filed for bankruptcy in August 2024. This means the tax dollars that went into the loan might keep on truckin' out into the sunset if the company defaults on it.

If you're a proponent of a safe, well-protected border, I've got some good news and some bad news: The good news is, the border is more secure than ever. The bad news is, it's Paraguay's. Yes, while the United States endures a border crisis, our leaders gave $2.1 million to Paraguay to beef up its border security. At least they're securing something, somewhere, right?

For years, consultants have preached to you about running your practice more efficiently. We can only hope the government eventually gets that message too.

— Walter Bethke
Editor in Chief

1. The Festivus Report: 2024.Available at: https://www.hsgac.senate.gov/wp-content/uploads/FESTIVUS-REPORT-2024.pdf. Accessed December 23, 2024.

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LIGHT ADJUSTABLE LENS INDICATIONS FOR USE AND IMPORTANT SAFETY INFORMATION

INDICATIONS: The Light Adjustable Lens™ (LAL™) and Light Delivery Device™ (LDD™) system is indicated for the reduction of residual astigmatism to improve uncorrected visual acuity after removal of the cataractous natural lens by phacoemulsification and implantation of the intraocular lens in the capsular bag in adult patients with preexisting corneal astigmatism of ≥ 0.75 diopters and without preexisting macular disease. The system also reduces the likelihood of clinically significant residual spherical refractive errors.

CONTRAINDICATIONS: The Light Adjustable Lens is contraindicated in patients who are taking systemic medication that may increase sensitivity to ultraviolet (UV) light as the LDD treatment may lead to irreversible phototoxic damage to the eye; patients who are taking a systemic medication that is considered toxic to the retina (e.g., tamoxifen) as they may be at increased risk of retinal damage during LDD treatment; patients with a history of ocular herpes simplex virus due to the potential for reactivation from exposure to UV light; patients with nystagmus as they may not be able to maintain steady fixation during LDD treatment; and patients who are unwilling to comply with the postoperative regimen for adjustment and lock-in treatments and wearing of UV protective eyewear.

WARNINGS: Careful preoperative evaluation and sound clinical judgment should be used by the surgeon to decide the risk/benefit ratio before implanting an IOL in a patient with any of the conditions described in the Light Adjustable Lens and LDD Professional Use Information document. Caution should be used in patients with eyes unable to dilate to a pupil diameter of ≥ 7 mm to ensure that the edge of the Light Adjustable Lens can be visualized during LDD light treatments; patients who the doctor believes will be unable to maintain steady fixation that is necessary for centration of the LDD light treatment; patients with sufficiently dense cataracts that preclude examination of the macula as patients with preexisting macular disease may be at increased risk for macular disease progression; and patients at high risk for future vitreoretinal disease that may require silicone oil as part of therapy. The Light Adjustable Lens must be implanted in the correct orientation with the back layer facing posteriorly.

PRECAUTIONS: The long-term effect on vision due to exposure to UV light that causes erythropsia (after LDD treatment) has not been determined. The implanted Light Adjustable Lens MUST undergo a minimum of 2 LDD treatments (1 adjustment procedure plus 1 lock-in treatment) beginning at least 17-21 days post-implantation. All clinical study outcomes were obtained using LDD power adjustments targeted to emmetropia post LDD treatments. The safety and performance of targeting to myopic or hyperopic outcomes have not been evaluated. The safety and effectiveness of the Light Adjustable Lens and LDD have not been substantiated in patients with preexisting ocular conditions and intraoperative complications. Patients must be instructed to wear the RxSight-specified UV protective eyewear during all waking hours after Light Adjustable Lens implantation until 24 hours post final lock-in treatment. Unprotected exposure to UV light during this period can result in unpredictable changes to the Light Adjustable Lens, causing aberrated optics and blurred vision, which might necessitate explantation of the Light Adjustable Lens.

ADVERSE EVENTS: The most common adverse events (AEs) reported in the randomized pivotal trial included cystoid macular edema (3 eyes, 0.7%), hypopyon (1 eye, 0.2%), and endophthalmitis (1 eye, 0.2%). The rates of AEs did not exceed the rates in the ISO historical control except for the category of secondary surgical interventions (SSI); 1.7% of eyes (7/410) in the Light Adjustable Lens group had an SSI ($p < .05$). AEs related to the UV light from the LDD include phototoxic retinal damage causing temporary loss of best spectacle corrected visual acuity (1 eye, 0.2%), persistent induced tritan color vision anomaly (2 eyes, 0.5%), persistent induced erythropsia (1 eye, 0.3%), reactivation of ocular herpes simplex Infection (1 eye, 0.3%), and persistent unanticipated significant increase in manifest refraction error (≥ 1.0 D cylinder or MRSE) (5 eyes, 1.3%).

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

Please see the Professional Use Information document for a complete list of contraindications, warnings, precautions, and adverse events.

RxSIGHT

Prostaglandins and CME: A Connection?

Cystoid macular edema following cataract surgery can be diagnosed fairly easily by clinical examination, OCT or fluorescein angiography. Once diagnosed, physicians must identify the culprit. Although the manifestation is not fully understood, some suspect that the administration of prostaglandin analogs may increase the risk of developing postoperative complications. In this case, physicians suspend the drug regimen. However, researchers recently conducted a study that showed there is no causal relationship between prostaglandin analogs and pseudophakic CME.

In a systematic review, researchers collected data from seven electronic databases. A total of 196 articles were identified, but only four met the criteria. Each selected study included patients who developed post-cataract CME where prostaglandin analogs were administered in the perioperative period.

"The results of the present systematic review of randomized controlled clinical trials show no causal relationship between pseudophakic cystoid macular edema in patients using prostaglandin analogs undergoing uneventful cataract surgery and suggest that they do not have to be suspended in patients without known risk factors of pseudophakic cystoid macular edema or intraoperative complications," said the researchers in their paper published in *Cureus*. "It would also be sensible to suspend prostaglandin analogs in this group of patients to diminish the number of exogenous prostaglandin analogs administered that could start or add to a major inflammatory cascade in these patients."

Although this study supports the researchers' hypothesis that prostaglandins do not directly affect the risk of developing pseudophakic CME, there are some limitations. Since the study's criteria included data where patients were diagnosed with either clinical examination, OCT or fluorescein angiography, then there may have been differences in the observations made in previous articles. Also, researchers excluded from their review any data on the use of NSAIDs or any additional procedures performed other than cataract surgery. This could have impacted the strength of the reviewed studies' results since these interventions were originally factors in the final outcomes.

Post-cataract CME does not develop overnight. It can take around five weeks for signs and symptoms to arise. With this in mind, the researchers believe that if future clinical trials have extended follow-up periods and consistently use the same diagnostic methods, then this disease can be further understood, and more systematic reviews can be conducted to confirm that there is no causal relationship between prostaglandin analogs and this disease. ◀

1. Santamaria AB, Vera L, Rebollo R, Hartleben-Matkin C. Cystoid macular edema related to uncomplicated cataract surgery and topical prostaglandin analogs: A systematic review of randomized controlled trials. Cureus 2024;16:11:e72920.

Has DeCivilization Begun?

Musings on life, medicine and the practice of ophthalmology.

MARK H. BLECHER
CHIEF MEDICAL EDITOR

An article appeared in December in *The Atlantic* entitled "Decivilization May Already be Underway." It was a piece written after the assassination of the CEO of UnitedHealthcare by a person with an agenda. Not only an agenda, but a manifesto. This manifesto was a rather well-constructed condemnation of the health-care insurance industry and the U.S. health-care system in general. None of these defects and critiques were new or unknown. The reaction on the web, in particular social media, was an unexpected idolization of this person.

There was pretty widespread and vocal support for the murder of a figurehead of the insurance and health-care system. Stories of horrific insurance company actions flooded the news: life-saving treatments denied, bills unpaid. Pain, suffering, illness and death as a result of heartless, and frequently anonymous, insurance company employees adhering to the rules of their game.

Somehow it now became clear that most insurance companies are for-profit entities. More sobering, some are publicly traded entities whose fiduciary responsibility is to their shareholders, not to their "clients." For those of us in the business, we've been long aware that cost cutting and maximizing profits trumped patient care—even for the so-called nonprofit companies such as the Blues. And while I could turn this column into another pitch for universal health care or even single-payor health-care, that isn't what I'm here to say.

What was different this time was that there was almost no sympathy for this CEO. In fact, there was much sympathy for the shooter, and the idea that he was doing this for us, for everyone impacted by the unique and uniquely dysfunctional health-care system in the U.S. There was the notion that we're all impacted at one point or another if we get ill, no matter where you live or what your insurance situation is. Even Medicare, which has been lauded during this period for its relative openness to pay is, as we know, far from perfect.

The groundswell of opinion against private insurers was so widespread it seemed to be on the verge of an uprising. We'd come to a point of frustration with the system so profound that to some people violence seemed to be an acceptable response, and the author of the article I referenced felt concern that this was the path to losing a civil society.

I have a couple of issues with that premise. The long and sometimes sordid arc of our civilization has all too often been marked by periods of violent change, sparked by good reasons and bad. And while I for one would love us to not need violence to adjust and repair the deficiencies of our world, we certainly aren't there yet. The shock of such violence, especially when it comes unexpectedly, may be enough to get attention paid without inciting a spiral of violence, and this incident most certainly got people's attention. The question is, is it enough to engender a real restructuring of health care and how it's paid for in this country? I hope so. I've said for years that our system is on the verge of collapse, not only for the way it provides care but financially as well. It's a Rube Goldberg mess (for those who get the reference).

The somewhat puzzling and amazing thing to me is that we have so many structural inequalities in this country I'm surprised it's health care that may spark the revolution.

Maybe I shouldn't be surprised. Income inequality is at its highest point in history in the United States and a look back over the centuries worldwide shows that this is what has sparked violent change. And while you can argue the merits or lack thereof of income redistribution, the reality is that you can't enjoy your "well-earned" wealth if your head is in the basket of the guillotine.

So, it behooves all of us to not get to that point, since self-righteousness won't save the day. But the American public made a rather clear statement with this election that they don't mind billionaires and oligarchs. They actually admire them. Surprisingly, it seems that the right to health care is more motivating. I guess my grandmother was right, your health is everything. At the end of the day while money may be able to buy happiness, you shouldn't have to spend all of it to buy your health care. ◀

This article has no commercial sponsorship. **Dr. Blecher** is an attending surgeon at Wills Eye Hospital.

MARY PAT JOHNSON, COMT, CPC, COE, CPMA

MEDICARE Q&A

2025 Ophthalmic Reimbursement Update

The important changes to Medicare's rules and regulations you need to be aware of going into the new year.

In recent months, CMS has announced important changes to the Medicare program that affect physicians and ASCs, including payment rate changes, new and revised codes and revised quality programs.

Here, we provide some practical suggestions to address this challenging situation.

Q What changes are in store for physician reimbursement?

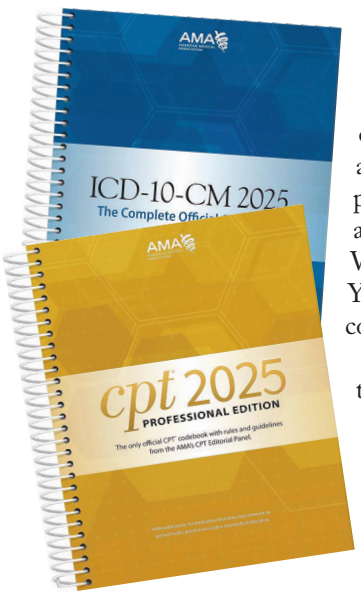
A The CMS Final Rule for the 2025 Medicare Physician Fee Schedule (MPFS) was published in the November 1, 2024, Federal Register.[1] The 2025 conversion factor is $32.3562 per RVU, which is a decrease of 2.8 percent. This doesn't count the impact of sequestration (-2 percent) that was reinstituted in 2023. CMS estimated the Medicare payments to ophthalmologists would decrease 2 percent and payments to optometrists would decrease 1 percent based on a weighted average calculation. Organized medicine has asked Congress to intervene and lessen this reduction; so far, that hasn't happened.

Our comparison of the 2024 and 2025 Medicare allowed amounts shows that payments for most procedures changed very little, but there were a few that changed a lot (*Tables 1,2,3*).

Only one surgical procedure increased significantly — 66680 (repair iridodialysis), going from $517 to $573.

Q What changes are planned for ambulatory surgical center and hospital outpatient department reimbursements?

A For 2025, Medicare increased the hospital outpatient department and ambulatory surgery center conversion factor by 2.8 percent. The new ASC rates are based on a CF of $54.895.[2] *Table 4* contains a selected list of some common ophthalmic procedures and their Medicare payment rates in 2024 and 2025 for facilities. With the exception of YAG capsulotomy, all codes listed increased.



Nearly all ASCs meet their quality reporting requirements. However, those that failed to meet their quality measures in the most recent reporting year will have their annual update factor reduced to $53.797. As with physician rates, ASC pay-

TABLE 1. OFFICE PROCEDURES THAT INCREASED SIGNIFICANTLY

CPT	Service	2024	2025
99242	Fluorescein and ICG angiography	$281	$315
99240	ICG angiography	$188	$229
65778	Placement of temporary amniotic tissue	$1,087	$1,218

TABLE 2. OFFICE PROCEDURES THAT DECREASED SIGNIFICANTLY

CPT	Service	2024	2025
92134	OCT retina	$40	$31
92284	Dark adaptation	$37	$29
92133	OCT optic nerve	$36	$30
92230	Fluorescein angioscopy	$137	$123
92287	Specular microscopy with fluorescein	$142	$128

*Reimbursement in office

TABLE 3. SURGICAL PROCEDURES THAT DECREASED SIGNIFICANTLY

CPT	Service	2024	2025
+67331	Strabismus surgery, add-on code	$153	$121
+67334	Strabismus surgery, add-on code	$151	$119

*Reimbursement in facility

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ments for most procedures changed very little. Those with significant changes, either up or down, are shown in *Tables 5 and 6*.

Q Are there changes to ASC quality reporting?

A Yes. QualityNet has the 2025 ASC Quality Specifications manual, version 14.0, available for download on their website. It retains measures ASC-1 through 4 (i.e., burns, falls, wrong-sited, hospital admission).

CMS kept ASC Quality measure ASC-11 for 2025 and it remains voluntary. If you choose to report this measure, use CMS' web-based tool after the reporting year ends and include all payors, not just Medicare.

This measure is defined as "Improvement in Visual Function within 90 days after cataract surgery." The professional societies continue to encourage not to report on this measure since, in their view, this isn't within the ASC's control.

Measure ASC-14, "Unplanned Anterior Vitrectomy" is mandatory, and reporting is via the HQR secure portal.

Measure ASC-20, "COVID-19 Vaccination Coverage Among Health Care Personnel" is mandatory and reporting is via the web-based tool, the National Healthcare Safety Network.[3]

The Outpatient and Ambulatory Surgery Consumer Assessment of Healthcare Providers and Systems (OAS CAHPS) survey is mandatory starting January 1, 2025. It's designed to measure the experiences of care for patients who visited HOPDs or ASCs. The goal is to produce comparable data on the patient's perspective that allows comparisons between HOPDs and free-standing ASCs, so consumers can make more informed choices and to facilitate quality improvement initiatives for HOPDs and ASCs.

The following types of patient experiences are included:

- communication and care provided by healthcare providers and office staff,
- preparation for the surgery or procedure, and
- preparations for discharge and recovery.

Facilities must contract with a CMS-approved vendor to conduct the survey.

Q What code changes are there to be aware of?

A The CPT Editorial Panel made more than 400 changes to the 2025 manual.[4] Only a few of them affect eye care. New CPT codes effective January 1, 2025, include:

92137 - Computerized ophthalmic diagnostic imaging (e.g., optical coherence tomography), anterior segment with interpretation and report, unilateral or bilateral; retina, including OCT angiography;

66683 - Implantation of iris prosthesis, including suture fixation and repair or removal of iris;

0936T – Photobiomodulation therapy of retina, single session.

Existing CPT codes for OCT, 92132, 92133 and 92134, were revised to remove the term "scanning" and add the term "optical coherence tomography" to clarify but didn't materially change the meaning.

Existing Category III CPT code 0615T was substantially revised to read, "automated analysis of binocular movements without spatial calibration, with interpretation and report."

A new drug eluting implant, iDose, to treat glaucoma was introduced in early 2024. CMS assigned J7355 - injection, travoprost, intracameral implant, 1 mcg, to report this supply.

CMS inaugurated a new HCPCS add-on code, +G0559 - Post-operative follow-up visit complexity inherent to evaluation and management services addressing surgical procedure(s), provided by a physician or qualified health care

TABLE 4. MEDICARE PAYMENTS TO ASCS AND HOPDS

CPT	Short Description	ASC		HOPD	
		2024	2025	2024	2025
15823	Blepharoplasty, upper lid	$946	$981	$1,739	$1,829
66821	YAG capsulotomy	$302	$295	$554	$549
66984	Cataract/IOL	$1,184	$1,214	$2,223	$2,281
67036	Pars plana vitrectomy	$2,045	$2,094	$3,878	$4,023

TABLE 5. ASC PROCEDURES THAT INCREASED SIGNIFICANTLY (19 TO 58 PERCENT)

CPT	Service	2024	2025
65785	Corneal ring segments	$1,891	$2,981
66180	Aqueous shunt with graft	$2,627	$3,424
0660T	Implant anterior segment drug eluting device	$1,626	$2,094
0661T	Remove/replace anterior segment drug eluting device	$1,626	$2,094
66175	Canaloplasty with stent	$3,563	$4,254

TABLE 6. ASC PROCEDURES THAT DECREASED SIGNIFICANTLY (19 TO 26 PERCENT)

CPT	Service	2024	2025
66155	Fistulization, cautery	$2,818	$2,094
0308T	Intraocular telescope	$14,261	$11,370
66225	Repair/graft eye lesion	$3,258	$2,618
68816	Probe NLD with balloon	$1,257	$1,026
65135	Insert ocular implant	$1,921	$1,587

professional who is not the practitioner who performed the procedure (or in the same group practice) and is of the same or of a different specialty than the practitioner who performed the procedure, within the 90-day global period of the procedure(s), once per 90-day global period, when there has not been a formal transfer of care.[5]

The long description of HCPCS code +G0559 specifies numerous required elements in the chart documentation including:

- reading the surgical note,
- assessing the affected anatomy,
- considering the potential complications of the surgery,
- determining the postoperative course,
- examining the patient, and
- communicating with the surgeon or proceduralist.

+G0559 is an add-on code that's listed separately in addition to office/outpatient E/M visits for new or established patients (i.e., codes 99202-99215).

The 2025 ICD-10 updates became effective October 1, 2024. Only a few of them affected eye care professionals. In the H44.2 series, a miniscule change in terminology was made to harmonize language with other ICD-10 codes: "Bilateral eye" was changed to "bilateral" with no change in meaning.

Q What was ophthalmology's Medicare claims error rate?

A The most recent report for the Comprehensive Error Rate Testing program covers July 1, 2022, through June 30, 2023.[6] Again ophthalmology did well with the accuracy of their claims for reimbursement and a low error rate. In the most recent report, the error rate for ophthalmology was 3.3 percent, which is up from 1.7 percent the prior year. This report also contained information on the error rate for cataract surgery (8.2 percent) and the error rate for claims submitted to the Durable Medical Equipment, Prosthetic, Orthotics, and Supplies (DMEPOS) program for post-cataract corrective lenses (70.7 percent).

TABLE 7. MIPS CATEGORY WEIGHTING

MIPS Category	2017	2018	2019	2020	2021	2022 to 25
Quality	60%	50%	45%	45%	40%	30%
Program Interoperability	25%	25%	25%	25%	25%	25%
Improvement Activities	15%	15%	15%	15%	15%	15%
Resource Use (Cost)	0%	10%	15%	15%	20%	30%

Q What changes occurred on the beneficiary side?

A Medicare Part A deductible is $1,676 in 2025, a $44 increase from 2024. The Medicare Part B deductible increased $17 to $257 and the Part B basic premium increased to $185 for most beneficiaries.

Part C Medicare (Medicare Advantage) continues to grow. Fifty-four percent of eligible beneficiaries were enrolled in an MA plan in 2024. The Congressional Budget Office estimates that enrollment will rise to about 64 percent of eligible beneficiaries by 2034.[7]

Q What changes occurred in the Quality Payment Program?

A QPP enters year nine with additional emphasis on resource use, particularly for cataract surgery. Exclusions for comorbidities are fewer, cost elements are more numerous, and the scoring methodology is tougher. In 2024, some surgeons were surprised by poor MIPS scores from CMS' determination of the cost of cataract surgery relative to peers. 2025's MIPS score, based on the 2023 performance year, may have more surprises.

The maximum negative payment adjustment remains 9 percent for the Medicare payments you get in 2025 and the minimum composite score to avoid a penalty remains 75 points. A MIPS Hardship Exception for weather calamities provides relief for some localities. The failure of a third-party intermediary in the reporting process is also grounds for relief. MIPS category weightings are unchanged for 2025 (*See Table 9*).

CMS is considering sunsetting MIPS in 2028 and mandating value pathways. In 2025, CMS proposed a value pathway for "complete ophthalmologic care."[8]

Q How can practices offset imminent cuts?

A While the new payment rates in 2025 for ASCs are good, the forecast for the Medicare Physician Fee Schedule is not. Our best suggestion to address this unfortunate situation is to increase revenue in practical ways. Assess your practice for options like offering new service lines, revising fees, expanding cataract surgery pre-testing, expanding office hours and dropping low-paying contracts or difficult payors.

If you have questions about the information in this article, please contact us. Happy New Year! ◀

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LIZ HUNTER
SENIOR EDITOR

Nearly 20 years ago, intraoperative floppy iris syndrome was a newly recognized phenomenon occurring during cataract surgery in patients who were taking alpha-1 antagonist medications.[1] Characterized by poor pupil dilation, iris billowing and prolapse, IFIS has been linked to other systemic medications and is no less rare than it was two decades ago. In order for cataract surgeons to successfully complete a case in which they notice iris prolapse or billowing, they must recognize the risks and be prepared to implement a few special techniques.

Risks and Characteristics Of Iris Prolapse

As discovered in 2005, the use of alpha-1 receptor antagonists, such as tamsulosin (Flomax) is one of the major risk factors contributing to intraoperative floppy iris. These medications are thought to decrease the tone of the smooth muscle in the iris, according to Marisa Schoen, MD, a cataract and cornea surgeon with Ophthalmic Partners and part of the Cornea Service at Wills Eye Hospital in Philadelphia. "Additional risk factors have been reported, including other systemic medications such as benzodiazepines, some antipsychotics, antidepressants, and medical conditions like hypertension and diabetes," she says.

A thorough history of medications will help bring these to a surgeon's attention, even if patients don't recall them by name. "During a cataract evaluation, I'll typically ask patients if they have a history of tamsulosin, or Flomax, use," Dr. Schoen says. "If they're unfamiliar with the medication name, then I'll ask if they've used anything for their prostate or urination problems. Even a one-time use of these medications can put a patient at risk for developing floppy iris syndrome."

Eye color could also heighten the risk. "Not all patients on Flomax will experience IFIS, however," says Derek DelMonte, MD, a cornea and cataract surgeon at Carolina Eye Associates in North Carolina. "Patients with lighter-colored irises—like blue or green—are more at risk than darker brown irises when taking Flomax."

A history of chronic intraocular inflammation leading to an abnormal iris tone is another preoperative risk, adds Dr. DelMonte. "While many of these patients will have iris fibrosis and limited movement, some mimic IFIS-like movement intraoperatively," he says. "Most of the other causes of iris prolapse are intraoperative, such as a very short wound or a wound that's located very far peripherally. These factors increase the likelihood of iris prolapse by placing the internal wound opening in close proximity to the iris. Additionally, any kind of iris trauma during surgery can make the iris more likely to prolapse. The more you manipulate or poke the iris, the more likely it is to lose its tone and become floppy as time goes by. And the longer the case goes it increases the chances of iris prolapse."

Dr. DelMonte also looks for any signs of pseudoexfoliation, which can also alter iris tone and stability leading to iris complications such as prolapse during surgery. But ultimately, dilation and a history of Flomax are the biggest red flags, he says. "What really raises my concern is if a patient on Flomax also doesn't dilate well," Dr. DelMonte says. "If the iris doesn't dilate properly during an exam, that's a clear sign that there could be an issue during surgery."

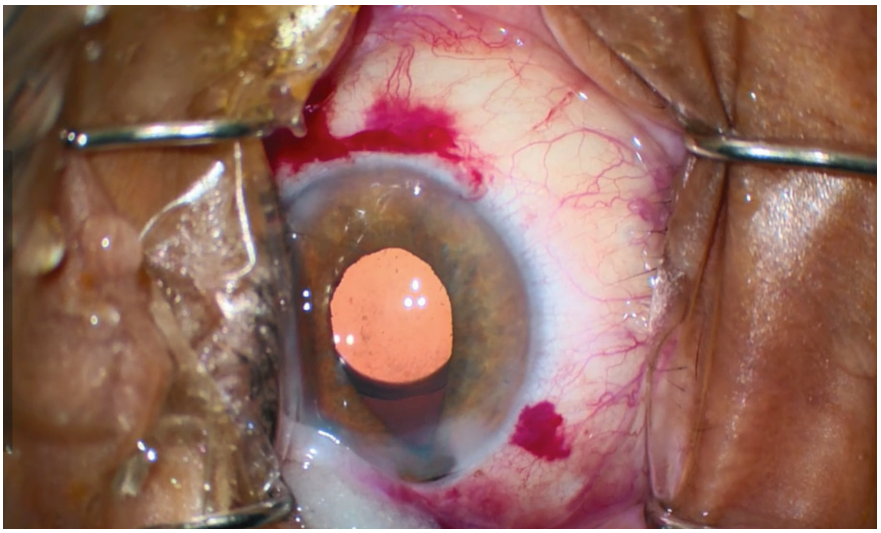
Dr. Schoen notes that IFIS has a spectrum of characteristics, even if the patient dilates normally in the preop period.

"Some patients may exhibit poor dilation during the preop exam, other patients may dilate well and only show characteristics intraoperatively, like billowing of the iris, iris prolapse and progressive miosis during the case," she says. "During cataract surgery, we expect the iris to dilate well and remain stable. If it doesn't dilate well, or even if it dilates well initially but starts to move around when we introduce instruments or irrigation into the eye, that can indicate floppy iris syndrome.

"Another sign is iris prolapse, where the iris moves toward surgical incisions—either the main wound or the paracentesis—during irrigation and changes in fluidics within the eye," continues Dr. Schoen. "These are the key ways floppy iris syndrome presents: poor dilation; billowing

This article has no commercial sponsorship.

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



Marisa Schoen, MD

Intraoperative floppy iris syndrome can present in various ways, including poor dilation; billowing or floppy movement of the iris; progressive intraoperative miosis; or iris prolapse (shown here), in which the iris moves toward incisions.

or floppy movement of the iris; iris prolapse; and progressive intraoperative miosis."

Management Strategies

IFIS isn't just a surgical complication that adds time to the case, it also has other implications.

"If a patient experiences poor dilation or develops miosis during surgery, that increases their risk for complications, which can subsequently affect their visual outcomes," explains Dr. Schoen. "For example, poor visualization of key structures during cataract surgery, like the capsule, can lead to capsule rupture. This can result in vitreous prolapse or dropped lens fragments, which are associated with visually significant complications such as cystoid macular edema, retinal tears and detachment, and endophthalmitis. Iris prolapse itself, depending on its severity and how it's managed, can cause iris defects, which may lead to visual problems like glare and sensitivity to bright lights. Floppy iris alone, without complications, is visually insignificant, but when it presents challenges that aren't managed well, it can cause lasting visual consequences."

Dr. DelMonte says that once the iris starts prolapsing, the surgery becomes much more difficult for a number of reasons. "First, once the iris begins to come out, it tends to want to keep coming out," he says. "It's already stretched to the point where it seems to have memory, and it will continue to prolapse with even minimal manipulation. Second, as the iris prolapses the pupil gets smaller and smaller, which distorts and obscures the surgeon's view of the cataract. And third, iris prolapse can also cause patient discomfort due to both the iris stretching and anterior chamber pressure changes. When the patient becomes uncomfortable during these situations, they're more prone to movement and squeezing which will often impact the surgical experience. The situation quickly spirals downhill if the wrong action is taken, such as trying to shove the iris back in. This approach will usually make things worse and cause the iris to continue to prolapse."

This makes prevention the primary strategy for cataract surgeons. Using epinephrine preoperatively is one strategy to consider. "Epinephrine is helpful in preventing the iris from becoming floppy by increasing iris tone," says Dr. DelMonte. "I'll use epinephrine, either in the infusion bag or intracamerally as part of a lidocaine-epinephrine combination (Shugarcaine). Typically, I assess the iris early in the procedure. If I notice the iris moving easily after I administer the Shugarcaine or epinephrine combination, that's a bad sign—it means the iris will be very floppy and prone to prolapse. If everything seems stable, that gives me some reassurance, but I remain cautious throughout the surgery."

Starting patients on atropine a couple of days before their surgery is another prevention method Dr. Schoen has implemented. "I don't pre-treat patients if they have good dilation during their preop exam," she says. "However, if they have risk factors for IFIS and poor dilation, or a known history of IFIS in their fellow eye, then I'd consider starting them on atropine prior to cataract surgery.

"One of my mentors, Samuel Masket, MD, published an article suggesting that preoperative treatment with atropine sulfate 1% three times a day for two days prior to surgery, in addition to intraoperative intracameral epinephrine, can reduce the risk of floppy iris syndrome and its associated complications," she continues. "Additionally, some studies suggest that pre-treatment with topical NSAIDs can help as well."

Despite these efforts, iris prolapse may still occur, however, both Dr. Schoen and Dr. DelMonte say that a surgeon's first instinct is incorrect.

"When iris prolapse begins, the natural instinct is often to try to force the iris back in by injecting BSS or a viscoelastic through the main wound at the iris," says Dr. DelMonte. "Unfortunately, this will only increase the pressure inside the eye and worsen the pressure gradient that forced the iris out in the first place. The key is to minimize manipulation of the iris. The more you touch it, the more inflammatory mediators are released, which makes it floppier as time goes on."

"The most important thing to remember is to resist the instinct to shove the iris back into the eye," Dr.

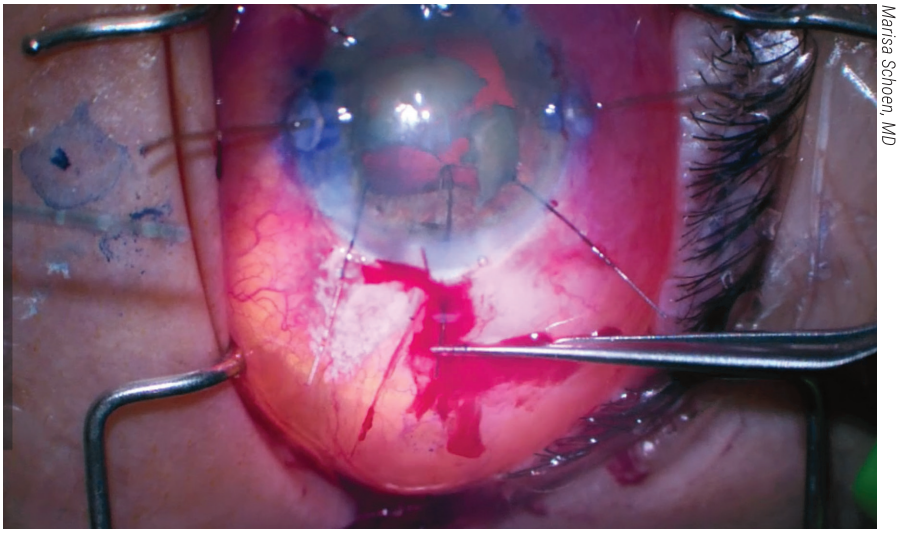
Schoen says. "That can cause a lot of trauma to the iris and create iris defects, which can lead to postop issues like glare. Iris prolapse usually occurs because the intraocular pressure is higher than the external pressure. The first thing is to decompress the eye and try to lower the pressure internally so that it's easier to get the iris back in. If you don't lower the intraocular pressure, the iris is just going to keep coming out."

Dr. DelMonte will initially attempt to burp out as much fluid as he can from the anterior chamber through the paracentesis to create a negative pressure environment. "Then I gently massage the iris back into the eye using a cannula or another instrument without injecting any substance into the eye," he says. "Alternatively, you could sweep the iris back into the eye with a cannula from the paracentesis incision when the pressure gradient has been eliminated. Typically, the iris will redeposit inside the eye at this point."

If lowering the pressure of the eye isn't sufficient, then sometimes tapping on the wound encourages the iris to fall back into the eye, says Dr. Schoen. "You could also try squirting BSS towards the wound without necessarily putting the cannula into the wound and touching the iris," she says.

Once the iris is back inside, the goal is to stabilize it to prevent further prolapse. "One of the most effective ways to do this is by using iris hooks," Dr. DelMonte says. "These are useful for enlarging the pupil in certain cases, but in the case of iris prolapse, I use them specifically to stabilize the area under the main wound. I make one or two small incisions around the main wound or slightly posterior to it, and then insert the iris hooks focally. This helps to hold the iris in place and prevent further prolapse."

Dr. Schoen says a subincisional iris hook can make all the difference. "Depending on the stage of the cataract surgery when the iris prolapse occurs, I'll consider placing a subincisional iris hook to try to keep the iris out of the way and prevent further prolapse of, and thus trauma to, the iris," she says. "To do that I'll create an incision with a paracentesis blade through the sclera 1 mm posterior to the limbus and parallel to the iris, and then you can just slip in a single iris hook, capture the edge of the iris, retract it back and keep it out of the way.



Marisa Schoen, MD

Surgeons say iris hooks are helpful tools when confronted with floppy iris syndrome. Inserting one subincisionally to the main wound will retract the iris back and keep it out of the way from further prolapse and trauma.

"I'll keep that iris hook in place until the IOL is in the bag, viscoelastic is removed, and I'm not planning to use the main wound anymore," she continues. "It's also important in these cases to come off irrigation prior to removing instruments from the eye to try to reduce the risk of further iris prolapse."

A Malyugin ring would would be helpful for preventing anticipated iris prolapse, notes Dr. DelMonte, but it's more difficult to use once the prolapse has already occurred. "If you notice a floppy iris early in the procedure, before any prolapse happens, that's the ideal time to insert the Malyugin ring," he says. "In these situations, iris hooks are usually a safer and more useful option."

Dr. Schoen says she's simply more comfortable with iris hooks. "I prefer iris hooks because they offer more flexibility and are friendlier in eyes with shallow chambers," she says. "They usually come in a pack of five, so I'll insert them in a pentagon configuration with one placed subincisionally. Others might do a diamond configuration, but no matter what, always aim to have at least one subincisional iris hook in place to reduce the risk of iris prolapse through the main wound. Proper management can go a long way in minimizing intraoperative and postoperative issues."

Surgeons should also be mindful of their wound construction, adds Dr. Schoen, who advises to err on the side of a longer wound.

Phaco settings can also play a role in managing iris prolapse. "In cases where iris prolapse is a concern, decreasing the aspiration flow rate to less than 26 mL/min, vacuum to less than 200 mmHg, and entering and exiting the wound without irrigation on can all be very effective in minimizing iris prolapse," recommends Dr. DelMonte. "Essentially, you want to slow down all movement within the eye to prevent further issues. Consider having a 'floppy iris' setting on your phaco machine that reduces flow rates, which can be very beneficial in these cases."

(Continued on p. 62)

A Look at the Latest Surgical Microscopes

This list will provide up-to-date information about ophthalmic surgical microscopes from leading brands in the industry.

ANDREW BEERS
ASSOCIATE EDITOR

A good surgical microscope allows surgeons to execute their intricate maneuvers, and several companies are pushing the boundaries of technology with new advances, both for standard and digital microscopes. Here, we'll go over what's currently available for ophthalmologists looking to upgrade their surgical suites.

Artevo 750 and 850 (ZEISS)

The two latest microscopes to come from Zeiss' line of surgical equipment include the Artevo 750 and the Artevo 850. The digital capabilities offered with Artevo 850 is the major difference between the two devices. Artevo 750 is an analog surgical microscope requiring the surgeon to look through eyepieces while performing the procedure. Conversely, the Artevo 850 is equipped with a 55-inch, high-fidelity screen for 3D digital visualization. There's no need for an eyepiece while performing operations such as vitreoretinal or cataract surgery.

"With Zeiss Artevo microscopes, physicians can support multiple surgical workflows in their practice, whether it's related to cataract or retina, enabling further practice development with the latest in ophthalmic innovation," shares Frank Seitzinger, the Head of Business Sector Surgery Anterior Segment for Zeiss Medical Technology. "The Zeiss Artevo 850 offers digital visualization with customizable digital color settings depending on the surgical procedure's requirements and intraoperative OCT allowing for real-time monitoring of the surgical process and decision-making. The Artevo 750 introduces advanced optical visualization technology, including new RGB LED illumination with adjustable light color temperature, as well as data overlays provided in the eyepiece with 40 percent higher resolution."

Zeiss surgical equipment is compatible with each other, so when surgeons need assistance with cataract surgery, they can use the Callisto along with the Artevo 750 or 850. This assistive technology provides a graphical interface displayed on a separate monitor for surgeons to use when placing intraocular lenses during surgery.

When surgeons use the Artevo 850, they may not want to view their patient through the 3D screen, which is why Zeiss added a hybrid mode for surgeons to change between analog and digital viewing. This allows OR teams to continue to view the surgery through the monitor without getting in the way of the surgeon operating on the patient.

Zeiss

Switch between analog and digital microscopy with Hybrid Mode.

LuxOR Revalia and Ngenuity (Alcon)

Clinics looking to upgrade their microscopes in the OR can look towards Alcon's Ngenutiy as an option. This is a digital microscope system that can be added to Alcon's LuxOR Revalia and other microscopes. For surgical viewing, it comes with a 55-inch, 3D high-fidelity display. "Instead of having to look through little one-inch oculars to do the surgery, we remove the eyepiece, replace it with a patented 3D surgical camera, and then surgeons can operate heads up and be untethered from the microscope, in essence," explains Chris Dyer, Alcon's Senior Brand Manager for U.S. Visualization.

The LuxOR already offers its own unique features that allow it to stand alone without the Ngenuity system. For instance, the red reflex zone was designed to expand the illumination field during surgery while minimizing the risk of phototoxicity by providing safer retroillumination. This provides advanced visualization and stability while operating, the company says. But, to enhance the experience with the LuxOR, the microscope should be upgraded with the Ngenuity system. The system is meant to further support surgeons during procedures through its Digital Detection modes.

"Digital Detection includes Tissue Detail Mode and Capsule Clarity Mode for the anterior segment," says Mr. Dyer, "and then for retina surgery, we have a Tissue Detail Mode that's slightly

This article has no commercial sponsorship.

Dr. Colvard is a surgeon at the Colvard-Kandavel Eye Center in Los Angeles and a clinical professor of ophthalmology at the Keck School of Medicine of the University of Southern California. **Dr. Charles** is the founder of the Charles Retina Institute in Germantown, Tennessee.

different for the posterior segment as well as Performance Green and Blue Boost Modes for greater visualization of the green and blue dyes that are used in posterior segment surgery."

Additionally, with a recent 1.5 update to the Ngenuity system, Alcon now offers a MIGS Mode. "We do what's called tone mapping, and that kind of highlights different anatomical structures within the eye," says Mr. Dyer. "So, MIGS Mode, for instance, highlights the trabecular meshwork when a surgeon is implanting MIGS devices."

Alcon designs their surgical equipment to work in tandem with each other. The LuxOR, whether the Ngenuity is installed or not, operates under the Alcon Vision Suite and can be connected to other Alcon devices such as the Centurion phaco machine or the Argos biometer. For example, when a physician or technician takes an image with Argos, it starts to recognize certain landmarks on the patient's eye. Then, if an IOL is needed, the surgeon can decide which lens to employ and where they'd like to make their incisions. Once the surgeon includes their markings to the image, they can then upload it to the LuxOR and use it to their advantage.

"When the surgeon's image-guided plan gets electronically sent to the OR and into the LuxOR, and if they don't have Ngenuity added on, then a reticle overlay comes through the surgeon's binocular," explains Mr. Dyer. "So, surgeons can optimize their outcomes based on the lens used, techniques applied and the uniqueness of the surgery itself."

Leica Microsystems

Leica's most advanced surgical microscope is the Proveo 8, but other models are available. Leica developed FusionOptics technology to enhance the visualization of the Proveo 8, which makes it stand out among the rest of Leica's models. According to the company, these optics offer two separate beam paths. One path provides 40 percent increased depth of field and the other provides high resolution for visualization. When the two images merge together in the surgeon's brain, it creates a single optimal spatial image.

Alcon

Integrate Ngenuity into the LuxOR Revalia system for digital microscopy.

In addition to the Proveo 8's FusionOptics, the lighting, focus and magnification for the procedure can be pre-programed to a footswitch. The light is constant and uncompromised through a coaxial LED illumination providing red reflex for a consistent image. For sensitive eyes or particular patients, the illumination diameter can be adjusted for each individual patient's eye.

To assist with anterior and posterior segment surgeries, Proveo 8 comes with a built-in optical coherence tomography system, EnFocus. This technology from Leica allows surgeons to use OCT intraoperatively, so they can view ocular tissue as they operate. Also, a 3D monitor for heads-up viewing is installed on the Proveo 8 system, allowing surgeons to view their patient using analog microscopy and then transmit OCT images onto the monitor.

As mentioned before, Leica offers other surgical microscopes in addition to the Proveo 8. These models include the following:

- M822 (Ophthalmic surgical microscope for anterior and posterior segment surgery)
- M844 (Ophthalmic microscope for advanced eye surgery)
- M620 F20 (All-around surgical microscope for ophthalmology)
- M220 F12 (Efficient surgical microscope for ophthalmology).

Metis and Hi-R NEO 900 (Haag-Streit)

In March 2025, Haag-Streit will be launching a new surgical microscope, the Metis. Hi-R NEO 900 models are still available, but the company will be moving forward with their latest model in the coming months.

What's to be expected from the Metis? This device will be equipped with coaxial red reflex for stable and bright illumination during procedures such as capsulorhexis and nuclear disassembly during cataract surgery. However, the microscope was designed with glaucoma surgery in mind. With motorized tilting and an eyepiece inclination lever, surgeons can position their microscope optimally for MIGS procedures, the company says.

Haag-Streit says it developed the Metis with the goal of improved surgical control. According to the company, the Metis' ergonomic design, motorized controls and hand and foot switches are meant to provide total control of the microscope's angles, illumination, magnification and other functions.

The Metis comes equipped with a 27-inch high fidelity touchscreen display, which can support the workflow of surgical teams. Integrated into the device is Haag-Streit's Microscope Imaging and Operation System (MIOS), which can be accessed using the touchscreen display. Clinics can save surgeon and patient profiles to the system, access records of procedures and maintain system settings.

When the Metis becomes available,

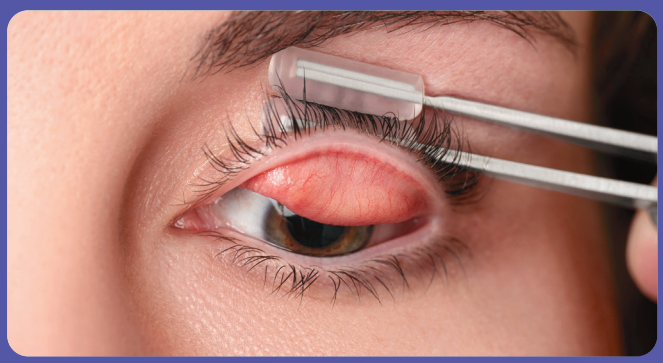
(Continued on p. 32)

Haag-Streit

Metis is designed to be fully upgradable as future devices and technologies emerge.

Meivertor™

US Patent 11,446,017



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STEPPING INTO THE RING OF PREMIUM PRACTICE

What's holding surgeons back from embarking on the premium IOL journey? Experts weigh in.

CHRISTINE YUE LEONARD
SENIOR ASSOCIATE EDITOR

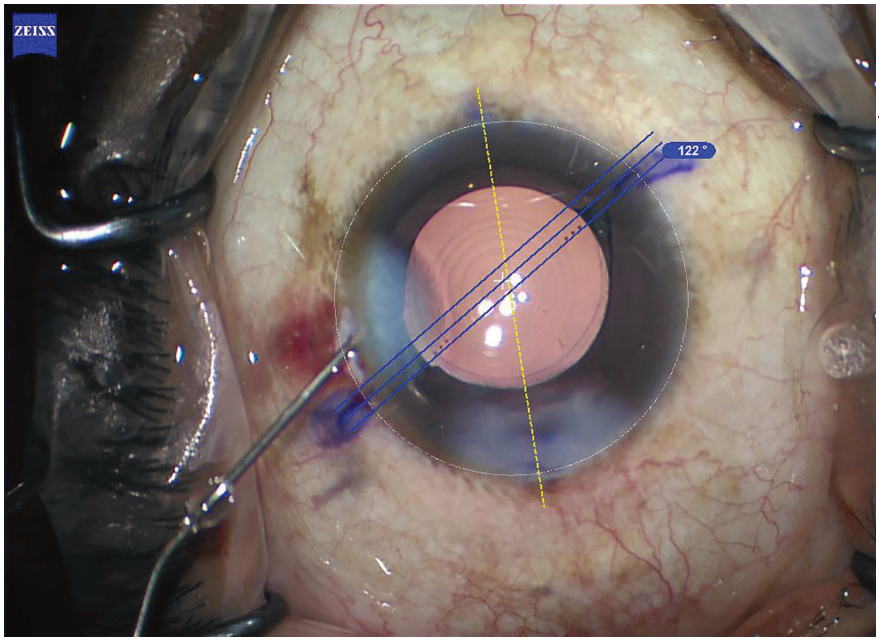
Soul searching isn't usually thought of as a prerequisite for performing cataract surgery, but when it comes to making big practice changes, experts say that confidence may lie at the heart of it. Vance Thompson, MD, founder of Vance Thompson Vision in Sioux Falls, South Dakota, believes that a lack of confidence is one of the biggest obstacles holding surgeons back from getting into premium IOLs. "Physicians took an oath to do no harm," he says. "I consider myself a physician first, an ophthalmologist second and a refractive surgeon third. When you think about the fact that we're physicians who don't want to disappoint our patients, I think that's the core of it. What would be the main reason we'd worry about disappointing our patients? Our confidence in the technology and our confidence in our ability to deliver it to its full potential."

This month, we spoke with premium IOL veterans about gaining confidence, and the tips and tools you need to get started with premium practice.

Preparation

William F. Wiley, MD, medical director of the Cleveland Eye Clinic and assistant clinical professor of ophthalmology at University Hospitals, Case Western University, agrees that a lack of confidence in achieving the outcome that patients are looking for is a major barrier to uptake.

The practice changes related to premium consults and workup, additional chair time and staff coordi-



Rahul S. Tonk, MD

An Alcon PanOptix toric IOL is aligned at the desired axis with guidance from the Zeiss Callisto.

This article has no commercial sponsorship.

Dr. Thompson is a consultant for RxSight, Precision Lens, Alcon and Zeiss. **Dr. Wiley** is a consultant for Alcon, J&J, Bausch + Lomb and RxSight. **Dr. Tonk** has no relevant financial disclosures.

nation can also feel like particularly tall obstacles. Having a mentor and observing how they manage premium lenses in their practice is a good way to get started, says Dr. Thompson. He also recommends attending national meetings, taking courses on the business of premium practice, and keeping abreast of the latest information published in the journals and trade journals.

"At our first Business of Refractive Cataract Surgery course in Dallas, we found that many practices felt overwhelmed by the complexity of the premium implant patient experience cycle," says Dr. Thompson. "The BRICS course at ASCRS includes forms and patient education materials for every step of the patient experience and checklists for the consult or follow-up exams, pearls for the surgery itself and for what to consider if the patient isn't seeing perfectly at their one-month or beyond postop visit.

"We break the patient experience cycle down from beginning to end step by step: from patients' online research phase to the phone interaction with your staff and the homework patients should complete before their consultation," he says. "On consultation day, it's essential to plan the greeting and first impressions, and coordinate with your team. Proper training for technicians on testing and patient communication is key. The consultation itself must set clear expectations, explaining the pros and cons of different implants. Additionally, it's crucial to address insurance coverage, additional charges and the value of the procedure so patients understand and feel confident in their investment. This process also involves educating patients about payment plans and preparing them for surgery."

Another challenge all surgeons point out is managing the unhappy premium IOL patient. "For every few satisfied patients, there will inevitably be one who's mostly happy but not fully, and another who's dissatisfied," says Rahul S. Tonk, MD, MBA, an associate professor of clinical ophthalmology at Bascom Palmer Eye Institute and medical director of The Lennar Foundation Medical Center in Florida. "That's part of the reality when you're not just correcting vision, but also promising freedom from glasses and contacts. Raising those expectations can set you up for an unhappy patient.

> **"You need several points of touch on the education aspect. It's not even a sell; it's simply educating patients on the options, so they understand what's available or potentially available for their situation."**
>
> ***—William F. Wiley, MD***

"Some surgeons, after a few dissatisfied patients, may get discouraged and back away from premium lenses," he continues. "In those cases, it's important to reevaluate the process—were the patient's expectations properly set? Were they the right candidate for that lens technology? Was the surgery done to the best of the surgeon's ability, and was postoperative care handled well to ensure a positive outcome? Proper attention to these details can significantly reduce dissatisfaction with premium lenses."

To smooth the way, select patients with relatively easy to hit refractive targets and relatively normal eyes, recommends Dr. Wiley. "Don't test out premium lenses in unusual eyes," he says. "Start out with virgin eyes with no previous surgery or eyes with a favorable prescription, such as a low hyperope. The chances of making that patient happy are pretty high. Tee yourself up for success. Once you have success in these patients, you can start gaining confidence to expand your patient offerings."

The Price Tag Issue

Dr. Tonk says that another of "the biggest hurdles is asking patients to pay out of pocket for something when most of what we do in medicine is covered by insurance. There's a perception that asking for payment means we're trying to sell a product.

"Discussing out-of-pocket costs is uncomfortable for many physicians, myself included, which is why I don't dwell on it," he continues. "I explain that insurance will cover certain lenses, and there are additional options for those interested in reducing their need for glasses after surgery. I assess their interest through questions and surveys, and if they're interested, I make sure they fully understand their options. The real issue would be a patient who would have wanted a premium lens but wasn't given the opportunity because their surgeon didn't offer it—this is something we need to avoid."

Invest in Patient Education

When performing refractive cataract surgery with premium intraocular lens implants, the primary goal is to meet the patient's refractive needs and visual expectations. Dr. Tonk says that the first step is largely technology-independent and relies more on having a systematic way of understanding the patient's visual goals. It's also key for the patient to understand their own goals.

"First, ensure patients are educated about the benefits of premium IOLs, which can reduce dependence on glasses and contacts," he says. "Use tools like the Dell questionnaire to help patients articulate their needs and involve office staff in discussing goals during the patient workup. Is it simply to get rid of the blur? Because someone told them they needed it? Or are they expecting to be free of or rely less on glasses and contacts? Additionally, gaining insight into the patient's lifestyle—such as their daily

activities, profession and recreational pursuits—will help match them with the right lens technology."

Dr. Wiley recommends that practices invest in education to show both patients and staff what can be achieved with new lens technologies. "I think a lot of patients just assume all cataract surgery is the same," he says. "If they're not educated about their options, they're not likely to choose an upgraded lens. It's hard for the surgeon to be the only one discussing it. We've found a multifaceted approach works well—you need your website to discuss it, you need literature that's mailed out to the patients ahead of time, your technicians need to talk about it and your referring ODs should discuss it. You need several points of touch on the education aspect. It's not even a sell; it's simply educating patients on the options, so they understand what's available or potentially available for their situation. I think that's a crucial step to increase adoption of premium lenses."

Meticulous Evaluation

As with any intraocular lens implant, but especially a premium IOL, performing careful diagnostics is essential for checking the overall health of the eye and confirming a patient's suitability for a premium intraocular lens. Dr. Tonk offers the example of a diffractive multifocal lens, which may not be appropriate for a patient with macular disease. "Macular disease can be challenging to detect due to cataracts," he says. "In such cases, an OCT of the macula can provide clarity."

For quality surgery, a premium implant needs a premium tear film, says Dr. Thompson. "The tear film is critically important—not only therapeutically but also optically. The air-tear interface focuses light two to four times stronger than the implant. Be sure to rule out tear film blur. If it's present, treat it preoperatively and perform a good ocular surface evaluation, including dry-eye questionnaires."

In addition to history, tear analysis and corneal topography, Dr. Thompson says it's important to have a way of quantifying the optics of the cornea. "You want to understand if you're dealing with a multifocal cornea or not," he says. "Using aberrometry, assess the higher order aberration state of the cornea. In general, you don't want to add a multifocal implant to a multifocal cornea. I also perform a macular and optic nerve OCT on every cataract patient, whether they're premium or not, because the only way for me to determine if they're a candidate for an advanced implant is to confirm that their eye is healthy from front to back. The exam helps, but you need these diagnostics to fully understand the state of the eye."

Another essential aspect of preoperative diagnostics is reliably measuring a patient's astigmatism. Dr. Tonk's workflow includes Placido disc topography, IOL biometry and macular OCT. Additional tools like wavefront aberrometry and tomography (e.g., Galileo or Pentacam) provide supplemental precision. He adds that "a high-quality IOL biometer and modern formulas are crucial investments for achieving optimal refractive outcomes."

Key Intraoperative Techniques

According to Dr. Tonk, managing astigmatism and having a consistent capsulotomy are among the most important intraoperative aspects for working with premium lenses. "Astigmatism can be addressed in two ways," he says. "One is with the lens implant itself. If you're putting in a toric lens implant, you should have a reliable way of implanting it on the appropriate axis. Good quality manual marking can be used, or you can employ devices such as Zeiss Callisto, Alcon Verion and ORA, and Lensar IntelliAxis. You'll also want to ensure that the implant doesn't rotate intraoperatively or postoperatively. The other way of managing astigmatism is with femtosecond laser arcuate keratotomies. I prefer to use the femto laser for low-grade astigmatism and torics for moderate or greater astigmatism, as I find astigmatism correction with a toric lens more reliable than with femtosecond laser."

A consistent, solid capsulotomy is also vital, says Dr. Tonk. "You want to achieve good capsular overlap of the IOL for 360 degrees to ensure consistent effective lens position," he says. "This minimizes the chance of refractive surprise postoperatively and minimizes the chances of the patient developing posterior capsular opacification. There are several ways of achieving a consistent capsulotomy: manually, with a femtosecond laser or with the Zepto device. Lastly, develop meticulous surgical technique with good cortical cleanup and avoid damaging the zonules or posterior capsule. No one wants these issues regardless, but you especially don't want them in a premium lens."

Planning for the Postoperative Obstacles

On average, premium lens patients require more postop care than standard monofocal cataract surgery patients.[1] Experts say to be prepared to look after these patients closely and ensure they have easy access to you and your staff. "These patients are paying not only for a premium intraocular lens but also for a premium experience," Dr. Tonk points out.

From the patient's perspective, the premium lens journey may involve "complications," so experts say it's a good idea to carefully explain what the postoperative period will look like and why these seeming "complications" are just part of the healing process.

Dry eye, for example, is common after ocular surgery, and it's a common premium patient complaint. "Dry eye may cause fluctuating or blurred vision, [and] an advanced-technology lens patient expects to

Premium lenses are a time committment for both the surgeon and the patient. Experts say it's important to prepare patients for what to expect in the days, weeks and months following their cataract surgery, from potential enhancements to dysphotopsias.

have spectacle freedom right out of the gate," says Dr. Tonk. "Some premium lenses [also] require neural adaptation, so you'll also want to be prepared to help patients going through that process."

Dr. Thompson says he has a three-step journey of education for premium patients. First, he discusses what the natural lens used to do: provide reading range and clarity. He explains that reading range is lost first, necessitating a need for reading glasses or bifocals, followed by loss of clarity with cataract formation. "I tell patients they have the choice to replace one of those things, the clarity, and then replace the reading range and any residual refractive error with trifocal glasses, or they have the choice to replace both of those lens functions with modern premium IOL technology."

If patients choose the premium route, Dr. Thompson thoroughly explains what to be prepared for. "I don't explain effective lens position and incisional healing astigmatism to every patient, but I do tell patients that their healing process can have them end up not being 20/20 as they hoped," he says. "I tell them that in traditional cataract surgery, we make that up with glasses. For advanced cataract surgery, we do an enhancement where we laser the leftover spherical refractive error and/or astigmatism or do an astigmatic keratotomy if the spherical equivalent is right where we want it. I also note that often the capsule behind the implant gets hazy and we'd need to do a YAG laser capsulotomy. So, it's not uncommon that the first four to six months are spent on the implant, the capsule, the residual refractive error and tear film optimization. I always consider the first six months as me optimizing the patient's optical system. Those are the first three steps, and if the tear film needs attention, that's another step.

"The main thing with a multifocal or extended depth of focus implant is that the part of the implant that helps patients see near and intermediate creates a typically very tolerable halo around lights at night, and that's to be expected," he continues. "However, this halo can be complicated by glare and starburst caused by dry eye, residual refractive error and posterior capsule opacification. It's up to the doctor to minimize the non-IOL-related dysphotopsias because the halo of modern day multifocals simply gets better with time. That's why patient satisfaction is so high with these lenses when expectations are properly set and doctors work hard to optimize the patient's optical system."

Negotiating dysphotopsias can be daunting for surgeons. "Bothersome nighttime glare, halo or starburst symptoms are among the biggest fears with premium IOLs," says Dr. Wiley. "We don't know which patients are going to be bothered by it. Thankfully, the newer lenses have helped mitigate some of that concern, though it's a question of balancing the amount of vision versus the amount of side effects. An EDOF lens, for example, mitigates the side effect profile but also dampens the amount of near vision achieved. Regardless of the optical strategy chosen, it's important to set proper expectations."

Since residual refractive error is the number one cause of patient dissatisfaction after premium cataract surgery, you need to be able to treat residual refractive error or refer patients for that, says Dr. Thompson. "We know that with good quality biometry, keratometry and measurements, especially with a healthy tear film, we can have very low enhancement rates. But nevertheless, it's important to think about the 'what if' patients need an enhancement and have a plan."

Dr. Tonk notes that laser enhancements aren't part of every surgeon's toolbox. "They may be cataract surgeons but not corneal refractive surgeons, or they may not have access to a laser," he says. "In these cases, partnering with someone in or

outside of your practice can work."

If surgeons are concerned about hitting refractive targets, implant-adjustable lenses such as the light-adjustable lens from RxSight could be a confidence-boosting alternative. Dr. Wiley points out that the LAL is also an option for providers who don't have access to LASIK for performing enhancements.

Experts also say that the IOL exchange and rotation procedures should be in the surgical repertoire for anyone working with premium lenses. "Most cataract surgeons have the skills to do bag-to-bag IOL exchange," Dr. Tonk says. "If you haven't done it before, there are surgical skills courses available at the major meetings such as the American Academy of Ophthalmology meeting or ASCRS to learn these specific techniques and pearls."

"Patient satisfaction six to 12 months down the road is so high, but it may not be that way in the first six months," Dr. Thompson emphasizes. "That's why you need to be able to tell the patient that we're embarking on a one-year journey, where the first six months is optical system optimization and the next six months is your brain adapting to their new optical system.

"Practices don't always have the confidence to be able to efficiently tell this story in a busy clinic," he continues. "That's why we created the BRICS course at ASCRS, because we know practice confidence is one of the main reasons that premium implants haven't grown. Doctors want to learn ways to increase their practice confidence and the confidence of their entire team of technicians, nurses, staff and doctors, and to also do that for their community and referral network through education. That's why we also have the doctor bring one or some of their team members to the course so they can help teach the rest of the team and implement the lessons to improve patient satisfaction and practice success."

Final Thoughts

"I like to emphasize to doctors, as the ASCRS president, that we work hard in Washington to try to limit Medicare cuts," says Dr. Thompson. "But third-party reimbursement is just going to continue to go down. This is the new normal. However, patients are also willing to invest in their own health care with advanced implants. The modern-day practice is one that understands that by blending third-party pay and patient pay, and that by patients investing in their health care, ophthalmologists can afford the technology that helps them take care of their Medicaid patients or enables them to do mission work. Premium implant cataract surgery makes for a healthy practice that also allows you to help those who can't afford to help themselves." ◀

1. Maloney RK, Doane J, Weinstock R, Donaldson KE; AECOS Postoperative Care Study Group. Work intensity of postoperative care following implantation of presbyopia-correcting versus monofocal intraocular lenses. Clin Ophthalmol 2023;17:1993-2001. Published 2023 Jul 17.

(Continued from p. 26)

surgeons will have the option to incorporate Haag-Streit's Eibos 2 fundus observation device. This will be adapted from the Hi-R Neo 900 microscope. One other feature from the Hi-R Neo 900 that could assist with procedures is Haag-Streit's Tocular, a rotatable wide-angle ocular to adjust the implantation angle for alignment of toric IOLs. It has yet to be announced whether this feature will be available with the Metis.

OMS-800 (Topcon Healthcare)

Topcon Healthcare offers their OMS-800 surgical microscope in three different models: OFFISS; Standard; and Pro. OFFISS stands for Optical Fiber Free Intravitreal Surgery System. Both the OFFISS and Pro models have the same exact features as the Standard edition. Each microscope is equipped with apochromatic optics to reduce chromatic aberrations and a built-in beam splitter and adjustable eyepieces for positioning the microscope and proper viewing.

The Pro and OFFISS models come with additional features. An electromagnetic locking system was added to both devices to support the positioning of the optical head by locking it in place instantaneously after the surgeon has adjusted their settings for the procedure. Furthermore, both models come with a coarse functioning mechanism that can quickly elevate the optical head intraoperatively.

The OFFISS feature enhances the microscope's observational system for vitrectomy procedures without the need for fiber optic illumination. Instead, Topcon developed lenses for OFFISS to allow the microscope head and indirect lens to move independently of each other. An image inverter integrated into the system will activate automatically when using the OFFISS feature to assist with visualization. The lenses available for the OFFISS system come in multiple different diopter strengths ranging from a 40-D lens to a small 120-D lens, as well as an anterior lens. These lenses are autoclavable.

Featherlite (Prescott's)

Ophthalmologists traveling for work or practicing at their own private office can opt for Prescott's Featherlite, a portable ophthalmic surgical microscope. According to Prescott's, this microscope can be disassembled and packed up in five minutes. Two luggage cases are provided for transportation of the equipment.

Featherlite comes with a five-step apochromatic magnification changer (0.4, 0.6, 1, 1.6 and 2.5). It uses LED illumination for visualization and comes equipped with an objective lens that works at focal lengths between 200 mm to 400 mm. Also, while it doesn't come equipped with its own display, it does offer optional 4K streaming with still image capturing. Simply plug in an HDMI cable into the microscope and connect it into any monitor display for visualization.

No matter what microscope ophthalmologists prefer, the industry is filled with the most advanced microscope technology to ensure procedures are done safely and effectively. ◀

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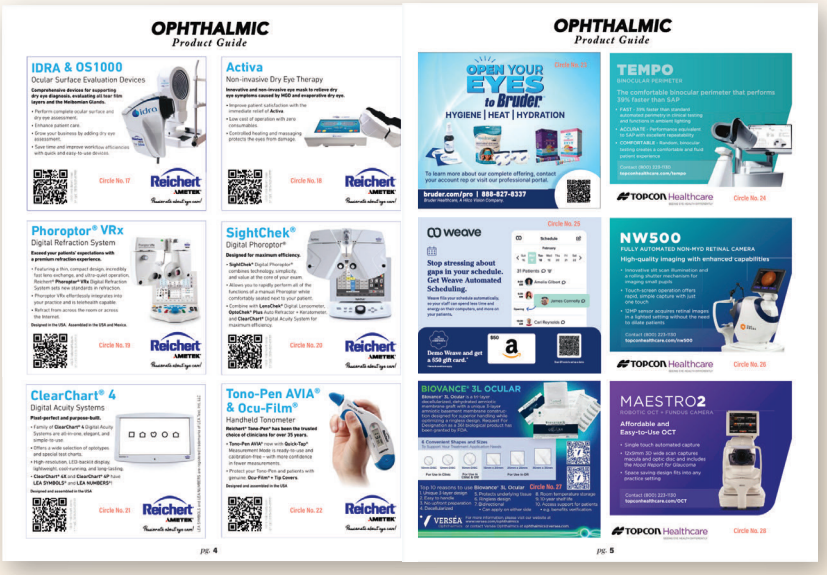

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REVIEW'S ANNUAL INTRAOCULAR LENS SURVEY

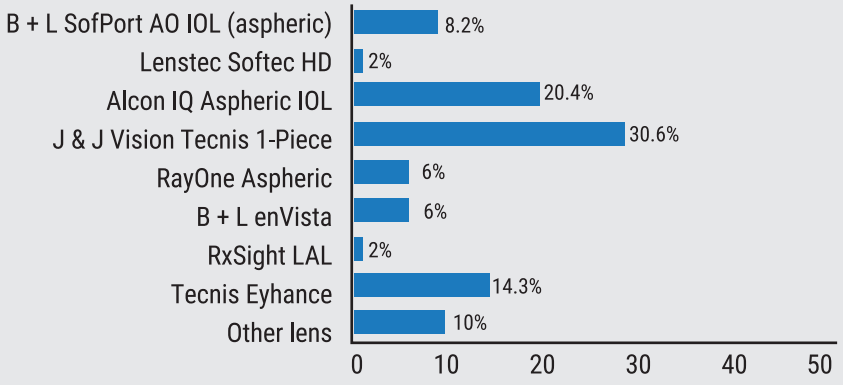
Cataract surgeons share their thoughts on the various lens options available, from monofocal and toric lenses to presbyopic and phakic IOLs.

WALTER BETHKE
EDITOR IN CHIEF

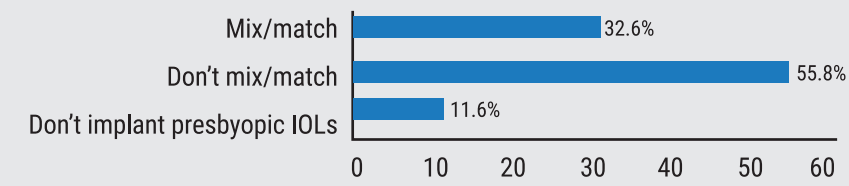
Each year, cataract surgeons are presented with a range of new intraocular lenses to choose from, both monofocal and premium. After reading the literature and trying these devices in their practices, physicians gravitate toward the ones that achieve the outcomes they're looking for. In this year's survey regarding IOL preferences, physicians were able to weigh in on such topics as the monofocal lenses they prefer, the lens features they value the most and which toric IOLs they use.

This year's e-survey was sent to around 14,700 physicians, and had a 28 percent open rate. Overall, 51 surgeons completed the entire survey. To find out about their IOL preferences and practice patterns, read on.

Preferred Non-premium IOL for Most Cases



Surgeons Who Mix/Match Presbyopic Lenses



Monofocal Menagerie

When it comes to monofocal, non-premium IOLs, the most popular option among respondents was the Tecnis one-piece, chosen by 30.6 percent of surgeons. They provided a variety of reasons for their choice.

"It's easy to implant, has excellent reliability, and good long term performance!" says a surgeon from Missouri. A surgeon from Iowa likes the Tecnis for its "Excellent visual quality and refractive predictability. Though I do experience more negative dysphotopsias than I like."

A physician from Maryland, however, says he likes the Tecnis' "optical quality, low level of dysphotopsias and pricing." A Mississippi surgeon agrees on the topic of optics. "It has great optics and you don't see that IOL reflex on your patient from across a room," he says.

The second most popular monofocal on this year's survey was the Alcon IQ Aspheric, selected by 20.4 percent of

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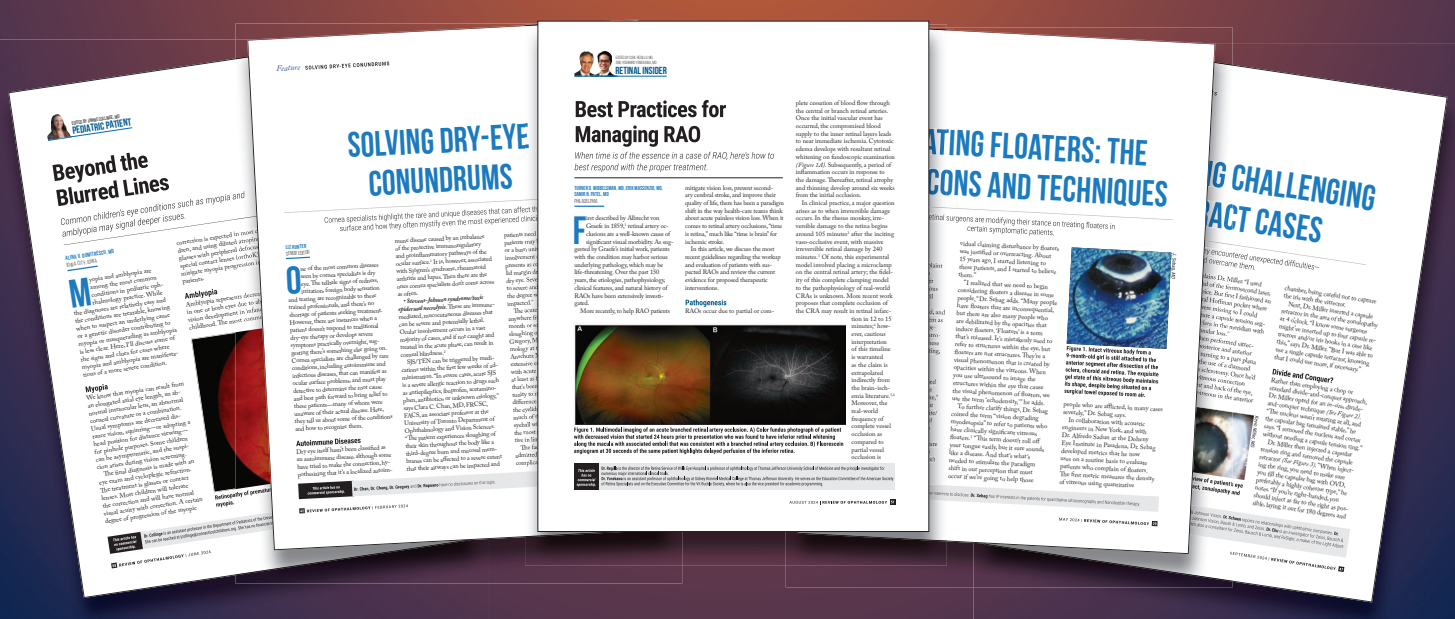


respondents.

"The SA60AT platform has been around for a long time and is very stable and predictable," says a surgeon from Kansas. Jonathan Adler, MD, of Bradenton, Florida, agrees, saying, "[It has] very clear optics with no deposits." Jeffrey Shaver, MD, of Edmond, Oklahoma, says he sees pros and cons to the lens. "[I like the] consistency," he says, "But it's hard for tech to load and slow to open." A surgeon from Missouri prefers the lens because it's "effective, safe, affordable [and comes with good] support," he says.

The rest of the respondents monofocal preferences appear in the graph on page 34.

Toric Lens Options

Surgeons also shared their toric IOL practices on this year's survey.

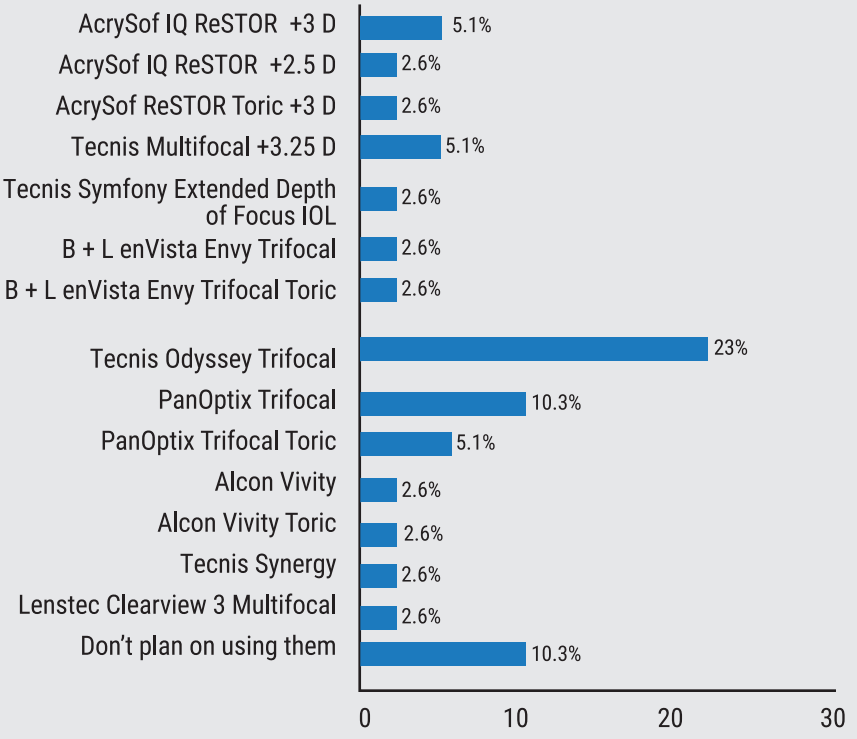
The most popular option was the Tecnis Eyhance Toric, chosen by 36 percent of the respondents. "It gives great results with a wide range of vision at a low cost," says a doctor from Wisconsin. A surgeon from Maryland says he chooses the lens because of "good stability and a mild EDOF function." A surgeon from Mississippi says he likes the lens due to its "excellent distance vision with great intermediate."

The next most popular toric option is the AcrySof toric, chosen by 16.7 percent of surgeons. Oklahoma's Dr. Shaver says he chooses it due to its "consistency and stability."

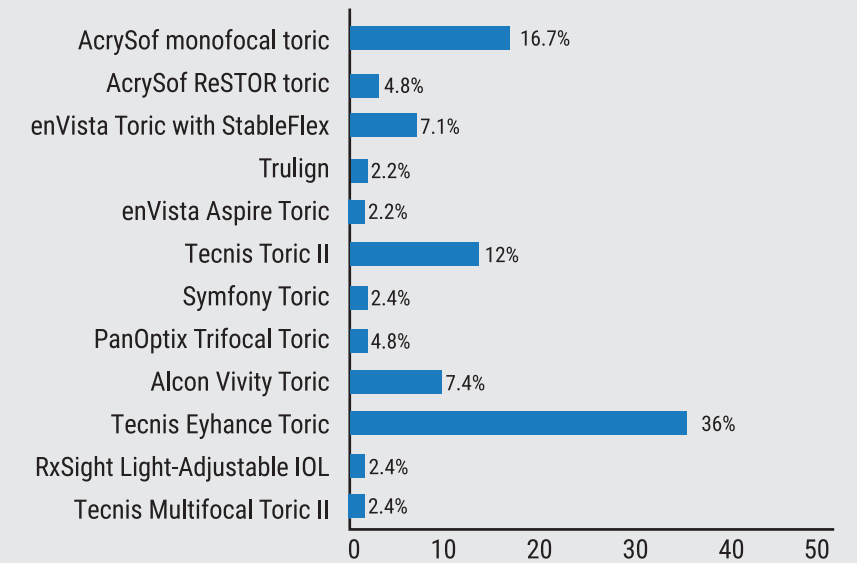
The third most popular choice is the Tecnis Toric II, preferred by 12 percent of the respondents.

"The durability, clarity, handling characteristics, as well as the pre-loaded injector and the rotational stability," are some of the reasons given by a New Hampshire surgeon who prefers this lens. Steven Dewey, MD, of Colorado Springs, says he uses the lens because it offers "zero levels of postop rotation, and exceptional color and contrast." A surgeon from Georgia uses the Tecnis Toric II frequently, saying, "I like its stability and the Tecnis IOL characteristics."

If Surgeons Get into Presbyopic Lenses, Which Will They Start With?



Preferred Toric IOL



The full list of toric options chosen by surgeons appears in the graph above.

Presbyopic Lens Roundup

Surgeons also shared their views on presbyopia-correcting lenses.

The Alcon PanOptix Trifocal IOL and the PanOptix Trifocal toric were the lenses chosen the most often, at 36.8 and 34 percent, respectively (surgeons chose more than one option).

Florida's Dr. Adler says, "As long as patients are chosen carefully, [I get]

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IOP = intraocular pressure; ITT = intent to treat.

*In the XEN® Gel Stent clinical study, baseline medicated IOP ranged from 20.0 to 33.7 mm Hg.[2]

†No clinically significant consequences were associated with hypotony, such as choroidal effusions, suprachoroidal hemorrhage, or hypotony maculopathy. IOP < 6 mm Hg was defined as an adverse event, regardless of whether there were any associated complications or sequelae related to the low pressure. Thirteen cases occurred at the 1-day visit; there were no cases of persistent hypotony, and no surgical intervention was required for any case of hypotony.[1]

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The most common postoperative adverse events included best-corrected visual acuity loss of ≥ 2 lines (≤ 30 days 15.4%; > 30 days 10.8%; 12 months 6.2%), hypotony IOP < 6 mm Hg at any time (24.6%; no clinically significant consequences were associated, no cases of persistent hypotony, and no surgical intervention was required), IOP increase ≥ 10 mm Hg from baseline (21.5%), and needling procedure (32.3%).

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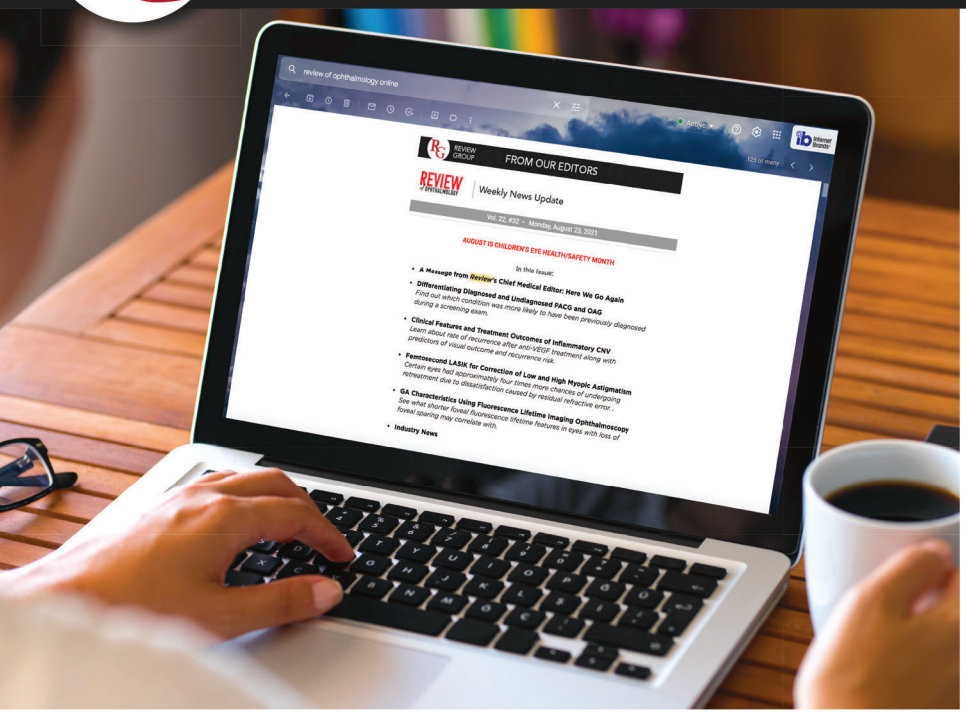

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REVIEW of OPHTHALMOLOGY | Weekly News Update

Vol. 25, #33 • Monday, August 19, 2024

AUGUST IS CHILDREN'S EYE HEALTH/SAFETY MONTH

In this Issue:

- **Corneal Epithelial Damage Findings After Switching from Concomitant Use of Brinzolamide and Brimonidine to Fixed-dose Combination**
  Find out if the fixed-dose combination had efficacy.
- **Effect of Brolucizumab and Aflibercept on Maximum Thickness of PEDs and sub-RPE fluid, in HAWK and HARRIER**
  Learn which agent achieved greater reductions in pigment epithelium fluid and sub-retinal pigment epithelium fluid thickness.
- **Outcomes of Donor Corneas of Different Thicknesses from Endothelial Keratoplasty in DALK for Keratoconus**
  Find out if there was parity among the corneas.
- **Digital Histology of Retinal Microaneurysms as Provided by Dense B-scan (DART) OCTA: Relevance in DR**
  Researchers determined that Dense Automatic-RealTime OCTA technology provided several new insights on retinal microaneurysm characteristics and their blood flow network connectivity.
- **Industry News**

Corneal Epithelial Damage Findings After Switching from Concomitant Use of Brinzolamide and Brimonidine to Fixed-dose Combination

Researchers assessed the effectiveness of switching from the concomitant use of brinzolamide 1% (BZM) and brimonidine 0.1% (BMD) to a BZM/BMD fixed-dose combination (BBFC) for the reduction of corneal epithelial damage.

The retrospective cohort study involved 52 eyes of 52 glaucoma patients (26 women, 26 men; mean

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great results with very happy patients for PanOptix. Do not use if [the patient is] post-refractive or has an epiretinal membrane or other macula pathology. With Vivity, I can use it in the instances where PanOptix isn't indicated."

"It's consistent," says a surgeon from Washington, D.C., who uses the PanOptix. "Tolerable halos. Good near, distance and intermediate. Can always get better with halos and glare." A surgeon from New Jersey who uses the PanOptix often, still sees room for improvement. "Still [doesn't have] the calculated accuracy I would like," he says. A Wisconsin surgeon chooses the PanOptix because she says it gets her, "Good results. Less halos." Oklahoma's Dr. Shaver says he's "very satisfied," with the PanOptix Trifocal toric.

The next most popular presbyopic lenses are the Alcon Vivity, chosen by 26 percent of surgeons and the Tecnis Odyssey Trifocal, selected by 21 percent.

"[The Odyssey Trifocal] gives excellent distance, tolerable dysphotopsias and good quality of vision," says a Maryland doctor. A Texas surgeon says he's "somewhat satisfied" with the Odyssey Trifocal, saying, "It still needs better intermediate and near without nighttime issues or decreased contrast." Dr. Dewey uses the toric version the most, appreciating its "wide visual range from distance to near, great contrast/color, low levels of pseudophakic dysphotopsias and rapid visual adaptation."

Surgeons also discussed the practice of "mixing and matching" presbyopic lenses in order to get a certain effect. The percentage of respondents who mix and match is 32.6, those who don't is 55.8 percent and 11.6 percent of the surgeons don't implant the lenses.

"Occasionally [I'll implant] an Alcon PanOptix Multifocal in the first eye, usually the non-dominant eye, and if the patient isn't completely satisfied, then a monofocal in the second, dominant eye," says a surgeon from Ohio. "It often saves having to exchange the multifocal out. I've occasionally implanted a Vivity in one eye and a PanOptix in the other eye, but the patient invariably prefers the near vision of the PanOptix, so I rarely do this anymore."

Dr. Shaver says, "I'll put an EDOF from Rayner in an eye with previous retina surgery or higher order aberrations and a PanOptix in the unoperated eye." A surgeon from Miami says his approach is, "Symfony in dominant eye for distance, Odyssey in the near eye." A physician from Texas declares, " I most commonly mix and match Synergy with Symfony to achieve best range of vision. Though I may not need to if the Odyssey turns out to be better."

IOL Attributes Surgeons Value
(1= least important, 8=most important)

Attribute	Average score
Asphericity/neutral asphericity	6
Extended Depth of Focus Design	6
Toric Design	6
Edge design to decrease PCO	5
Bifocal Multifocality	5
Blue-light Blocking	5
Violet-light blocking	5
Trifocality	5
Ability to adjust IOL power post-implantation	4

Phakic IOLs

Some surgeons on the survey (18 percent), implant phakic IOLs. Seventy-eight percent of these surgeons implant the EVO/EVO+ ICL, while the rest implant the Artisan/Veriflex.

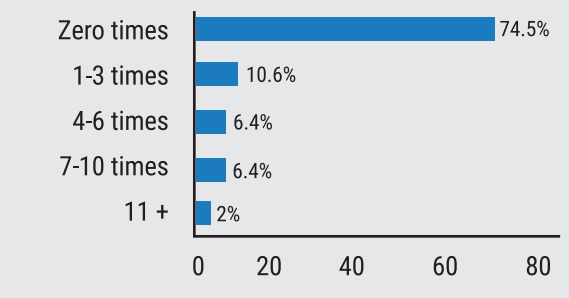
"[They're] a very good option to LASIK or PRK; I refer these out," says Dr. Adler. A surgeon from Georgia, however, doesn't implant them, saying, "I'm concerned about endothelial health."

Lens Fixation

Surgeons also touched on situations where they need to suture a lens *(see graph to the left)*.

"The most common reason for sutured IOLs is the lack of adequate capsule support," says a surgeon from Ohio. "Most cases are referred in. I never use AC IOLs due to the high incidence of glaucoma afterwards." Syamala Reddy, MD, of Slidell, Louisiana, says the most common reason for suturing is "a lack of stability," and that "scleral fixation" is his preferred method of dealing with it. A Tennessee surgeon says his reason for suturing a lens is usually when "[the patient is] left aphakic after complex cataract surgery." Jimmy Hu, MD, of Englewood, New Jersey, says the main reason for suturing and his approach is often "dislocated IOL or inadequate capsular support. I favor the Yamane technique for scleral fixation." ◀

How Often Surgeons Suture an IOL in a Year

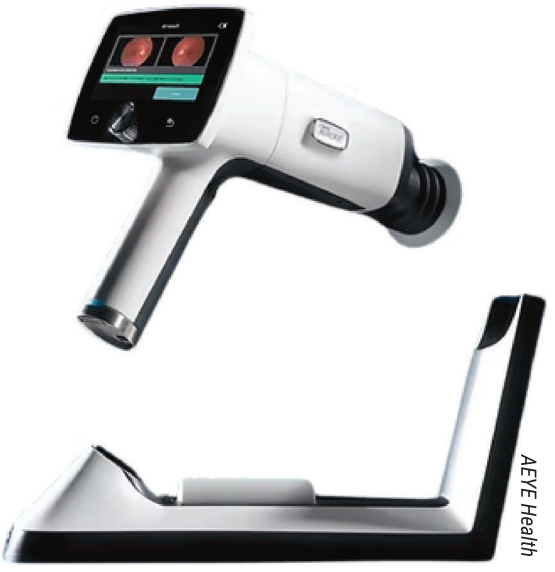


ADVANCEMENTS IN DR SCREENING TECHNOLOGY

These innovations may help catch more patients with diabetic retinopathy, including those in underrepresented populations.

ANDREW BEERS
ASSOCIATE EDITOR

Performing comprehensive screening for diabetic retinopathy can be challenging for many patients, especially those with inadequate insurance or access to care. With proper fundus photography, optical coherence tomography and ultra-widefield imaging, however, physicians can catch DR before it worsens in these and other patients. The only problem is getting this screening technology to the masses and ensuring patients adhere to routine follow-up. Fortunately, advances have been made to screening for DR that can increase awareness and diagnosis for all patients, including those from historically underrepresented groups looking for care.



AEYE Health

Optomed Aurora AEYE portable fundus camera uses AI to automatically examine and diagnose patients for diabetic retinopathy.

Streamline Screening with AI

Artificial intelligence is one of the latest technologies to be used for diagnoses in eye care. There are several AI systems that were developed and FDA approved for the identification of mild to visually threatening DR with fundus photography.

"IDx-DR, EyeArt and AEYE Diagnostic Screening are among the FDA-approved systems," says Paolo Antonio Silva, MD, an ophthalmologist with the Joslin Diabetes Center in Boston. "These are autonomous programs capable of identifying referable DR from high-quality retinal images. They're useful for their rapid, standardized screening that reduces reliance on specialist availability and enables early intervention." These systems are primarily intended for use in a general practitioner's office, to help with the recognition of diabetic retinopathy and referral to a specialist or retina subspecialist.

• ***IDx-DR (Digital Diagnostics)***. This AI system is indicated for the automatic detection of mild nonproliferative DR in adults diagnosed with diabetes, but without any previous history of DR, analyzing images taken with a Topcon NW400 retinal camera. The camera operator must take two images per eye to ensure the AI's algorithm can understand what's being presented to it. One image of the centered disc and one image of the centered macula are needed.

To use IDx-DR, the user takes images of a patient's eyes and sends them to the AI client online. Results should be expected within one

This article has no commercial sponsorship.

Dr. Silva provided research support for Optos and Optomed. **Dr. Haug** has no relevant financial disclosures.

minute, according to the company. The AI will provide results along with suggested follow-up instructions for management. If the results are negative for mild DR, Digital Diagnostics suggests rechecking in 12 months rather than re-submitting images back into the system in accordance with the American Diabetes Association's guidelines for DR screening and management.

This AI was designed to streamline workflow for physicians. It can interface directly with electronic health record systems, so retina specialists can attach the results to their patients' files. If interested, physicians can take an operator training session by a certified IDx trainer to better understand how to use the AI and ensure their images meet the protocol needed for the AI's algorithm.

According to FDA data, the IDx-DR has a sensitivity of 87.4 percent, and a specificity of 89.5 percent. It shouldn't be used in patients with a history of laser treatment, ocular surgery or injections, per the FDA labeling.

• ***EyeArt (Eyenuk)***. This AI system is indicated for the automatic detection of more severe forms of DR in patients with diabetes who have no previous diagnosis of DR. EyeArt can distinguish images taken with Canon CR-2 AF, Canon CR-2 Plus AF and Topcon NW400 retinal cameras. Good quality images focused on the centered disc and the centered macula are needed for the AI to observe any signs of DR.

Image quality is important for EyeArt to be successful. Poor imaging can result in a false positive or insufficient results. In this case, Eyenuk suggests retesting the subject by dilating their pupils, reimaging and submitting new, clearer images. If the patient's pupils can't be dilated properly, then other screening methods should be employed, or the patient should be referred to a specialist for diagnosis of DR.

In one clinical study, EyeArt demonstrated a sensitivity of 96 percent and a specificity of 88 percent. The study protocol excluded patients with persistent visual impairment in one or both eyes, contraindication to fundus photography or pharmacologic mydriasis, and/or history of retinal vascular occlusion, ocular injections, laser treatments to the retina, or prior intraocular surgery other than uncomplicated cataract extraction.[1]

After analyzing fundus images, EyeArt suggests a management plan for what medications and treatment options should be considered for patients with different severity levels of diabetic retinopathy.

EyeArt's RESTful application programming interface is HIPAA compliant. This interface allows physicians to integrate results from the AI test into a third-party software such as an EHR or other communication systems.

• ***AEYE Diagnostic Screening (AEYE Health)***. This AI system was designed to be used for point-of-care screening. Depending on the physician's preference, they can either choose to image with the Topcon NW400 retinal camera or Optomed's Aurora IQ handheld fundus camera. Both systems only require one image per eye for the AI's algorithm to detect signs of DR.

The Aurora camera is much different than using the AI with the NW400, the company says. Instead of presenting the findings through the AI client on the physician's desktop, the Aurora is equipped with its own screen and interface to provide results straight to the user in approximately a minute.

As mentioned earlier, AEYE is meant to be used for point-of-care screening. Dedicated CPT codes for testing with this AI have been created to allow physicians to use this technology outside of the clinic. This can give patients the opportunity to be screened more frequently at their primary care service or through teleretinal screening, rather than spending all the time and money to make it to a clinic, especially in rural areas.

According to the company's FDA clearance documents, the device's sensitivity was in the range of 92 to 93 percent, and its specificity was 89 to 94 percent. In the clinical trial, patients with a history of laser treatment of the retina or injections into either eye, or any history of retinal surgery were excluded.[2]

"There are some downsides to using AI," says Dr. Silva. "They require high-quality images—blurred or poorly illuminated images can impact the accuracy of results. And, although they're quite intuitive, they're limited on their ability to detect artifacts. Systems are improving but they still require human oversight for non-referable findings.

"In order for AI to be successful as a screening tool for diabetic retinopathy, some things need to be considered," he continues. "Training staff members, figuring out where the AI can be integrated into the workflow and addressing regulatory requirements are critical for successful implementation."

Imaging for DR

Quality images are imperative for properly screening patients for DR. Fundus cameras, OCT and UWF imaging devices have all improved the accuracy of diagnosis, and the technology is continuing to evolve.

• ***OCT***. "Ultra-widefield imag-

Disparities in Screening for Diabetic Retinopathy

According to the American Diabetes Association, patients with mild, non-proliferative diabetic retinopathy should be screened every one to two years.[4] As the disease worsens, patients should be screened more frequently. For instance, proliferative DR patients should be screened every month to ensure symptoms are managed. This can be time-consuming, especially for patients in rural areas or without access to transportation. In turn, many patients end up with worsening DR.

"I practice in Durango, which is in Southwest Colorado, and we service the Navajo Nation and Indian Health Service," says Sara Haug, MD, an ophthalmologist with Southwest Eye Consultants, "and a lot of those patients don't have electricity, they don't have running water, they technically have free health care, but the way to access the system is really hard, and transportation is difficult. So, by the time they get to me, often it's almost too late.

"Then, I have patients who see me every year that have no retinopathy," she continues. "They're educated and have more money and insurance, and they know that they're supposed to stick to their follow-up visits, and they do it."

Studies have shown that socioeconomic status, household income, education, geography, race and ethnicity factor into the level of access for DR screening. Historically, older minority patients in rural areas who have Medicare/Medicaid, or no insurance, are less likely to be screened regularly compared to others. For example, the American Indian and Alaskan Native patients are amongst those who are underrepresented in screening.

Stephanie J. Fonda, PhD, and her co-workers conducted a study in 2023 which observed the disparities in screening for DR in American Indian and Alaskan Native patient populations.[5] Researchers partnered with the Indian Health service to collect data between 2015 and 2019 through a telemedicine program. A total of 8,374 individuals were included in this study.

After examining their findings, the researchers concluded that as long as patients comply with their follow-up visits and their visual acuity isn't jeopardized, then the time between DR reevaluations for patients can be extended. However, in this study, 7,097 subjects were screened in 2015 without DR, and 18 percent of those subjects developed mild NPDR, and 0.1 percent developed PDR. Furthermore, 61.2 percent of subjects adhered to the follow-up guidelines and 38.8 percent of subjects weren't reexamined between 2016 to 2019.

"The reality is that I see 80 to 100 patients a day, and it's too much," shares Dr. Haug. "There's no one else to see them. We need more help to make sure we're delivering the proper care to people, and so technology might have the answer. But there needs to be a way to make it worth our while. I would love a system that makes sure everybody gets their check at least once a year and everybody gets their glycemic control medicines and all of that. We're not even considering adding any of those things in our area."

ing captures more than 80 percent of the retina, improving detection of peripheral DR lesions, which are critical for identifying disease progression," shares Dr. Silva. Some widefield cameras available include Optos' line of cameras, the Spectralis (Heidelberg Engineering), the Clarus 700 (Zeiss), the Eidon (iCare) and the RetCam Envision (Natus).

The aforementioned devices have been around for some time now, but there are two that are working with AI to improve diagnosing diseases, including DR. Heidelberg Engineering partnered with RetinAI to integrate their AI portfolio into the Spectralis. This will allow users to submit a larger volume of scans and images to the AI system for analysis right after using the Spectralis, rather than sifting through all the results by hand.

Optos has incorporated their own AI system into their UWF cameras. According to their website, their AI's accuracy for DR detection sensitivity was over 96 percent and specificity was over 93 percent in trials. Currently, this AI only has a CE mark in the UK and European Union.

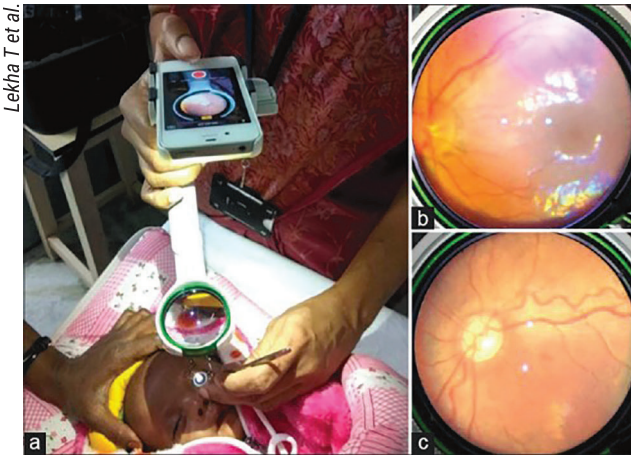
• ***Fundus photography.*** Although it's a powerful screening tool, UWF imaging isn't the only method for imaging the retina. Traditional fundus photography has been a mainstay in retina specialists' armamentarium for imaging. No matter what method of imaging physicians prefer, the cost of these devices can be the deciding factor for what technologies they ultimately use in the end. However, there are more affordable options for imaging.

One approach physicians can do to cut costs is to use their smartphone for fundus photography. Smartphone fundus photography doesn't require an application to download. Rather, a 20-D condensing lens is used to focus the phone's camera lens on the fundus after positioning the camera. The smartphone's flashlight should remain continuously on during the imaging process, but users say that the location of the camera lens and the flashlight in relation to the camera lens can affect the quality of the images.[3]

"Smartphones are great for fundus imaging because they're portable, low-cost and accessible, but the image quality may be variable and proper training and pupil dilation are essential for reliable results," says Dr. Silva. There are smartphone applications available for download that can assist with imaging. These include EyeTakes (Sarah Maki, MD) and Ullman Indirect (Michael Ullman, MD), which both provide assistance to perform smartphone fundus photography.

Not every doctor will want to sit down with their patients and spend the time moving a 20-D lens and their smartphone camera back and forth to focus the image properly. Companies such as Mii Ret Cam and oDocs Eye Care have developed handheld adapters to assist with focusing the image. The visScope 2.0 from oDocs comes with a 20-D lens fixated at the end of the adapter. The 3D printed device allows iPhone and Samsung users to attach their phone to the other end for fundus photography. The Mii Ret Cam adaptor doesn't come with a 20-D lens, but it does offer support and stability when imaging with a smartphone.

Essentially, smartphone fundus photography is something that everyone can perform. Patients can be given



Lekha T et al.

(A) Mii Ret Cam-assisted fundus imaging in a pediatric setting. Physicians imaged retinas with a normal posterior pole (B) and with plus disease (C). *(Creative Commons License: https://creativecommons.org/licenses/by-nc/4.0/.)*

oDocs Eye Care

The visoScope 2.0 comes equipped with a 20-D lens. If it needs to be replaced, oDocs offers lenses on their website in 20 D and other powers.

instructions on how to take the images themselves if they want to, and this form of imaging for DR could also be used for a point-of-care screening test. However, there are some downsides to this technique, especially for underrepresented patient populations.

"The people who would be able to access any sort of app are not the patients that are having trouble accessing health care," says Sara Haug, MD, a retina specialist at Southwest Eye Consultants in Durango, Colorado. "A lot of my patients in dire need aren't savvy with technology. A lot of my Native patients don't have electricity. They don't have cell reception. They can't use their phone." Providing a solution to certain patient populations is critical to ensure that the number of undiagnosed diabetic retinopathy cases decreases.

Screening with Telemedicine

In most cases, patients at risk for developing diabetic retinopathy rely on a visit to their doctor. Patient adherence to office visits can make or break a diabetic retinopathy case, but some patients' nearest retina specialist is a fair distance away. Rather than forcing patients to make their appointment at a distant clinic, a teleretinal approach and constant communication with patients could alleviate screening discrepancies.

"I have people go over huge mountain passes to come see me in the winter," shares Dr. Haug. "The onus is on us to then reach out to the patient and make sure that we follow up appropriately. We have better technology for patients to take a home OCT so that they can send their image to their doctor rather than having to come in four times a year. Telemedicine imagers can take the picture and send the image to a retina specialist or ophthalmologist for screening."

Dr. Silva's work with the Joslin Diabetes Center includes teleretinal services through the Joslin Vision Network. "Teleretinal screening programs extend access to populations different from those seen in traditional in-person examinations," says Dr. Silva. "This method typically accesses patients earlier when they have less severe disease when medical management is most effective."

With the Joslin Vision Network, image technicians are trained on how to image the eye. These specialists are employed at primary care practices and smaller offices to take fundus images and report them to the Joslin Vision Network for analysis. Expert retina specialists then go through each image and assess what management options are needed for each patient.

Hope for the Future

Both Drs. Silva and Haug are hopeful for the future of screening for diabetic retinopathy. Maybe the technology still needs some more time to mature, but there have been some major advances towards a solution to provide screening to all those in need.

"In the future, it's looking like there's some emerging AIs with broader capabilities, like predicting DR progression and integrating systemic health data, and portable imaging tools," says Dr. Silva. "Technologies like AI and handheld devices will improve screening rates, especially in underserved areas, but a more inclusive, equitable approach to screening through telemedicine, low-cost tools, and AI integration can significantly reduce blindness rates worldwide." ◀

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HOW SUSTAINED-RELEASE IS IMPACTING GLAUCOMA

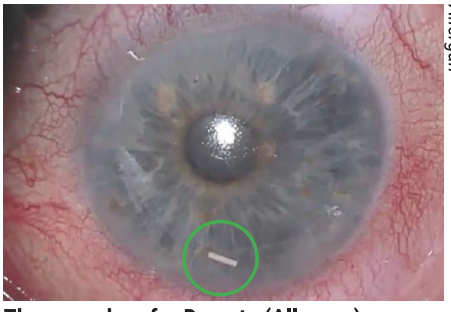
FDA-approved systems are transforming care by offering long-term relief and alleviating the burden of daily drops. Here's a look at the real-world experience.

BY LIZ HUNTER
SENIOR EDITOR

The advent of sustained-release drug delivery in the glaucoma space has been highly anticipated as patient adherence to topical medication instillation remains a challenge.

"Long-term drug delivery and sustained release will continue to be very important in glaucoma treatment moving forward, for a variety of reasons, but primarily because we know non-adherence to glaucoma drops can be as high as 60 percent," says Emily Schehlein, MD, a glaucoma and cataract surgeon who's in private practice in Michigan. "This is due to a variety of factors such as cost, side effects, difficulty in instilling the drops, forgetfulness, complicated regimens and lack of motivation. One study on adherence and persistence with glaucoma therapy shows that up to 90 percent of patients don't consistently refill their drops.[1] Therefore, adherence is a significant challenge, and sustained-release therapy has the potential to solve many of the difficulties we face with topical medications."

Currently, two sustained-release delivery systems are approved by the Food and Drug Administration: Durysta (bimatoprost, Allergan) and iDose (travoprost, Glaukos). The systems differ in their mechanisms of action and implantation method, yet they aim to provide consistent IOP reduction over a prolonged period of time and relieve patients of at least some of the burden involved with drops. To find out how these systems are being used in clinical practice, we spoke with several glaucoma specialists about their real-world experience and what else is in the treatment pipeline.



Allergan

The procedure for Durysta (Allergan), a polymer cylinder containing a prostaglandin analog, can be performed in the clinic. The device is injected into the anterior chamber of the eye where it adheres to the iris surface near the angle.

Where Sustained-Release Fits

When a patient is first diagnosed with glaucoma, there are a variety of first-line treatments available, and for decades eye drops were the mainstay. However, over the course of the disease, one drop can turn into six or more. The impact this regimen has on a patient's daily life has put the idea of interventional glaucoma at the forefront of treatment, including sustained-release.

"We're beginning to pay more attention to the lifestyle impact that our treatments have on our patients," says Karen Chen, MD, a glaucoma specialist with The Permanente Medical Group in San Francisco. "Personally, I think it's hard for me to take a daily vitamin every morning, so for our patients to be doing five to six eye drops every single day is essentially a full-time job. Thankfully, many of them are retired, but the question is whether that's how they want to be spending their time. If we have options where they don't need to be tied to a strict schedule of constant eye drops or other treatments, and they can just focus on living their life, wouldn't that be the best thing possible? Of course, aside from finding a full cure for glaucoma,

This article has no commercial sponsorship.

Dr. Chen has no disclosures. **Dr. Schehlein** consults for Glaukos. **Dr. Schuman** has no disclosures for products mentioned.

or completely ending the disease."

Dr. Schehlein says, as more interventional glaucoma treatments are developed, sustained-release is going to be a cornerstone of that. "These therapies are essential for ensuring patients receive the IOP-lowering and disease modification they need, rather than just relying on what we prescribe, which they may or may not be able to take," she says. "When treating glaucoma, we must focus on disease modification—finding the most consistent way to lower IOP and prevent disease progression—while also ensuring that patients maintain the quality of life they deserve. Interventional glaucoma allows us to intervene earlier in the disease process so we work to preserve the vision that patients want to maintain for the rest of their lives. I approach glaucoma with an interventional mindset, emphasizing to my patients that we have multiple options and will utilize them over their lifetime."

Sustained-release fits into the toolbox that glaucoma specialists can access, which includes surgery and eye drops, and adapts to the patient's needs over time. "Interventional glaucoma and sustained-release therapies are part of this evolving mindset that glaucoma specialists need to have," continues Dr. Schehlein. "We're looking to find the right balance of convenience, safety and efficacy, which may involve adjusting our workflow to accommodate new technologies. For example, when SLT became a first-line therapy, it changed how we treated patients—rather than simply writing a prescription, we now sit down with the patient to explain the procedure in the informed consent process and then perform the laser. Similarly, as new technologies like sustained-release implants emerge, we owe it to our patients to adjust our workflow to accommodate them."

Dr. Chen agrees, adding that patients deserve to be informed about all of the options. "Personally, I try to have this conversation with my patients early in their disease process about different types of interventions," she says. "I talk to them about glaucoma as a journey, and we start with the most conservative treatments before moving on to more aggressive options as the disease progresses. We take it step by step."

In those conversations, she introduces selective laser trabeculoplasty and Durysta, regardless of whether or not they find SLT to be an acceptable first-line treatment or if patients want to hear about first-, second- or third-line treatments. "I can go over the different time points where Durysta can come into play," continues Dr. Chen. "It can be used at various stages, depending on the patient's situation. It plays a role in mild, moderate and severe diseases for different reasons at each stage. For most of my patients, I like to introduce the topic early so they can become familiar with it. We may not do it right away, but it's important for them to be aware of it so when the time comes, they feel comfortable moving forward with it."

Durysta, iDose and Patient Selection

There are several methods for controlled-release delivery of drugs. With both Durysta and iDose, the medication resides either on or inside the eye and is delivered over a long period of time. Although this approach isn't limited to glaucoma; it applies to a variety of eye conditions, says Joel Schuman, MD, FACS, the Kenneth L. Roper Endowed Chair and co-directors of the glaucoma service at Wills Eye Hospital in Philadelphia. "Specifically for glaucoma, drugs are injected into the anterior chamber of the eye. These drugs may be encapsulated in polymers that dissolve over time, slowly releasing the medication, or they may be delivered using a system that not only encases the drug in a polymer but also places that polymer inside a device to ensure it remains in place."

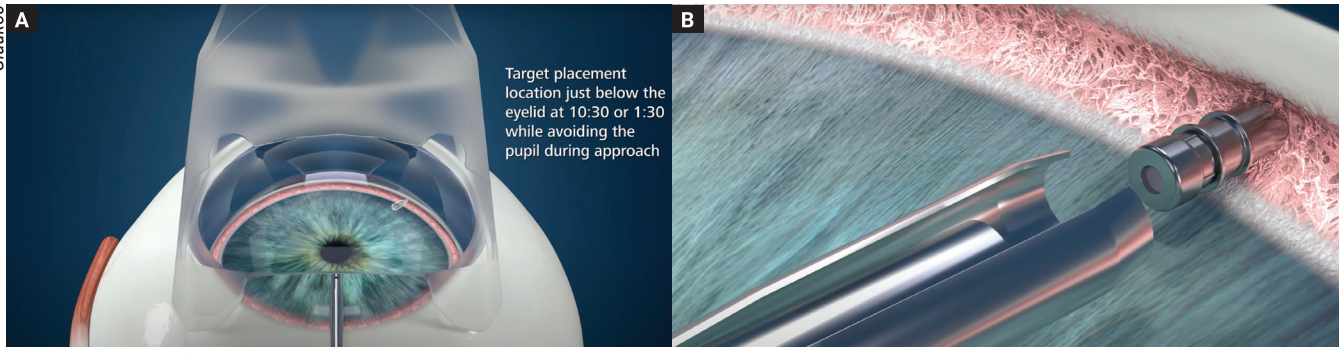
Durysta was the first FDA-approved sustained-release treatment for ocular hypertension and open-angle glaucoma in 2020. As Dr. Schuman explains, this system is a prostaglandin analog contained in a polymer cylinder and can be administered in the clinic. "This device is injected into the anterior chamber of the eye, where it adheres to the iris surface near the angle and remains in place without moving," he says. "Durysta is designed to release its medication for up to six months. The FDA has approved it for single use, meaning it can only be administered once per eye, according to the approval guidelines."

In some rare cases, the Durysta implant has been dislodged from the interior angle. "What people worry about is the potential damage to the corneal endothelium if the Durysta implant moves and is in contact with the corneal endothelium," he continues.

Early trials showed a 10.2-percent incidence of ≥20 percent endothelial cell density loss with a 10-µg implant.[2] "There are ongoing clinical trials to determine the optimal timing between implants to minimize effects on the corneal endothelium," Dr. Schehlein says. "Some issues with corneal endothelial loss in earlier trials were due to stacking implants, and researchers are working on ways to avoid this. My hope is that, in the future, we'll have more guidance on how to safely use multiple implants and understand the best timing for them."

Even so, there are patients who can benefit from a one-time use of Durysta, she continues. "Particularly those with transient IOP spikes due to steroids or those who need a 'drug holiday' and bridge to prepare for incisional surgery," continues Dr. Schehlein.

iDose, which was FDA approved in late 2023, involves encapsulating the drug in a polymer and placing it within a device implanted in the eye. "This device is inserted through a procedure that uses a spike to puncture the trabecular meshwork," says Dr. Schuman. "Once inserted, the device is anchored in the eye and the drug is released slowly over time. Theoretically, the iDose delivery system can be replaced after the drug is depleted."



The iDose system (Glaukos) features a titanium canister with a drug-eluting membrane that's surgically implanted in the trabecular meshwork. Surgeons say the procedure requires a clear view of the trabecular meshwork through a gonioscopy lens for placement (A). The trabecular meshwork is punctured by a spike on the tip of the canister (B) where it should stay parallel to the iris plane.

iDose differs from Durysta in that it uses a titanium canister with a drug-eluting membrane, which is anchored in the trabecular meshwork. "In contrast, Durysta's bimatoprost SR implant floats freely in the anterior chamber, usually settling into the inferior angle," Dr. Schehlein says. "iDose requires a clear view of the trabecular meshwork for placement, needing a gonioscopy lens, which means it's generally placed in the operating room rather than in the office. It offers long-term IOP lowering, with clinical trials showing that 81 percent of patients were free of medications at 12 months. The data extends to three years, and we also know that the travoprost canister can be replaced to provide longer-term IOP control."

A majority of patients with primary open-angle glaucoma and normal eyes—a deep chamber and visible trabecular meshwork—may be good candidates for sustained-release therapies, say surgeons. "However, patients with corneal issues, particularly with their corneal endothelium or prior corneal transplants, narrow angles, or those with inflammation, infections or previous trauma, aren't suitable candidates," says Dr. Schehlein.

When considering patients, it's important to talk to them about their preferences. "For example, if a patient has undergone SLT and doesn't need major surgery at that point, but still requires eye drops, sustained-release options might be appropriate," she continues. "I always discuss the potential side effects of eye drops with patients and emphasize that data shows up to 60 percent of them won't be adherent to their prescribed drops. With sustained release, we can ensure 100-percent adherence because we're directly placing the implant. As long as there's no contraindication, anyone in need of eye drops could be considered a candidate for sustained-release."

On the first exam, Dr. Chen says she's looking for a few key characteristics to guide her treatment plan. "I'm looking for a deep angle with no peripheral anterior synechiae," she says. "I want to ensure the patient has a clear cornea, no prior corneal transplants, no Fuchs' dystrophy or any other condition that could cause unwanted side effects. The goal of interventional glaucoma is to disrupt the patient's lifestyle as little as possible, so I want them to have a seamless and positive experience. I also make sure the anterior chamber is quiet, with no anterior uveitis or any questionable inflammation."

One factor that would steer her toward Durysta is if the patient is already on eye drops and having difficulty with them, such as experiencing significant conjunctivitis, dermatitis or erythema around their eyelids. "But even if they don't have those symptoms, I think the majority of early, mild glaucoma patients are still candidates, and I'll still bring it up with them," Dr. Chen says. "Even using one drop a day compared to not having to think about it at all can be beneficial."

She also looks at the patient's lifestyle and how they're managing their current eye drops. "I have many patients over the age of 90 who have debilitating rheumatoid arthritis, making it difficult for them to squeeze the bottles and get the drops into their eyes," she continues. "This is especially challenging with smaller prostaglandin eye drops, which many patients might not even realize they're not squeezing the drop out of the bottle. Sometimes, I observe them in the clinic while they apply their eye drops, and if they have trouble, I'll lean toward offering Durysta."

When she first started offering Durysta, Dr. Chen says it was beneficial to use as a bridge for surgery. "For patients preparing for a trabeculectomy, tube shunt surgery or a Xen implant where inflammation could affect the outcome, I try to reduce the number of preserved eye drops they're using," she says. "I might put them on oral medications and steroids temporarily, and Durysta has been a great addition in getting them into a quiet, happy state prior to surgery, ensuring better long-term outcomes."

Real-World Experiences

Although the trial data shows the effectiveness of Durysta and iDose, there are still nuances of each system that can only be gleaned from real-world use.

One such nuance is drug duration. Dr. Chen, who has only used Durysta until iDose is available through Kaiser

Permanente, says she's been surprised to see Durysta lasting longer than expected.

"Initially, I was telling patients that it would last around three months, but I've found that for some patients, the effects can last up to a year," she says. "Even when I do need to add more eye drops after that period, I don't typically see their eye pressure return to baseline. This has been really interesting, and it aligns with the research showing that bimatoprost concentration is related to extracellular matrix gene expression, which is dose-dependent. This leads to an increase in matrix metalloproteinases, which could play a role in changing the structure of the trabecular meshwork. This, in turn, may have a long-term effect on the outflow pathway, though we don't fully understand the mechanism. It's possible that Durysta is creating chronic changes that help the trabecular meshwork maintain its function over time."

She says this is one of the reasons she's become more comfortable offering Durysta to patients earlier on in the disease. "If you have a patient with glaucoma and some trabecular meshwork dysregulation, the question is: Would you rather intervene early when the trabecular meshwork might still have the ability to reorganize," she says, "or wait until the disease has progressed to a severe stage where the dysregulation is more pronounced? Early intervention could change the trajectory of the patient's disease and ultimately prevent further damage to their vision."

Dr. Schuman has noticed this, as well. "The interesting thing with the intracameral controlled-release is that it often seems to provide pressure lowering for a longer period of time than it was designed for," he says. "So there's some talk about whether these agents are in some way disease modifying, in addition to just pressure lowering, as long as the drug is available. However, I'd say that the evidence for disease modification is lacking. It's interesting that it works longer in some people, and that may just have to do with the rate of decay of the polymer."

Dr. Chen mentions she has also adapted her method for inserting Durysta. "I initially started by using it at the slit lamp, and I found that it was very well-tolerated by all my patients, even those who were quite nervous," she says. "They didn't feel pain during the insertion. The technique is similar to an anterior chamber tap at the slit lamp. Over time, I've shifted away from doing them under the slit lamp as I've become more comfortable and now I treat it similarly to how I would an intravitreal injection. I lean the patient back at a 45-degree angle, prep the eye with Betadine and insert a speculum. After that, I place the medication without magnification or loops.

"I still check the placement at the slit lamp afterward, but I find that this technique works well in improving clinic visit efficiency," she continues.

Although Dr. Chen is currently practicing in San Francisco, she previously worked in Hawaii, where the life expectancy is much higher than the national average. "I had many patients over the age of 90 who were still very functional with their daily activities, including driving," she recalls. "There's also a large Japanese population in Hawaii, and while Durysta isn't typically used for normal-tension glaucoma, I've found it to be beneficial in these patients.

"Some normal tension glaucoma patients, similar to patients with other types of glaucoma, can experience fluctuations in their eye pressure, and when I monitor their eye pressure at home, I've seen that their pressure can go up significantly during certain times of the day," continues Dr. Chen. "For these patients, Durysta can smooth out these fluctuations and reduce the frequency of pressure spikes. It's been an effective tool in managing these diurnal variations."

Dr. Schehlein says the procedure for implanting iDose is one most glaucoma specialists will feel comfortable doing. "Although I haven't yet had the opportunity to place iDose in my practice, I've been trained and have observed the process," she says. "As glaucoma specialists, we're already familiar with working in the angle, so placing an implant in the trabecular meshwork isn't too far from what we already do. As with any procedure, there are nuances, but if surgeons are comfortable with intraoperative gonioscopy and working in the angle, they will be able to apply their existing skills to this procedure."

Barriers to Patient Adoption

Despite the excitement and promise surrounding these sustained-release therapies, there are a few notable barriers to their widespread adoption.

"For both Durysta and iDose, the ideal candidates depend on various factors, including the patient's adherence to medication and insurance coverage," says Dr. Schuman. "Durysta, for example, is FDA-approved for single-use, which presents a challenge for many clinicians and patients. Since insurers often only cover one use, the cost can be prohibitive for patients without sufficient insurance coverage. In clinical practice, however, some clinicians may choose to use it off-label, as the drug could be beneficial for patients who are non-adherent to daily therapies or those who require a surgical intervention that must be delayed. In such cases, Durysta can be an effective option, as it offers a one-time solution to maintaining drug delivery.

"In contrast, the iDose delivery system allows for replacing the drug payload without removing the part of the device that's attached to the eye," he continues. "This system does require intraocular surgery, making it a more invasive option compared to Durysta. The decision between using iDose or other glaucoma treatments is a clinical one, dependent on the patient's specific needs and circumstances. This may include whether the patient requires a more extensive surgical procedure or a combined approach with minimally invasive glaucoma surgery. Insurance coverage also plays a crucial role in these decisions, as some insurers may

(Continued on p. 57)

Monitoring Blebs

Practical tips for establishing and maintaining a well-functioning bleb after a Xen procedure.

LORRAINE M. PROVENCHER, MD
OMAHA, NEBRASKA

Following a minimally invasive bleb surgery, proper formation of a bleb is crucial for long-term success. However, postoperative challenges such as bleb fibrosis, cyst formation, or bleb leak can arise, compromising the surgery's effectiveness. As such, blebs require early and ongoing monitoring and may necessitate medication adjustments, clinic intervention or even surgical revision. Coupled with variable patient healing responses, a one-size-fits-all approach is often ineffective.

In this article, I'll explore the intricacies of bleb management following MIBS and share practical tips for monitoring blebs and optimizing patient outcomes.

MIBS Options

In the United States, the only option for minimally invasive bleb surgery is the Xen gel stent (AbbVie), which has been available since 2017. FDA approval for Preserflo (Santen) is pending, and the stentless MIMS procedure (SanOculis) is currently in U.S. clinical trials.

In Xen glaucoma surgery, the formation of a healthy bleb is essential for effective intraocular pressure management. The Xen has a 45-µm lumen and creates a controlled outflow pathway from the anterior chamber to the subconjunctival space, resulting in a low lying and often diffuse, uniform bleb. This bleb morphology, along with the controlled outflow of the Xen stent, is generally associated with a low risk of complications such as hypotony and infection, making postoperative management simpler. Early postoperative monitoring is crucial to ensure establishment of a well-functioning, sponge-like bleb. Longer-term postoperative monitoring is then required to address any potential issues, such as chronic bleb fibrosis or stent occlusion.

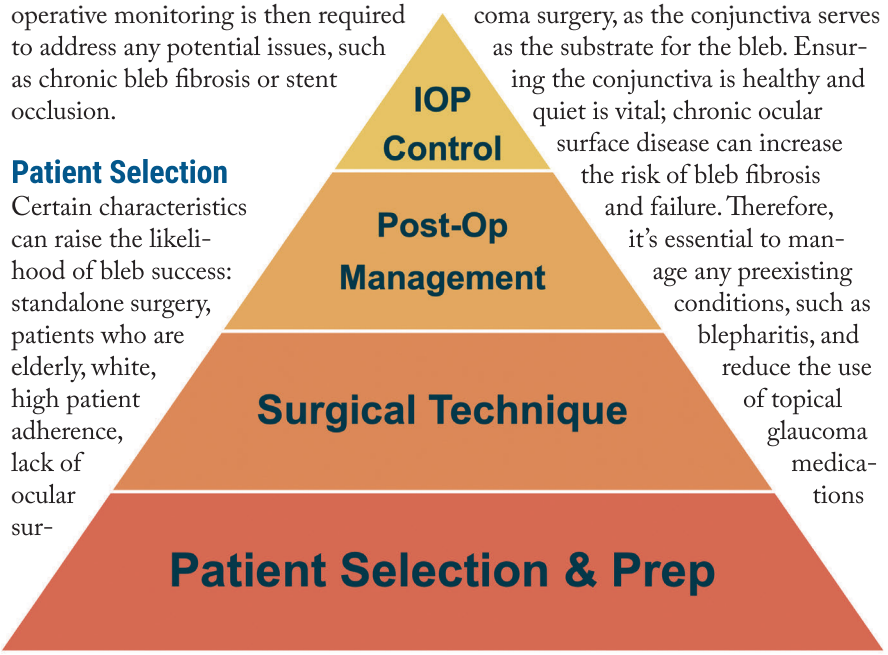
Patient Selection

Certain characteristics can raise the likelihood of bleb success: standalone surgery, patients who are elderly, white, high patient adherence, lack of ocular surface disease and/or virgin conjunctiva. Other characteristics may lower the likelihood of success: young patients, ocular surface disease, Xen combined with cataract surgery, prior conjunctival surgery and/or black patients. None of these are absolute contraindications but should be considered when choosing patients.

I do consider a few situations absolute contraindications. Extremely non-adherent patients are at high risk for failure, as bleb success depends heavily on postoperative medication adherence and close monitoring in clinic. Additionally, those at high risk for bleeding are poor candidates, as significant bleeding sets off an inflammatory cascade that ultimately leads to bleb fibrosis.

Ocular Surface Prep

Preparing the ocular surface is crucial for successful bleb formation in glaucoma surgery, as the conjunctiva serves as the substrate for the bleb. Ensuring the conjunctiva is healthy and quiet is vital; chronic ocular surface disease can increase the risk of bleb fibrosis and failure. Therefore, it's essential to manage any preexisting conditions, such as blepharitis, and reduce the use of topical glaucoma medications



The Bleb Success Pyramid. The formation and maintenance of a healthy bleb require a strong foundation, beginning with careful patient selection and ocular surface preparation.

This article has no commercial sponsorship.

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

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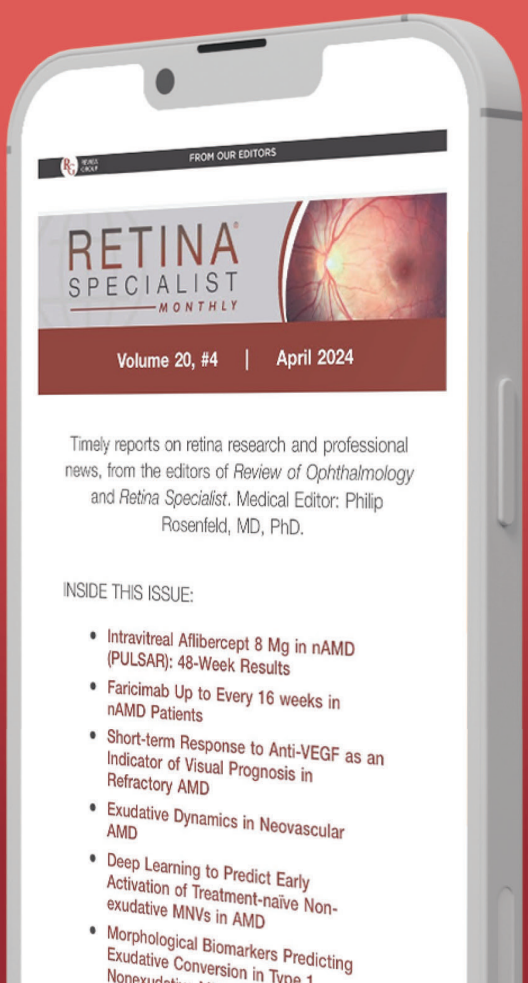

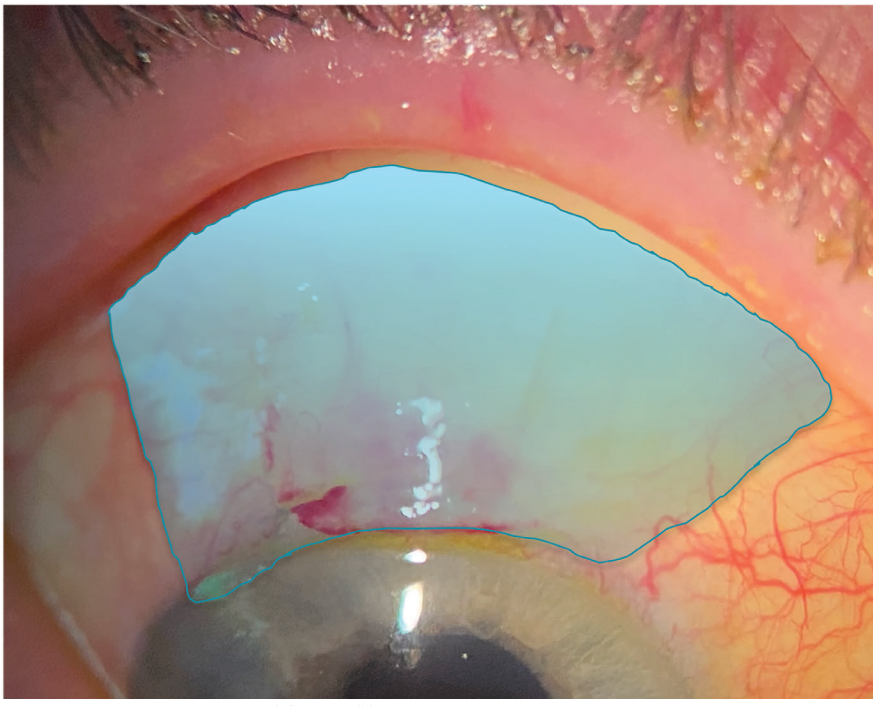

Figure 1. The bleb's extent of flow or "footprint" should ideally span several clock hours superiorly. Three to four clock hours is ideal.

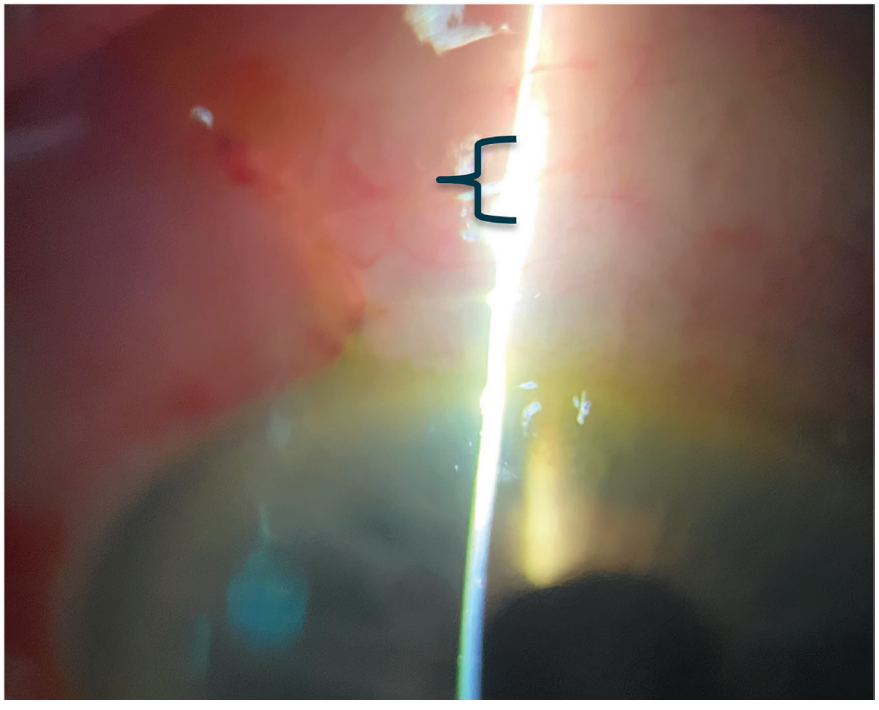

Figure 2. An ideal bleb height is low to moderate. A flat bleb is not desirable, while excessive height can indicate cystic change.

whenever possible, with options like acetazolamide being particularly useful. Additionally, starting preoperative topical steroids a few weeks prior can help quiet the eye. However, if, despite these efforts, the ocular surface condition remains unsatisfactory, I'm prepared to reconsider the surgical plan and may opt for alternative procedures, such as a tube shunt, to ensure the best outcome for the patient.

Intraoperative Tips

There are several techniques for implanting the Xen, but the primary focus should always be ensuring patency on both ends of the stent. Once implanted, verify that the internal portion of the Xen is positioned in the anterior trabecular meshwork and is free from contact with the iris and cornea. The distal part of the stent should also demonstrate patency, either through visible bleb formation/flow or, if the conjunctiva is open, one can observe a small bead of aqueous forming at the tip of the stent. If the intraocular pressure is too low after inserting the stent (due to peritubular flow), you may not see flow through the stent. This design feature helps ensure safety, as the stent is intended to prevent flow at very low pressures. To address this, you might need to raise the pressure slightly using balanced salt solution.

Before concluding the case, I recommend performing primary needling if the conjunctiva is closed. If it's open, you can gently dissect Tenon's capsule and push it back bluntly or even excise a portion of it. With either method, the goal is to create a window in Tenon's around the stent.

At the end of surgery, after I close the conjunctiva, I inject a small amount of cohesive viscoelastic (Healon is my preference) around the stent. This not only helps to displace any blood or Tenon's away from the stent but also opens up the potential space, promoting early flow.

Postoperative Day 1

On postoperative day one, it's essential to see an intraocular pressure of 9 mmHg or lower. This pressure range is a strong prognostic indicator for long-term bleb survival and reduced need for needling.[1] If the pressure exceeds 9 mmHg, it's important to troubleshoot potential issues either in the anterior chamber or within the bleb itself that could be contributing to the elevated IOP. Anterior chamber issues may include the presence

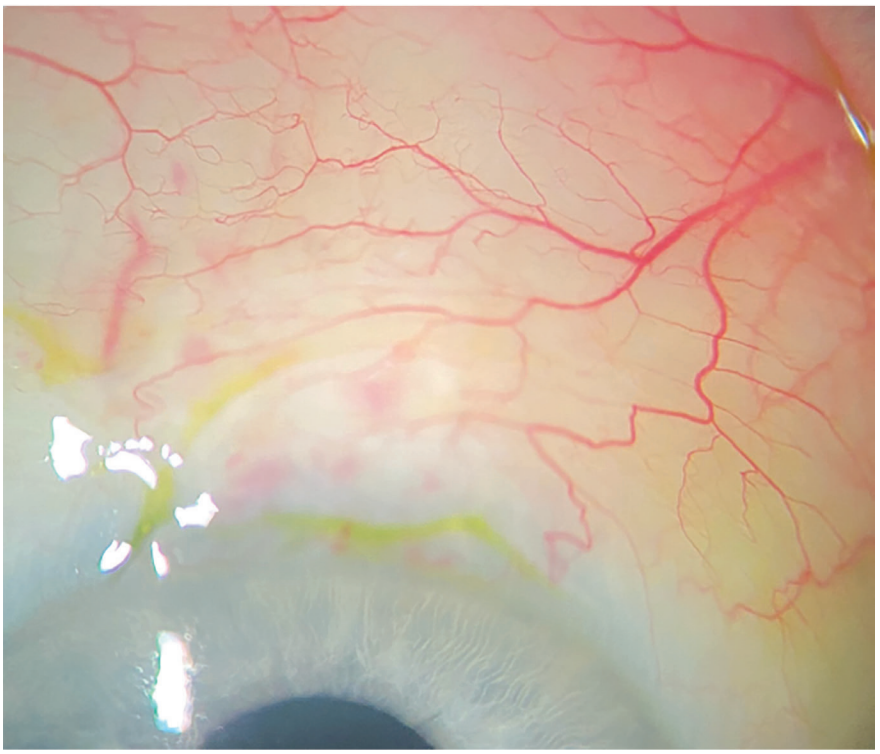

Figure 3. VEGF is involved in the signal cascade that leads to fibroblast migration. Any amount of vascularity greater than that shown in this image should raise concern.

of blood, pigment, viscoelastic, iris or Descemet's membrane. The bleb itself may have increased resistance to flow if blood is present or if the stent is obstructed by Tenon's capsule. One should address these issues promptly, either by medication alteration or Xen manipulation.

Bleb Evolution

It's vital to document bleb characteristics meticulously and consistently from visit to visit to understand how the bleb is evolving and therefore how to respond. While there are published methods for tracking blebs,[2-4] I've developed my own system, which I find easier to remember, to ensure I accurately capture any changes over time. Here are the external and internal features to be aware of:

• ***External features.*** These include extent, height and vascularity of the bleb. When assessing the bleb at the slit lamp, run an oblique thin slit beam across the conjunctiva to visualize the bleb footprint, i.e., extent (*Figure 1*). I typically document this in clock hours (E1 = one clock hour); a bleb extending for three to four clock hours superiorly is ideal.

In terms of height, I also use the slit lamp to gauge how tall the bleb is (*Figure 2*). A low to moderate height is good. A totally flat bleb may be failing (via acute stent occlusion or chronic fibrosis), while excessive height often indicates cyst formation. For my documentation, I categorize height as H0 (flat) to H4 (tall), which is somewhat subjective based on my own assessment.

Similarly, I evaluate vascularity using a scale of 0 to 4, with 0 indicating avascularity and 4 indicating significant vascular injection (*Figure 3*). Mild vascularity is acceptable, but excessive vascularity is a cause for concern, as it may suggest ongoing inflammation and the potential for scar tissue development which could compromise the bleb's filtration over time.

• ***Internal features.*** Using AS-OCT and confocal imaging[5] will help you evaluate tissue density and its capacity to facilitate fluid transmission. A healthy bleb appears low, diffuse, translucent and uniform, resembling thin-walled microcystic spongey tissue. This is sometimes evidenced by microcysts,[6] which can be visualized using fluorescein and cobalt blue light. Conversely, Tenon's cysts present a problem in intraocular pressure control due to their thick, poorly permeable cyst walls, which fail to filter fluid well and are often associated with high pressures.

Postop Modifications

There are various strategies to optimize bleb function during the postoperative phase. My approach includes closely monitoring the bleb over time, adjusting steroid dosages based on vascularity and tissue response, and adding needling and anti-metabolite injections as needed to maintain optimal pressure control. This multifaceted strategy helps encourage bleb function and addresses complications proactively, ensuring better outcomes for patients.

• ***Steroid drops.*** Be generous with steroids. I prescribe high-dose steroid drops (prednisolone q2h or difluprednate q.i.d.) for the first month, gradually tapering the dosage over two to three months as long as the bleb remains healthy. If the bleb demonstrates thickening or increased vascularity or if there's anterior chamber inflammation, you can increase or leave the steroids at a high dose until the bleb appearance improves. Lower the steroids if there's a steroid response, conjunctival staining or wound leak.

Aqueous in the bleb is also pro-inflammatory, so aqueous suppressants such as timolol also play a vital role in reducing inflammation and fibrotic responses associated with flow through the stent. I often use these if I note cystic changes or in cases of persistent wound leak to help manage flow through the incision.

• ***Needles.*** I rely most heavily on 5-FU injections. If I notice increasing vascularity or other unfavorable characteristics like flattening or thickening, I administer 5-FU into the far superior and posterior bleb. This can be done weekly PRN barring corneal

decompensation. Early needling is also crucial—if I identify any targetable anatomic issues, such as stent curling or Tenon's tissue obstructing the Xen, I needle promptly, often with antimetabolite (5-FU if within the first two months, or mitomycin-C if later). Be cautious with antimetabolite if the bleb has low vascularity or is avascular. It's better to needle early—don't wait until the pressure goes up. I prefer to needle with a 27-ga. needle at the slit lamp. The patient is anesthetized beforehand with lidocaine gel, and they tolerate the procedure well. If needling fails, or if the bleb is already completely scarred flat, an open revision in the operating room may be more appropriate.

• ***YAG laser.*** Clinicians may mistakenly attribute pressure spikes to bleb failure. Consider gonioscopy-assisted YAG shockwave laser treatment for cases of acutely elevated IOP, which may be due to visible or occult occlusion of the Xen lumen. YAG can effectively clear blockages, such as those caused by posterior capsule remnants, restoring function to the stent.[7] YAG may also be followed by same-day needling to reform a bleb that has collapsed due to collusion.

Long-term Monitoring

While the Xen procedure has good success rates, late issues may occur months to years postoperatively, such as bleb fibrosis, Xen encapsulation or Xen occlusion. Regular follow-up is critical to detect early signs of bleb dysfunction or failure, which may include changes in bleb morphology, IOP spikes or insufficient pressure reduction despite more recent control.

In summary, formation and maintenance of a well-functioning bleb is pyramidal, with each step building upon the last. By understanding the nuances of postoperative bleb care, surgeons can enhance the success of MIBS procedures and ensure better long-term management of glaucoma. ◀

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ABOUT THE AUTHOR

Dr. Provencher is a cataract surgeon and glaucoma specialist who practices at Vance Thompson Vision. She is a consultant and speaker for AbbVie.

IOL Calculation in Eyes With Corneal Dystrophy

Scientists evaluated the accuracy of several intraocular lens formulas for patients with endothelial dystrophy without edema, treated with cataract surgery alone, at an academic tertiary referral center, as part of a comparative retrospective cohort study.

Scientists assessed the predicted refractive results of ED patients who underwent cataract surgery and compared them to a matched control group. The accuracy of five different IOL formulas Haigis, Holladay 1, Barrett Universal II, SRK/T and Kane was evaluated and compared between the groups. The standard deviations of the prediction error of all formulas were compared.

The study included 221 eyes: 50 (23 percent) eyes of patients with ED and 171 (77 percent) control eyes.

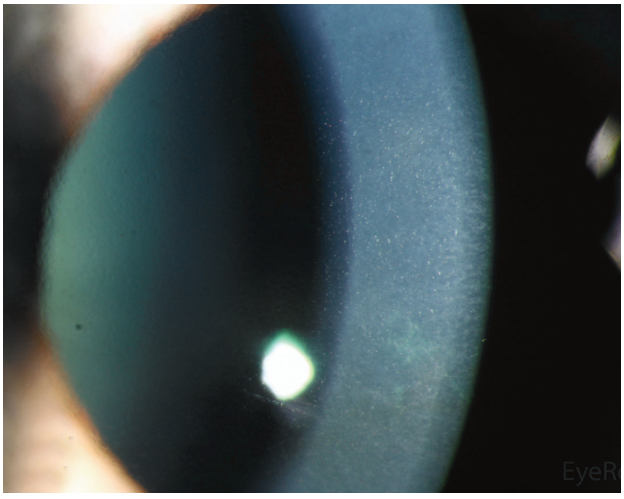
• No significant difference was found between the two groups in clinical and demographical characteristics (p>0.05).

• The postoperative spherical equivalent was -0.37 D in the ED and -0.30 D in the control group (p=0.8).

• Overall, both groups had a comparable standard deviation of the prediction error (PE) and absolute PE (APE) in all formulas (p>0.05).

• In the ED group, APE was 0.34 D for Haigis, 0.32 D for Holladay1, 0.32 D for Barrett Universal II, 0.38 D for SRK/T and 0.32 D for Kane formulas.

• No statistically significant difference between formulas was found.



Researchers say IOL calculations in certain corneal dystrophy patients can still be as accurate as in healthy eyes.

Scientists found the prediction accuracy of intraocular lens power calculation in patients with endothelial dystrophy was comparable between formulas and with healthy controls. They noted the finding suggests that in patients with guttae without edema intraocular lens power calculations are as effective and accurate as in healthy eyes.

J Cataract Refract Surg 2024; Nov 6. [Epub ahead of print].
Shemer A, Fradkin M, Dubinsky-Pertzov B, et al.

PC Phakic ICLs in Keratoconus

Scientists assessed the safety and efficacy of phakic implantable collamer lenses in patients with keratoconus, as part of a systematic review and meta-analysis.

They conducted a pre- and post-intervention single-arm systematic review and meta-analysis in line with guidelines from the Cochrane Collaboration and the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) 2020 Consensus Statement. Scientists searched five electronic databases and the gray literature for any studies evaluating ICLs in the setting of keratoconus. Primary outcomes were the corrected distance visual acuity, uncorrected distance visual acuity and manifest cylinder astigmatism. Secondary outcomes included uncorrected near visual acuity, spherical equivalent, refractive astigmatism, higher-order aberrations, endothelial cell density, intraocular pressure and incidence of adverse events. Scientists summarized analyses by calculating standardized mean differences (SMDs) with associated 95 percent confidence intervals using random-effects meta-analysis.

Sixteen observational studies, totaling 397 eyes, were eligible. Here are some of the findings:

• Postoperatively, no statistically significant improvement was found in CDVA (SMD: -0.97; CI, -1.99 to 0.05; p<0.06).

• A statistically significant improvement was found in:

o UDVA (SMD: -5.41; CI, -0.704 to -3.78; p<0.05);

o manifest cylinder (SMD: 2.27; CI, 1.83 to 2.70; p<0.05);

o spherical equivalent (SMD:-4.66, CI, -5.63 to 3.68; p<0.05); and

o refractive astigmatism (SMD: 2.22; CI, 1.03 to 3.41; p<0.05).

• No significant adverse events occurred.

Scientists determined that use of implantable collamer lenses in

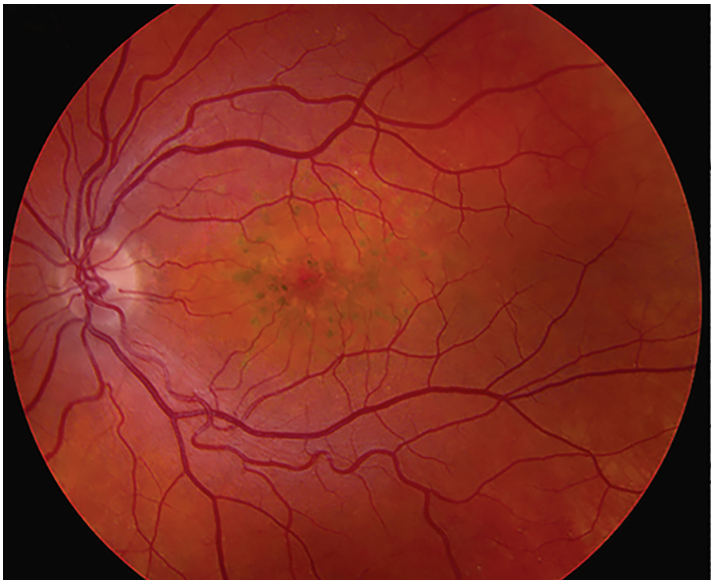
This article has no commercial sponsorship.

patients with keratoconus was safe and effective. They added that the results remain limited by the observational design of included studies as well as the limited follow-up duration.

Am J Ophthalmol. November 27, 2024. [Epub ahead of print].
Alkhabbaz AA, Karam MH, Pollmann AS, et al.

Persistent AEs from Pentosan Polysulfate

The maculopathy associated with chronic pentosane polysulfate use can pose serious risk to vision and, alarmingly, continues to progress even after drug cessation. Authors of a recent study reported on this and found that functional and structural outcomes continue to deteriorate even several years after stopping PPS. The team's paper on the work was recently published in the *American Journal of Ophthalmology*.



The maculopathy associated with pentosan sulfate can continue after drug cessation, researchers say.

A total of 23 eyes of 12 participants (11 of them women) diagnosed with PPS maculopathy were included; median age was 58. Participants were followed for four years. Changes in visual function and structure were the primary outcomes measured. Patient-reported outcomes were assessed with the Visual Function Questionnaire (VFQ-39) and the Low Luminance Questionnaire (LLQ). Structural outcomes included the presence of complete RPE and outer retinal atrophy (cRORA), atrophic lesion size (in mm^2), macular central subfield thickness and subfoveal choroidal thickness.

The findings of this study suggest that PPS maculopathy continues to progress many years after drug cessation, with broad-ranging and disabling impacts on retinal structure and visual function. The majority of eyes exhibited macular cRORA by the final visit, with some developing new onset atrophy years after PPS cessation.

All participants exhibited retinal function and structure decline between the baseline and four-year visits. The VFQ-39 composite scores at four years (52, range: 44 to 60) were lower than previously reported in patients with geographic atrophy (61.7 ±16.3) and diabetic macular edema (65.0 ±19.7). On subscale analysis, the greatest declines occurred in the "dependency" and "role difficulties"'subscales. LLQ composite scores at four years were significantly lower than those reported in patients with intermediate and advanced AMD, with the greatest declines occurring in the "emotional distress" and "extreme lighting condition"'subscales.

All eyes with cRORA at baseline demonstrated lesion growth. The median growth rate of atrophic lesions (0.23 mm/year) was lower than, yet comparable to, others reported in previous studies (0.32 mm/year and 0.26 mm/year). The median growth rate did not significantly differ from the rate seen at the two-year visit (0.23 mm/year). For context, a meta-analysis reported the mean growth rate for geographic atrophy in patients with AMD to be 0.33 mm/year (SD, 0.17 mm/year).

Additionally, five eyes developed new-onset cRORA during the study period, with one participant developing it eight years after stopping PPS at the age of 49. It should be noted that the development of cRORA years after PPS cessation has been found in prior studies as well.

Disease progression following drug cessation is not unsurprising, as similar findings have been observed in other toxic maculopathies, most notably hydroxychloroquine toxicity, the authors noted in their paper on the research. Additionally, many other diseases demonstrate that once present, cRORA lesions tend to grow.

The authors concluded that regardless of mechanism, this finding of new-onset atrophy years after drug cessation is "alarming" and should be investigated further. "For instance, to better guide screening programs and prognostication, it would be helpful to identify early signs of toxicity at which patients do not ultimately progress to atrophy if PPS use is halted.

"Additionally, with these findings of continued atrophy progression," the authors continue, "it may be worthwhile to investigate the potential role of existing therapies that may slow the progression of geographic atrophy in age-related macular degeneration, including Age-Related Eye Disease Study antioxidants, complement inhibitors and photobiomodulation."

Amer J Ophthalmol. December 3, 2024. [Epub ahead of print.]
Hall BP, Shiromani S, Jung EH, et al.

Common Meds' Effects on DME

As the number of adults with type 2 diabetes mellitus grows, so does the

incidence of diabetic macular edema. Recent drug approvals for diabetes have made notable strides against the systemic condition; does this carry forward to protection against its ocular consequences? Specifically, the drug semaglutide, a glucagon-like peptide-1 (GLP-1) for type 2 diabetes, has sparked interest in its broader impact on diabetic eye complications.

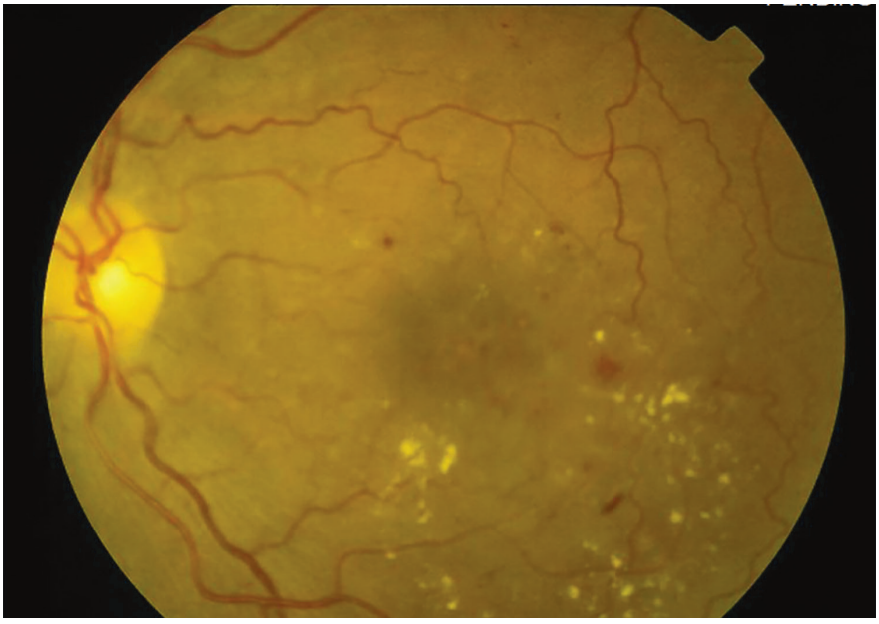
In a recent study conducted in Texas, researchers aimed to assess the impact of systemic medications, including GLP-1 receptor agonists, fenofibrates, thiazolidinediones and calcium channel blockers on the risk of developing DME in patients with type 2 diabetes.

Ultimately, the investigators found that patients on GLP-1 agonists and fenofibrates each experienced a lower risk of diabetic macular edema diagnosis, while those on calcium channel blockers experienced an increased risk. The team's paper on the work was recently published in *Ophthalmology Retina*.

In this retrospective cohort study, data from over 200,000 type 2 diabetes patients who were newly initiated on GLP-1 agonists, fenofibrates, thiazolidinediones or calcium channel blockers were included; the researchers looked at follow-up records for one to two years post-medication initiation to determine the rates of DME development. The study used propensity score matching (controls) to adjust for baseline characteristics and comorbidities.

The study found that patients on GLP-1 drugs and fenofibrates experienced a lower risk of DME diagnosis (hazard ratios of 0.77 and 0.83, respectively), suggesting a protective effect against DME development, while those on calcium channel blockers experienced an increased risk (HR: 1.66).

One member of the GLP-1 receptor agonist class, semaglutide, recently received an FDA label to reduce the risk of cardiovascular death, heart attack and stroke in adults with cardiovascular disease and either obesity or overweight status. A mouse model suggested beneficial effects of semaglutide on endothelial cells and antioxidant pathways, and identified differential regulation of T cells and interferon-γ. The authors suggest this could be the reason for the protective effect of GLP-1 medications on DME development.



Scientists looked at the effect of commonly prescribed medications, such as GLP-1 receptor agonists and calcium channel blockers, on DME development.

Hence, in addition to enhanced blood glucose control, the researchers explained in their paper, GLP-1 receptor agonist therapy may confer additional benefits. They noted that a literature review "shows an absence of basic science investigation on the effect" of such meds on retinal cells and retinal metabolic pathways. "Hopefully, this finding of a potentially protective clinical effect will stimulate a focus on this potentially rewarding avenue of basic science study."

Regarding the adverse effect of calcium channel blockers on diabetic macular edema development, studies have shown increased peripheral extremity edema in patients taking these drugs. "The mechanism of peripheral edema is unknown but may share vascular regulatory pathways with diabetic macular edema," the authors wrote, as the meds "may increase VEGF concentrations in retinal cells."

Since millions of patients with diabetes take calcium channel blockers, "even a small differential risk in DME development could translate to a significant DME disease burden," they wrote.

"Further research is needed to elucidate the mechanisms underlying these associations, determining whether the observed effects are due to the direct pharmacological impact of the drugs or the improved systemic control achieved by their use," the authors concluded. "Additionally, further study of the effect of these systemic medications on retinal cells, retinal metabolism and clinical behavior of DME is warranted. Enhanced systemic management may prove less burdensome and more cost-effective than high frequency intravitreal anti-VEGF therapy while also reducing non-ocular morbidity and mortality." ◀

Ophthalmology Retina. December 3, 2024. [Epub ahead of print.]
Muayad J, Loya A, Hussain ZS, et al.

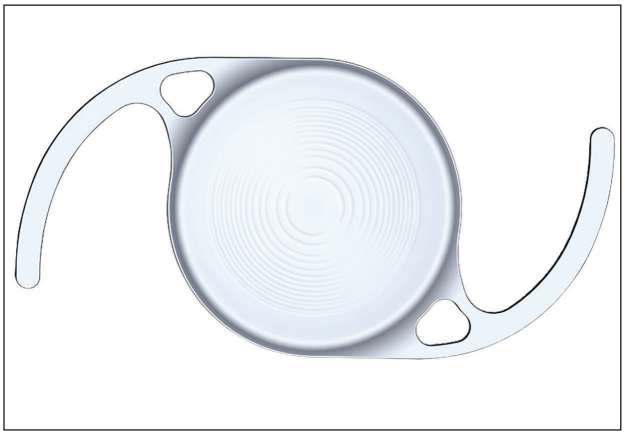
PRODUCT NEWS

New items on the market to improve clinical care and strengthen your practice.

INTRAOCULAR LENSES

Bausch + Lomb Gets FDA Approval for enVista Envy IOLs

Bausch + Lomb announced the FDA approved the enVista Envy intraocular lens, which the company says offers a continuous range of vision with excellent dysphotopsia tolerance.



A multicenter, randomized and controlled clinical trial evaluating 332 subjects demonstrated excellent long-term outcomes with the enVista Envy IOL in the United States, the company reports. The company says Envy also enables surgeons to treat a wider range of astigmatic patients with more accuracy and precision with 0.5-D steps (or less) throughout the cylinder range. For more information, visit bauschsurgical.com/cataract/envista-envy/.

RETINAL TREATMENT

Valeda Gets FDA Nod for Dry AMD Patients

LumiThera announced the FDA authorized marketing of Valeda Light Delivery System for treatment of patients with dry age-related macular degeneration. The therapy is the first FDA-authorized treatment for vision loss in dry AMD patients, the company says. Valeda has been shown to provide an improvement in best-corrected visual acuity over 24 months of >5 letters or equivalent to a line on the eye chart; in the LIGHTSITE III trial, the Valeda treatment met its primary endpoint and was shown to be safe and effective in increasing and maintaining improved visual acuity.

For information on the Valeda Light Delivery System, visit lumithera.com.

PHARMACEUTICALS

Eyenovia Launches New Drug

Eyenovia recently announced the U.S. launch of Clobetasol (clobetasol propionate ophthalmic suspension 0.05%), approved by the FDA for the treatment of inflammation and pain following ocular surgery.

For information, visit eyenovia.com.

IMAGING & DIAGNOSTICS

Spectralis Flexes its Muscles

Heidelberg Engineering announced U.S. Food and Drug Administration clearance for the Spectralis Flex Module, a diagnostic imaging-only platform designed for imaging the posterior segment of pediatric and adult patients in a supine position.

The Flex Module mounts the optical coherence tomography device to a movable stand with an articulated adjustable arm, offering flexibility that extends imaging capabilities to various patient positions and acquisition environments, according to a statement from Heidelberg.

For information on the Spectralis Flex module, visit business-lounge.heidelbergengineering.com/us/en/products/spectralis/flex-module/.

The Heidelberg Engineering Flex Module allows OCT imaging for patients in a supine position.

Konan Medical Launches objectiveFIELD Visual Field Analyzer

Konan Medical announced the commercial launch of its objectiveFIELD (OFA) visual field analyzer. According to Konan, unlike traditional subjective standard automated perimetry, which relies on a patient's manual responses to visual stimuli, the device uses a novel method called Multifocal Pupillographic Objective Perimetry (mfPOP), which is analogous to multifocal ERG/VEP but without electrodes.

For information, visit konan-medical.com. ◀

(Continued from p. 47)
cover the cost of iDose but not its combination with other treatments."

The iDose costs $13,950 for one dose (implant). A 10-mcg Durysta implant reportedly costs $2,102 for one dose. "iDose is a higher cost, and certainly somebody who's uninsured would have a very hard time paying for it, but I think that many insurers are currently covering iDose," says Dr. Schuman. "However, it's obviously something that the clinician and patient would need to investigate prior to the surgery."

Dr. Schehlein says the cost of iDose should be brought into perspective compared to alternatives. "I think some of the discussion about costs of iDose may come from a lack of knowledge about costs of other types of treatments in medicine," she says. "When we break down the cost of iDose year over year, it's comparable to (or less than) the cost of monthly infusions for other inflammatory disorders, such as multiple sclerosis, or other chronic diseases. Glaucoma is a chronic disease, and iDose provides a long-term drug elution for up to 36 months."

Future Therapies in The Pipeline

A variety of options are currently in the pipeline, such as contact lenses, punctal plugs and intracameral implants, some of which haven't progressed significantly or may be stalled.

"Contact lenses may not be ideal because many of our patients are older and may not be comfortable wearing them," suggests Dr. Schehlein. "Similarly, patients who struggle with eye drops may also struggle with contact lenses."

Some options on the horizon include:

• ***Paxtrava (OTX-TIC, Ocular Therapeutix):*** A biodegradable, anterior chamber implant consisting of microparticles with travoprost embedded in the hydrogel, providing four to six months of medication. The company reported Phase II clinical trial results showing a 24 to 30 percent reduction in mean IOP through six months.

• ***L-PPDS (Mati Therapeutics):*** A platform that uses an L-shaped plug with a nonbiodegradable latanoprost core which can be inserted at the slit lamp.[3] A Phase II study found that the L-PPDS reduces IOP by 5.7 mmHg after four weeks, and 60 percent of subjects saw a reduction of at least 5 mmHg.[4] Dr. Schehlein notes that there have been some issues with retention and consistent drug elution with this option.

• ***Bimatoprost Ocular Ring (AbbVie):*** An insert made of a silicone-polymer matrix to be placed directly on the ocular surface under the eyelid. According to one clinical trial, mean IOP reduced by 5.2 mmHg after one month, which was sustained over six months.[5]

• ***SpyGlass (SpyGlass Pharma):*** an intraocular lens implant with drug-eluting pads attached to the haptics, designed to release bimatoprost for up to three years. A single-center study of 23 subjects monitored over three years showed a mean IOP decrease from baseline (post-washout pressure) of 25.1 ± 2.5 mmHg to 13.9 ± 2.3 mmHg.[6] The company is currently enrolling patients in Phase I/II studies.

The glaucoma specialists we spoke with say SpyGlass' design is interesting. "It allows us to treat glaucoma by completing the most commonly performed surgery in the world—cataract surgery," says Dr. Schehlein. "This could put interventional glaucoma and sustained-release on the market for many different types of surgeons and patients. There are still questions about how long the drug delivery would last and how and if it could be replaced. I think it's an innovative platform."

"The initial clinical studies have shown promising results, although it's still in the early stages of development," Dr. Schuman says. "I recently heard an update from Malik Kahook, MD, the founder, and he reported that they're testing a newer model of the system which may allow for swapping out the drug-containing pads for new pads that would be attached to the lens somehow, but that still hasn't been used in clinical trials, as far as I'm aware."

Ultimately, the longer these sustained-release treatments can last, the better. "It would be ideal to have a modality where we can place implants more than once, if needed, or a one-time intervention that could have lasting effects for a longer duration," says Dr. Chen. "Having that discussion with patients can be challenging when you explain that the medication might only last for three to six months. I've changed the way I speak to patients about it because I've observed more long-term benefits. However, some patients might still ask, 'Why don't we just move on to something else if this is only temporary?' All of our glaucoma treatments have an expiration date to some degree, which is why we monitor patients long term."

"Although the new controlled-release approaches are not without their challenges, they offer a great deal of promise," concludes Dr. Schuman. "It's important for clinicians to work closely with patients to determine the best treatment option, as there is no one-size-fits-all solution. Ultimately, the choice of therapy should be made based on the individual patient's needs, preferences and circumstances, including considerations about cost and insurance coverage." ◀

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Back To Basics: Scleral Buckling Pearls

This sometimes overlooked procedure can still be effective.

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Scleral buckling is a surgical technique that has been in use for more than 75 years since it was first introduced by Ernst Custodis in 1949.[1] Since then, the technique has evolved considerably. Significant contributions were made by Charles Schepens, MD, who promoted the encirclage concept, and by Harvey Lincoff, MD, and Ingrid Kreissig, MD, who advocated the minimal approach of segmental buckling. Their refinements reduced complications common with earlier techniques, and their efforts at teaching this technique led to widespread acceptance. With the recent popularity and applicability of vitrectomy for a wide range of vitreoretinal situations, however, scleral buckling for retinal detachment has been relegated to a minor role. This is unfortunate for both patients and surgeons, as scleral buckling can be a minimal surgery with very limited instrumentation needs, negligible expenditure, almost no disturbance of the intraocular milieu and fast recovery.

Scleral buckling requires a tailored approach with careful case selection and meticulous planning. When done correctly, reported anatomical and functional outcomes of scleral buckling surpass those with any other technique of retinal detachment repair. It does, therefore, require a measure of expertise—*the art of scleral buckling*—that is sadly diminishing.

In this piece, we highlight a few important surgical pearls in a question-and-answer format with three surgeons who are passionate about scleral buckling.

Q1. Dr. Karpe (APK): If buckles are so great, why are they used less frequently?

Dr. Shroff (DS): The *sine qua non* of this art is accurate indirect ophthalmoscopic examination, which unfortunately isn't taught in residencies and fellowships with the rigor of years past. One of the factors for this could be the availability of near-peripheral ultra-widefield imaging.

Dr. Kothari (ARK): It all comes down to training during your fellowship. What you assimilate, you simulate. Preoperative time and reimbursement concerns have led to less time being spent on detailed indirect ophthalmoscopy and fundus drawings. Without this preparation, buckles are performed less these days. Trainees are less exposed to this technique, and therefore inadequately trained and understandably hesitant later in their practice.

Dr. Bhatia (GB): Vitrectomy with its smaller and smaller gauges and faster cut rates is perceived as more glamorous and less invasive than a buckle. Also, since vitrectomy can address a wider variety of cases, it's perceived as an answer to all detachments.

Q2. APK: What are your indications for scleral buckling in 2025?

GB: The primary indication of scleral buckling is rhegmatogenous retinal detachment in patients who are young, phakic, high myopes, have an absence of PVD, have breaks anterior to the equator or retinal dialyses.

ARK: Cases of retinal detachment with breaks in one or two quadrants and breaks that have at least the anterior edge depressible during the clinical exam are ideal for application of a scleral buckle. For more extensively spread breaks, I prefer vitrectomy. Visualization of the entire retina is important to avoid failures from missed breaks, and this is an important aspect I look at. If significant vitreous hemorrhage or peripheral capsular opacification precludes a thorough examination despite my best efforts, I'm wary of committing to a buckle alone. Good pseudophakia or even aphakia and previous refractive surgery aren't contraindications for buckling. Very high up on my list for buckles are patients with orthopedic or spine issues, pregnant women, patients destined for traveling early after surgery, very high myopes and the very young.

DS: I totally agree with the above indications. I would like to add that extremely chronic retinal detachments with subretinal gliosis also do well with buckles. The pearl is that PVR under the retina can settle well with a buckle, and we get away without the retinotomies which would have been required if we did a vitrectomy. This is a subset of cases that would require multiple interventions and silicone oil if we go in. But a humble buckle can do the trick in these cases. However, eyes with extensive retinal PVR causing fixed

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

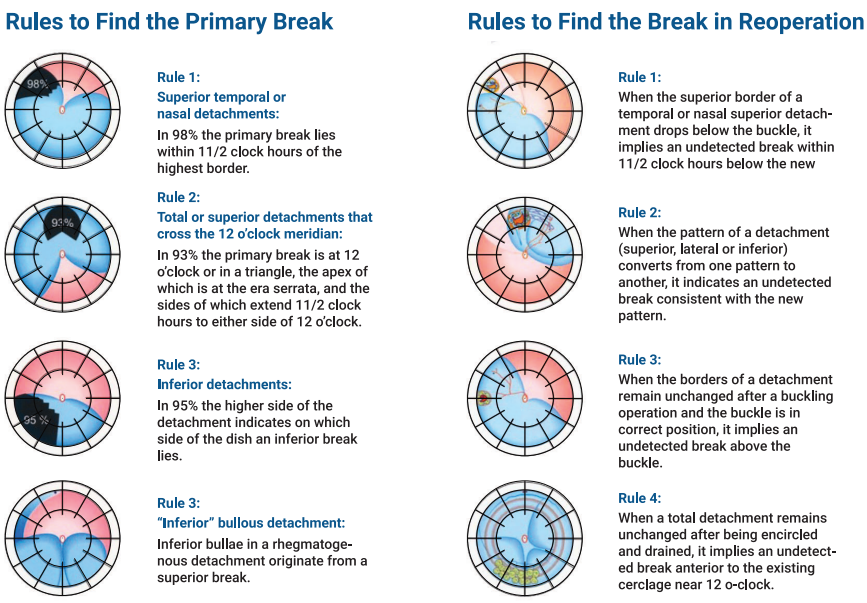

Figure 1. The Eight Rules to find the break.[1]

folds would need vitrectomy. The most important step in scleral buckling is judicious case selection. The good news is that, unlike vitrectomy, scleral buckling is very forgiving and always offers the surgeon and the patient a very favorable second chance in case of failure.

Q3. APK: Any pearls for localizing the break pre- and intraoperatively?

ARK: The success of a scleral buckle is scripted outside the OR. A meticulous fundus drawing with vessel marking up to the breaks goes a long way in ensuring that intraoperative frustration is avoided. To quote Dr. Kreissig, a giant in the field of scleral buckling, "A good diagram helps you to find the break even when the media is obscured, just follow the vessels like Boy/Girl Scouts from one branch to the other till you reach the break."

The next preoperative canon is to look carefully at your detachment diagram. Do the breaks marked explain the configuration of the detachment? The eight rules put forth by Drs. Lincoff and Kreissig *(Figure 1)* not only help us look for the breaks during the examination of a detachment, but they also help us seek out breaks that may have been missed.[2,3] The detachment drawing sheet, with meticulously marked breaks, vessels and other significant findings, is quite literally the sheet anchor for localizing the breaks and ensuring surgical success *(Figure 2)*.

Another technique I occasionally use to look for tiny or difficult to visualize breaks intraoperatively in areas where I strongly suspect them to be is a cryosearch. A gentle cryotherapy application intraoperatively reveals a dark retinal break against the contrasting white cryo mark.

GB: After the initial preparation, the fundus is examined using binocular indirect ophthalmoscopy using a sterile technique. This step is very important as anatomical localization of the break becomes easier under anaesthesia. If there's a single break, it can be marked with a single spot *(Figure 3)*. However, if the break is large, such a large horseshoe tear or a lattice with holes at edges, it's important to mark the anterior, posterior and lateral edges in order to ensure that no part of the break is unsupported or falls on the posterior edge of the buckle.

Q4. APK: Do you prefer retinopexy with cryo or laser?

ARK: Cryotherapy with a light reaction (early ice ball) is usually my go-to retinopexy technique. It works even in the presence of a little subretinal fluid around the break, and can even be performed in situations with a suboptimal view. Depression with the probe helps to reaffirm the retinal examination findings. Having said that, excessive cryopexy should be avoided to prevent pigment release and undue inflammation that can lead to postoperative proliferative vitreoretinopathy.

Laser photocoagulation is usually not possible in cases of detachments with significant fluid and presents intraoperative challenges. It's usually reserved

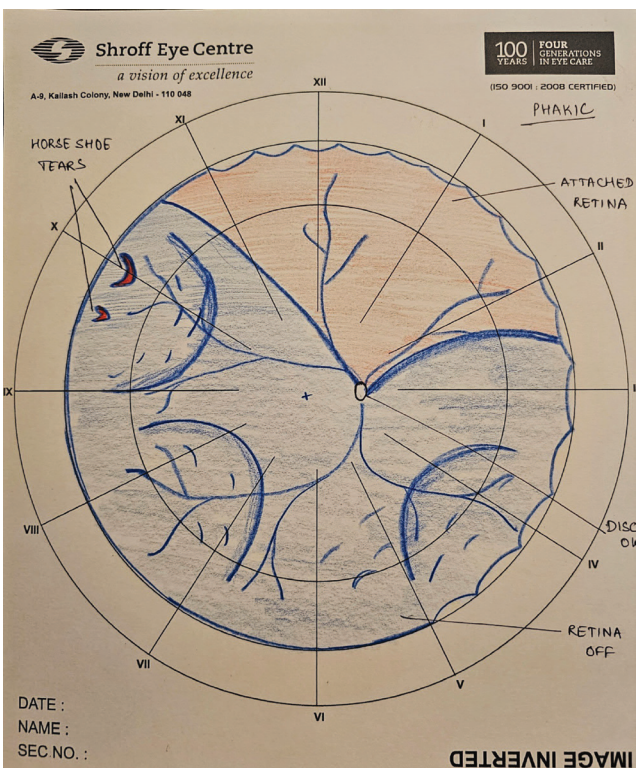

Figure 2. A retinal detachment drawing can ensure surgical success.

for the first postop day to create adhesions around the break. I do use laser for breaks or lattices in attached retina during surgery.

Q5. APK: A million-dollar question—Which is better: Encirclage or segmental buckle?

DS: We generally prefer an encircling solid silicone element. An encirclage can support the vitreous base and possibly compensate for anteroposterior vitreous traction. An overlooked break may still be supported by a 360-degree buckle. Solid silicone may have a lesser risk of buckle infection and exposure. This also ensures that the area of SRF drainage remains well-supported by being made within the bed of the buckle element.

ARK: I prefer to use a segmental buckle in most cases. A segmental sponge necessitates a limited peritomy of 100 to 120 degrees only, along with limited rectus muscle tagging, leading to less postoperative inflammation. A sponge element gives excellent buckle height due to its elastic compressible nature. My preferred orientation for such a sponge is radial, which has several advantages, including the fact that scleral sutures used to place a radial element are relatively easy to master and need less dependence on an assistant. For circumferential placement of a buckle, the posterior suture bites can sometimes be difficult due to access issues, and requires a top-notch assistant.

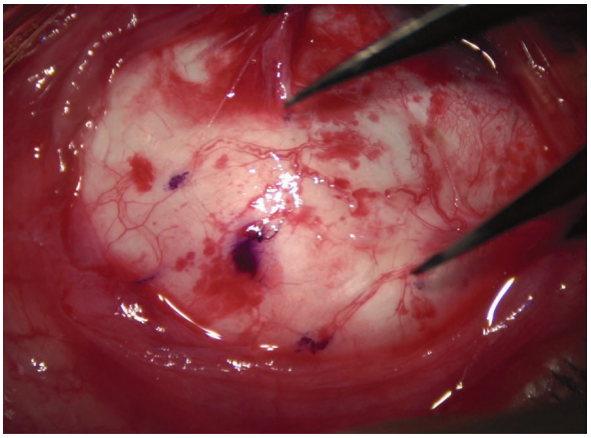

Figure 3. Single mark on the sclera to represent the small horseshoe tear. Adjacent marks to guide needle passage during suture application.

Q6. APK: How do you select the explant?

DS: The dimensions of the buckle depend on the location and size of the break(s). We use solid silicone tires as the main elements. The width of the circumferential buckle should be around 2.5 mm greater than the distance of the posterior-most break from the muscle insertion. The circumferential extent is usually one clock hour beyond the lateral margins of the break on both sides.

For breaks significantly apart in the same or adjacent quadrant, a single continuous element is usually used. One unique modification we've made is we sometimes fashion our own buckles based on the case. For example, by trimming 1 mm off the anterior aspect of a 280 type SB we get a 9-mm buckle (280 cut) with maximum posterior indentation; something that our group has been doing for decades. We use a 240 band for the complete encirclage to ensure the permanence of the buckle.

ARK: For radially placed explants, we choose an element that extends 1 to 1.5 mm beyond the lateral margins of the break on each side. This means that a 3-mm break would need a buckle with 5-mm width. The posterior extent of the buckle is about 2 mm beyond the posterior margin of the break. For breaks far apart, separate radial elements can be used. In cases with high myopia, if the intended suture track falls in the area of unusually thin sclera, then a broader suture may be taken to avoid going through the thin sclera which can tear during tightening. In these cases, a wider element is preferred to counteract the tendency for lateral displacement of a smaller buckle in a broader suture. The height profile of the sponge may be altered by cutting the sponge in half where minimal buckle height is needed.

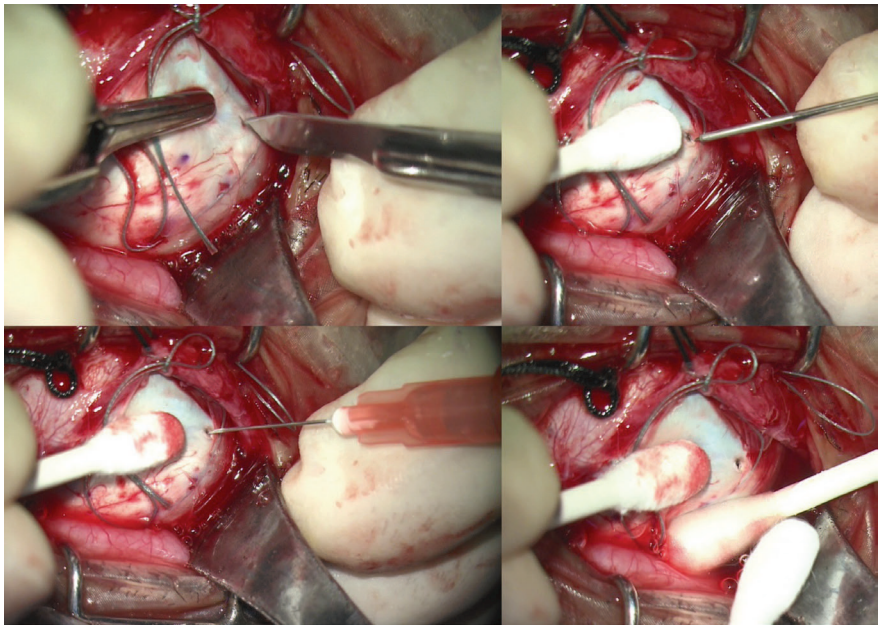

Figure 4. Subretinal fluid drainage: Scleral cutdown followed by light cautery and then needle drainage. Note the light compression using cotton-tipped applicators to maintain intraocular pressure during drainage.

Q7. APK: Any tips for subretinal fluid drainage?

DS: Drainage is a critical but unpredictable step in any buckling procedure. We can take certain steps to make it safer. We perform indirect ophthalmoscopy to determine the area of the high-

est height of the detachment. We then perform a slit shaped cutdown of the sclera and expose the choroid to ensure that no large vessel is present at our drainage site. We lightly cauterize the overlying scleral fibres and choroid and then perforate the choroid with a solid needle, once drainage starts, we tighten our grip on the bridle sutures to avert hypotony. Post drainage, we perform a fundus examination to ensure that drainage complications like subretinal hemorrhage or incarceration haven't occurred. We also always prefer to drain in the bed of the buckle. *(Figure 4)*.

GB: I use a hollow needle, 26 or 27 G, without a scleral cutdown. The site is determined by the location of significant fluid. We choose sites above or below the recti muscles to avoid vortices and larger choroidal vessels. We don't puncture repeatedly nor try to drain aggressively to prevent complications.

ARK: I prefer not to drain at all. Subretinal fluid drainage is the only intraocular step of an otherwise extraocular procedure, and its blind nature predisposes it to serious complications that, though infrequent, can adversely affect results. We prefer to let physiology do the dirty work. Even with chronic retinal detachments, macular attachment can be obtained fairly quickly without drainage. In recent onset detachments, most non-drainage cases have the retina reattached in a day or two. The presence of a little residual inferior fluid away from the break and macula is of no practical concern. Recent studies also indicate that a physiological settling of the retina may lead to less displacement and better functional outcome. If break coverage is adequate, drainage becomes unnecessary.

A corollary is that if subretinal fluid remains for significant time after a non-drainage procedure, this means that a break has been missed and the change in the fluid contours can guide you during any future corrective surgery.

Q8. APK: What are the common complications encountered during scleral buckling?

GB: A common complication while applying sutures for the scleral buckle is scleral perforation. When sclera is thin or the scleral bite is deep or when anatomical considerations make manipulation of the needle difficult while passing the suture, one can have a full-thickness bite. Most often, this leads to unintended subretinal fluid drainage. Occasionally, this can lead to subretinal hemorrhage or retinal injury. At this point it's important not to lose your confidence and crucial to achieve hemostasis. Ways to increase the IOP are by pulling on the muscle sutures and applying pressure on the globe with a cotton-tip applicator. The best way to avoid this complication while passing the suture is to use spatulated needles and to keep the intrascleral needle tip always under direct view *(Figure 5)*.

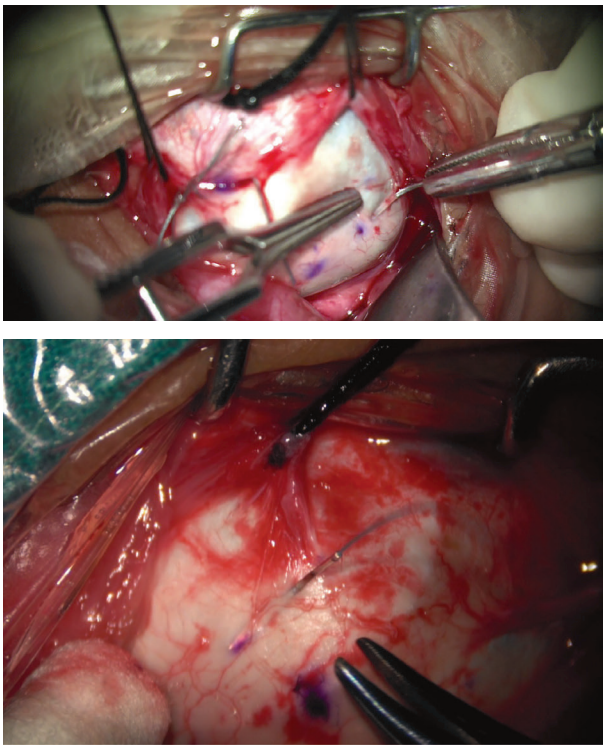

Figure 5. Needle pass through sclera: circumferential pass (top) radial pass (bottom).

DS: The most dreaded complication of scleral buckling is subretinal and choroidal hemorrhage during drainage of subretinal fluid. Avoidance of the impulse to drain till dry and prevention of hypotony can reduce the risk of this mishap. If minor and away from the macula and the break, the hemorrhage can be observed. If significant hemorrhage occurs that threatens the macula or lifts the break, then either a gas bubble or, in severe cases, a vitreous surgery may be needed.

ARK: Non-drainage surgery can avoid potentially serious complications like subretinal hemorrhage and retinal incarceration. Additionally, application of radial buckles needs radially passed sutures that are easier to apply, thereby reducing the risk of suture perforation. The occurrence of strabismus after buckle surgery can be averted by using the lowest profile of the buckle element under the recti muscles or using two separate buckles on either side of the rectus muscle if breaks are present in two quadrants.

Q9. APK: Do buckles fare better than vitrectomy? Why or why not?

DS: Long-term results of buckles are excellent, and our own long-term data is very convincing as to the high success rates of buckles in properly selected cases.

I love this quote that I picked up from Jay Sridhar, MD, of the United States: "You can't lose to the vitreous if you make the vitreous work for you," and this is something that a scleral buckle does! Another important quote by Dr. Kreissig goes, "The retina behaves logically," implying the successful nature of a properly applied buckle.

ARK: The surgical procedure selected for a particular detachment should offer three advantages: First, it should have a very high single operation success rate. Second, it should post a minimum morbidity and quality of life degradation. Third, the procedure should

accomplish retinal reattachment most economically, with minimal follow-up procedures necessary to restore vision.

Multiple studies and meta-analyses bear out very high success rates of scleral buckling that are equal to those obtained with vitrectomy and superior to pneumatic retinopexy.[4] In clinical settings, these rates can be bettered with tailored case selection. Scleral buckling surgery has low complication rates and the lowest postoperative PVR occurrence rates among all techniques of retinal detachment repair.[5] The need for positioning and limitation of activity and travel with other methods of detachment repair are avoided with buckling. The frequent necessity of tamponade removal and cataract extraction after vitrectomy poses an additional economic burden and morbidity on the patient. These reasons make buckling an invaluable and irreplaceable technique to have in one's armamentarium.

Q10. APK: How can the learning curve for buckling be made less steep for trainees and young surgeons?

GB: Proper focus on preoperative examination and indirect ophthalmoscopy skills is important to ease difficulties faced initially in buckling surgery. Observation of surgeons who routinely perform this surgery is essential to improve familiarity with buckling.

ARK: Preoperative fundus diagrams *(Figure 2)* should be compulsory for trainees, even for cases destined to undergo vitreous surgery. The time spent on this activity would translate into better clinical assessment, decision making and intraoperative ease of localization. Familiarity with different materials used in buckling and animal wet labs to practice scleral suturing can remove the hesitation in younger surgeons. Above all, thorough knowledge of the rules to find breaks will enhance the uptake of this artful technique for retinal detachment. ◀

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(Continued from p. 24)

Ending the Case and Patient Recovery

Surgeons say there are a couple of additional steps for closing cases involving iris prolapse.

For one, if an iris hook has been used, it shouldn't be removed until a surgeon is done using the main wound, says Dr. Schoen. "I'll also inject a miotic agent, like acetylcholine (Miochol-E) or carbochol (Miostat), to bring the pupil down," she says. "Depending on the case and the patient, I might consider placing a 10-0 nylon suture in the main wound to prevent the risk of iris prolapse postoperatively, which can occur with eye rubbing or Valsalva maneuvers. It's crucial to avoid being too aggressive when hydrating the wounds and pressurizing the eye, as this could lead to further iris prolapse."

And although routine, uncomplicated cataract surgery would have surgeons removing all viscoelastic before closing the eye, a different approach may be warranted here. "In cases of iris prolapse, I may leave a small dollop of viscoelastic just beneath the main wound to help keep the iris in place," Dr. DelMonte says. "This is because, when I hydrate the wound at the end of the procedure, there's a risk that fluid could get inside the eye, creating positive pressure that could cause the iris to prolapse again. Leaving a little viscoelastic under the wound can help prevent this."

After the surgery, patients with iris prolapse tend to experience more inflammation, especially in the first couple of days. To manage this, Dr. DelMonte often uses more aggressive steroids and NSAIDs, with a longer course than he'd typically prescribe for a standard cataract surgery. "These patients are also at a slightly higher risk for cystoid macular edema due to the increased inflammation, which can lead to long-term complications," he says. "I usually prescribe a steroid twice a day after surgery, but for these patients, I may increase the dosage to three or four times a day and extend the course from two weeks to three or four weeks."

If there was significant trauma to the iris resulting in transillumination defects or loss of iris tissue, patients might experience glare or sensitivity to light, Dr. Schoen says. "If symptoms of glare or photophobia persist despite resolution of inflammation in the eye, then options like colored contact lenses or surgery could be discussed to address large iris defects," she says.

In conclusion, surgeons say the most crucial lesson is to resist the urge to push the iris back when iris prolapse occurs during surgery. "This reflex can cause significant trauma to the iris and lead to lasting defects," says Dr. Schoen. "When iris prolapse occurs, pause, take a breath, decompress the eye and allow the pressure to balance out. Sometimes, that alone will allow the iris to fall back in. If not, use gentle techniques like tapping, BSS or sweeping. Managing the iris gently is key to ensuring good outcomes." ◀

DISCLOSURES

Dr. DelMonte and **Dr. Schoen** have no relevant disclosures.

EDITED BY ERIK MASSENZIO, MD

WILLS EYE RESIDENT CASE REPORT

A patient presents with atypical, bilateral choroidal nevi.

SAMANTHA S. MASSENZIO, MD, TATYANA MILMAN, MD, AND JACQUELINE R. CARRASCO, MD
PHILADELPHIA

Presentation

A 37-year-old African-American female was referred to the Ocular Oncology Service at Wills Eye Hospital for atypical, bilateral choroidal nevi.

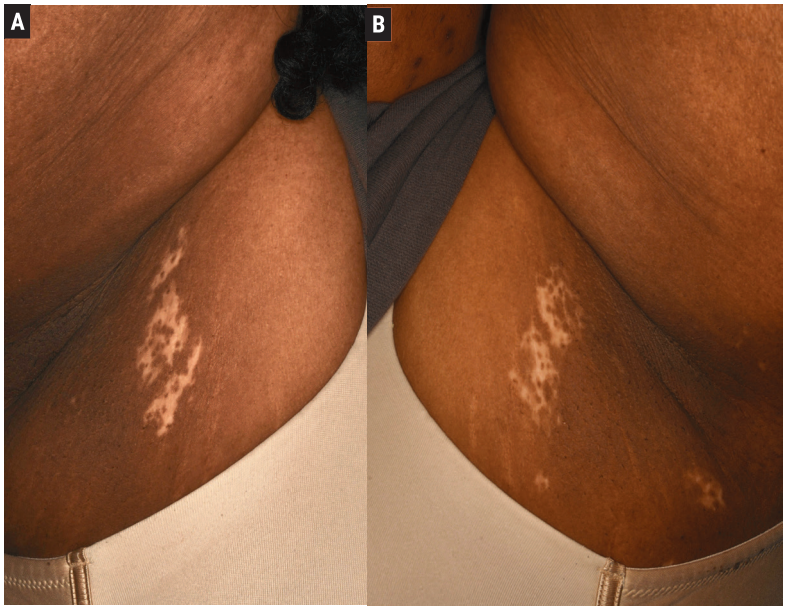

Figure 1. Photographs showing areas of depigmentation, or vitiligo, of the right (A) and left (B) axilla.

History

Past ocular history was unremarkable other than refractive error with contact lens and spectacle use. Past medical history was significant for hypertension, asthma, chronic migraine headache and dermatology-diagnosed vitiligo of the axillae and on the chest skin midline. She reported a birth history of having gray hairs on her arms and a tuft of gray hair present near the nape that resolved over time. Her surgical history involved cesarian section and hysterectomy. She denied a personal history of hearing loss, Hirschsprung disease, other congenital abnormalities and cancer. There were no known drug allergies. She noted drinking one alcohol beverage per day and denied a history of smoking and recreational drug use. Family history revealed malignant histiocytoma (mother), lung cancer (maternal aunt), uterine cancer (maternal aunt), Hirschsprung's disease (cousin) and a vague history of a white forelock in several relatives. Current medications included Valsartan 320 mg daily for hypertension.

Examination

On examination, uncorrected visual acuity was 20/80 in each eye and corrected visual acuity was 20/20 in each eye. The pupils were round and reactive to light with no relative afferent pupillary defect. Intraocular pressure was 13 mmHg in the right eye and 12 mmHg in the left. On skin examination, the Fitzpatrick skin type was six (darkly pigmented) and there were areas of skin depigmentation in both axillae *(Figure 1)* and on the midline chest wall.

Slit lamp examination of each eye was normal, exhibiting brown irises without depigmentation or heterochromia *(Figure 2)*. There was no identified cutaneous or scleral melanocytosis. Dilated fundus examination revealed a cup-to-disc ratio of 0.2 in each eye. The retina appeared normal and the choroid demonstrated patches of hypopigmentation posteriorly and hyperpigmentation more peripherally with no evidence of solid tumor *(Figure 3)*. Optical coherence tomography, ultrasound biomicroscopy, and A-scan and B-scan ultrasonography were unremarkable. Fundus autofluorescence revealed mild hyperautofluorescence in the hypopigmentation areas and mild hypoautofluorescence in the hyperpigmentation areas.

What's your diagnosis? What management would you pursue? The case continues on the next page.

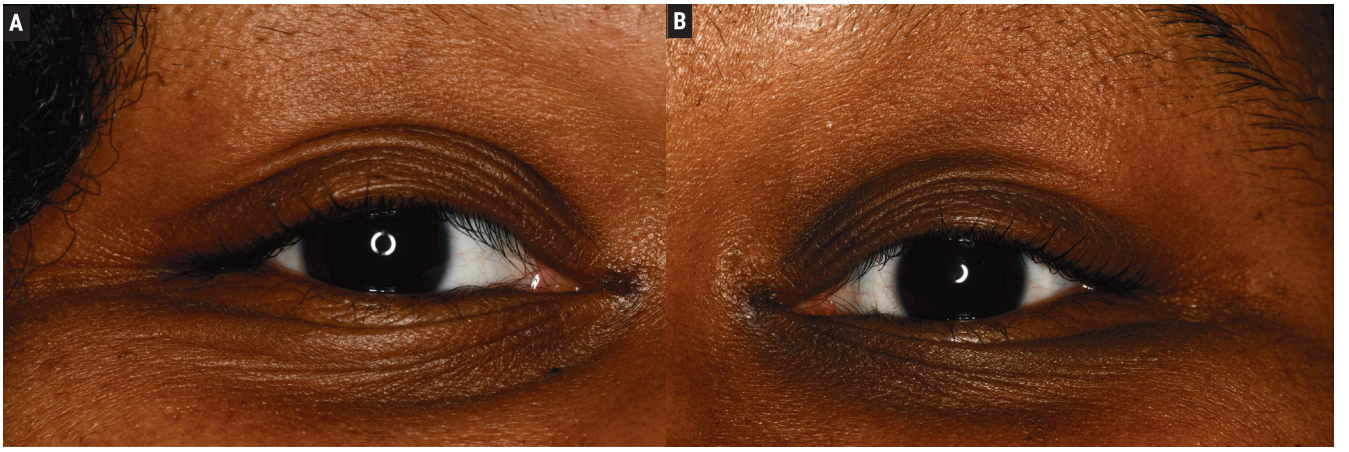

Figure 2. Slit lamp photographs showing normal, brown-colored right (A) and left (B) iris without depigmentation or heterochromia.

Diagnosis

This patient was referred due to concerns for atypical, bilateral choroidal nevi. On first inspection, the fundus appeared to have interspersed areas of choroidal melanocytosis with normal choroid in each eye. However, considering the clinical context, including family and personal history, Fitzpatrick skin type, cutaneous vitiligo of the axillae and chest wall, and the tuft of white hair noted at birth, it was determined that the choroidal hyperpigmented regions were normal areas and the hypopigmented regions were abnormal, suggesting congenital choroidal depigmentation or vitiligo. This constellation of findings was consistent with Waardenburg syndrome. The patient was advised to obtain a formal hearing test and additional genetic testing for confirmation.

Discussion

Waardenburg syndrome is a rare, primarily autosomal dominant, genetically heterogeneous disorder characterized by varying degrees of depigmentation, or vitiligo, of the newborn hair, skin and uvea, along with sensorineural hearing loss and facial abnormalities including telecanthus, tubular nasal bridge and small nasal alae.[1] The incidence of Waardenburg syndrome is estimated to be 1 in 42,000.[2]

There are four subtypes of WS, and each is differentiated by the presence/absence of syndromic features, in addition to genetic composition. Those with WS1 and WS2 are autosomal dominant, WS3 is primarily autosomal dominant but occasionally sporadic, and WS4 is autosomal recessive.[3] WS1 and WS2 are diagnosed using major and minor criteria, where one must have two major, or one major plus two minor criteria to meet the diagnosis.[3] The major criteria include sensorineural hearing loss, pigmentary changes of the iris (heterochromia, partial heterochromia, hypoplastic blue eyes), hair hypopigmentation and dystopia canthorum. The minor criteria include congenital leukoderma (areas of hypopigmented skin), synophyrys, broad and high nasal root, hypoplasia of the alae nasi and premature graying of hair.[3]

Those with WS1 involve mutations in PAX3, often presenting with pigmentary changes, dystopia canthorum,

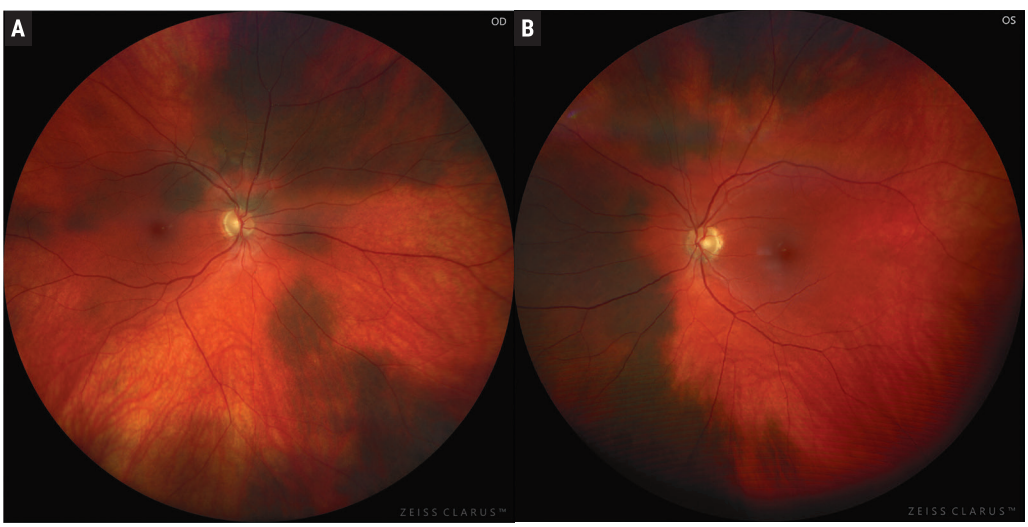

Figure 3. Wide-angle fundus images of the right eye (A) and the left eye (B) demonstrating a normal, darkly pigmented choroid with interspersed broad areas of choroidal hypopigmentation.

broad nasal bridge and synophrys.

Those with WS2, caused by mutations in *MITF* or *SOX10*, present with similar pigmentary changes but typically lacks dysmorphic features like dystopia canthorum, which is present in the majority (95 to 99 percent) of WS1 patients. Hearing loss is highly prevalent in WS2, occurring in 92 percent of cases compared to 52 percent in WS1.[4-6]

WS3, also known as Klein-Waardenburg syndrome, involves mutations in the *PAX3* gene and shares many features with WS1, though it's distinguished by musculoskeletal abnormalities, including limb contractures or synostosis.[7]

WS4, or Waardenburg-Shah syndrome, is associated with mutations in *EDNRB*, *EDN3* or *SOX10* genes. Clinically, WS4 is similar to WS2, but can be associated with Hirschsprung disease.[7] In our case, the patient had a cousin with Hirschsprung disease, leading to suspicion for WS4.

Though the initial description and categorization of Waardenburg syndrome didn't include a criterion for choroidal depigmentation, this finding has since been described in a few case series, citing the presence of choroidal depigmentation in 66 to 71 percent of Waardenburg patients.[8-9] Our patient presented with depigmentation of the skin and choroid, a history of a tuft of gray hair at birth, gray hairs on her extremities and a family history of Hirschsprung disease, likely correlating with WS4. These findings underscore the importance of thorough clinical and genetic evaluation in patients with atypical pigmentary changes, highlighting the significance of choroidal depigmentation alongside iris depigmentation in identifying and differentiating Waardenburg syndrome subtypes. ◀

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ADVERTISER INDEX

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

INDICATIONS AND USAGE

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

CONTRAINDICATIONS

Ocular or Periocular Infections
SYFOVRE is contraindicated in patients with ocular or periocular infections.
Active Intraocular Inflammation
SYFOVRE is contraindicated in patients with active intraocular inflammation.

WARNINGS AND PRECAUTIONS

Endophthalmitis and Retinal Detachments
Intravitreal injections, including those with SYFOVRE, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering SYFOVRE in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.
Retinal Vasculitis and/or Retinal Vascular Occlusion
Retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation, have been reported with the use of SYFOVRE. Cases may occur with the first dose of SYFOVRE and may result in severe vision loss. Discontinue treatment with SYFOVRE in patients who develop these events. Patients should be instructed to report any change in vision without delay.
Neovascular AMD
In clinical trials, use of SYFOVRE was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (12% when administered monthly, 7% when administered every other month and 3% in the control group) by Month 24. Patients receiving SYFOVRE should be monitored for signs of neovascular AMD. In case anti-Vascular Endothelial Growth Factor (anti-VEGF) is required, it should be given separately from SYFOVRE administration.
Intraocular Inflammation
In clinical trials, use of SYFOVRE was associated with episodes of intraocular inflammation including: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, and anterior chamber flare. After inflammation resolves patients may resume treatment with SYFOVRE.
Increased Intraocular Pressure
Acute increase in IOP may occur within minutes of any intravitreal injection, including with SYFOVRE. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

ADVERSE REACTIONS

Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.
A total of 839 patients with GA in two Phase 3 studies (OAKS and DERBY) were treated with intravitreal SYFOVRE, 15 mg (0.1 mL of 150 mg/mL solution). Four hundred nineteen (419) of these patients were treated in the affected eye monthly and 420 were treated in the affected eye every other month. Four hundred seventeen (417) patients were assigned to sham.
The most common adverse reactions (≥5%) reported in patients receiving SYFOVRE were ocular discomfort, neovascular age-related macular degeneration, vitreous floaters, and conjunctival hemorrhage.

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

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

PM: SYFOVRE monthly; PEOM: SYFOVRE every other month
*The following reported terms were combined:
Ocular discomfort included: eye pain, eye irritation, foreign body sensation in eyes, ocular discomfort, abnormal sensation in eye
Neovascular age-related macular degeneration included: exudative age-related macular degeneration, choroidal neovascularization
Punctate keratitis included: punctate keratitis, keratitis
Intraocular inflammation included: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, anterior chamber flare

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

Postmarketing Experience
The following adverse reactions have been identified during postapproval use of SYFOVRE. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Eye disorders: retinal vasculitis with or without retinal vascular occlusion.

USE IN SPECIFIC POPULATIONS

Pregnancy
Risk Summary
There are no adequate and well-controlled studies of SYFOVRE administration in pregnant women to inform a drug-associated risk. The use of SYFOVRE may be considered following an assessment of the risks and benefits.
Systemic exposure of SYFOVRE following ocular administration is low. Subcutaneous administration of pegcetacoplan to pregnant monkeys from the mid gestation period through birth resulted in increased incidences of abortions and stillbirths at systemic exposures 1040-fold higher than that observed in humans at the maximum recommended human ophthalmic dose (MRHOD) of SYFOVRE (based on the area under the curve (AUC) systemically measured levels). No adverse maternal or fetal effects were observed in monkeys at systemic exposures approximately 470-fold higher than that observed in humans at the MRHOD.
In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.
Lactation
Risk Summary
It is not known whether intravitreal administered pegcetacoplan is secreted in human milk or whether there is potential for absorption and harm to the infant. Animal data suggest that the risk of clinically relevant exposure to the infant following maternal intravitreal treatment is minimal. Because many drugs are excreted in human milk, and because the potential for absorption and harm to infant growth and development exists, caution should be exercised when SYFOVRE is administered to a nursing woman.
Females and Males of Reproductive Potential
Contraception
Females: It is recommended that women of childbearing potential use effective contraception methods to prevent pregnancy during treatment with intravitreal pegcetacoplan. Advise female patients of reproductive potential to use effective contraception during treatment with SYFOVRE and for 40 days after the last dose. For women planning to become pregnant, the use of SYFOVRE may be considered following an assessment of the risks and benefits.
Pediatric Use
The safety and effectiveness of SYFOVRE in pediatric patients have not been established.
Geriatric Use
In clinical studies, approximately 97% (813/839) of patients randomized to treatment with SYFOVRE were ≥ 65 years of age and approximately 72% (607/839) were ≥ 75 years of age. No significant differences in efficacy or safety were seen with increasing age in these studies. No dosage regimen adjustment is recommended based on age.

PATIENT COUNSELING INFORMATION

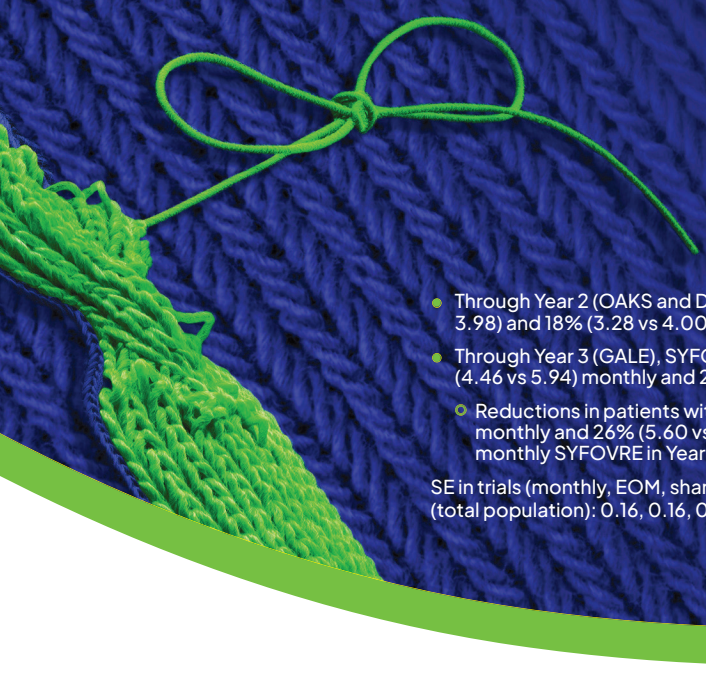
Advise patients that following SYFOVRE administration, patients are at risk of developing endophthalmitis, retinal detachments, retinal vasculitis with or without retinal vascular occlusion and neovascular AMD. If the eye becomes red, sensitive to light, painful, or if a patient develops any change in vision such as flashing lights, blurred vision or metamorphopsia, instruct the patient to seek immediate care from an ophthalmologist. Patients may experience temporary visual disturbances associated either with the intravitreal injection with SYFOVRE or the eye examination. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

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

SYF-PI-30NOV2023-2.0

12/23 US-PEGGA-2200163 v4.0

SYFOVRE®
(pegcetacoplan injection)
15 mg / 0.1 mL



Save more retinal tissue

Through Year 2, in OAKS and DERBY, SYFOVRE slowed GA lesion growth vs sham pooled.[1]

SYFOVRE slowed GA lesion growth with **increasing effects over time** up to **42%** in Year 3 (GALE) vs projected sham in patients without subfoveal lesions[1,2]

- Through Year 2 (OAKS and DERBY), SYFOVRE slowed GA lesion growth (mm^2) vs sham pooled by 22% (3.11 vs 3.98) and 18% (3.28 vs 4.00) monthly, and by 18% (3.26 vs 3.98) and 17% (3.31 vs 4.00) EOM[1,2]
- Through Year 3 (GALE), SYFOVRE slowed GA lesion growth (mm^2) vs sham pooled/projected sham by 25% (4.46 vs 5.94) monthly and 20% (4.74 vs 5.94) EOM. The greatest differences were observed in Year 3[2]
  - Reductions in patients without subfoveal lesions at baseline through Year 3: 32% (5.10 vs 7.54 (n=95)) monthly and 26% (5.60 vs 7.54 (n=104)) EOM. In this subset of patients, there was a 42% reduction with monthly SYFOVRE in Year 3 vs projected sham

SE in trials (monthly, EOM, sham pooled/projected sham): OAKS: 0.15, 0.13, 0.14; DERBY: 0.13, 0.13, 0.17; GALE (total population): 0.16, 0.16, 0.19; GALE (without subfoveal): 0.26, 0.31, 0.41[1,2]

EOM=every other month; GA=geographic atrophy; SE=standard error.

GALE Trial Limitations: GALE is an ongoing open-label, multi-center extension study, subject to patient dropouts over time. The analysis for the first year of GALE utilized a projected sham and may not reflect rate of change of all patients with GA. Projected sham assumes linear growth rate from Months 24-36 (GALE Year 1) based on the average of the mean rate of change of each 6-month period of sham treatment in OAKS and DERBY and natural history studies, which have shown there is a high correlation between prior 2-year growth rates of GA lesions and subsequent 2-year growth rates. This is a prespecified analysis but there is no statistical testing hierarchy, therefore the results on the individual components need cautious interpretation. Open-label studies can allow for selection bias.[2,3]

Discover more at SyfovreECP.com

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

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- **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

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

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

OAKS and DERBY Trial Design: SYFOVRE safety and efficacy were assessed in OAKS (N=637) and DERBY (N=621), multi-center, 2-year, 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 every other month, sham monthly, or sham every other month, for 2 years. Change from baseline in the total area of GA lesions in the study eye (mm^2) was measured by fundus autofluorescence (FAF).[1,2]

GALE Trial Design: GALE (N=790) is a multi-center, 3-year, Phase 3, open-label extension study to evaluate the long-term safety and efficacy of pegcetacoplan in subjects with geographic atrophy secondary to age-related macular degeneration. Patients enrolled in GALE include those who completed OAKS or DERBY after 2 years and 10 patients from Phase 1b Study 103. Patients with GA (atrophic nonexudative age related macular degeneration) with or without subfoveal involvement, secondary to AMD were assigned to receive 15 mg/0.1 mL intravitreal SYFOVRE monthly or SYFOVRE EOM for 3 years. The first visit was required to be within 60 days of the final visit in OAKS and DERBY.[2]

References: 1. SYFOVRE (pegcetacoplan injection) [package insert]. Waltham, MA: Apellis Pharmaceuticals, Inc.; 2023. **2.** Data on file. Apellis Pharmaceuticals, Inc. **3.** Sunness JS, Margalit E, Srikumaran D, et al. The long-term natural history of geographic atrophy from age-related macular degeneration: enlargement of atrophy and implications for interventional clinical trials. *Ophthalmology*. 2007;114(2):271–277. doi:10.1016/j.ophtha.2006.09.016.

Apellis

iStent infinite®

THE POWER OF 3

The Beginning of the
Interventional Glaucoma Revolution

infinite possibilities

Brought to you by the founder of MIGS, iStent infinite® is the first-ever micro-invasive, standalone implantable alternative. Built on the #1 MIGS platform worldwide, it is designed to provide powerful technology that delivers foundational, 24/7, long-term IOP control in glaucoma patients who have failed prior medical and surgical intervention.[1]

REFERENCE

1. Glaukos Data on File.

iStent infinite® IMPORTANT SAFETY INFORMATION

INDICATION FOR USE. The iStent infinite® Trabecular Micro-Bypass System Model iS3 is an implantable device intended to reduce the intraocular pressure (IOP) of the eye. It is indicated for use in adult patients with primary open-angle glaucoma in whom previous medical and surgical treatment has failed. **CONTRAINDICATIONS.** The iStent infinite is contraindicated in eyes with angle-closure glaucoma where the angle has not been surgically opened, acute traumatic, malignant, active uveitic, or active neovascular glaucoma, discernible congenital anomalies of the anterior chamber (AC) angle, retrobulbar tumor, thyroid eye disease, or Sturge-Weber Syndrome or any other type of condition that may cause elevated episcleral venous pressure. **WARNINGS.** Gonioscopy should be performed prior to surgery to exclude congenital anomalies of the angle, PAS, rubeosis, or conditions that would prohibit adequate visualization that could lead to improper placement of the stent and pose a hazard. **MRI INFORMATION.** The iStent infinite is MR-Conditional, i.e., the device is safe for use in a specified MR environment under specified conditions; please see Directions for Use (DFU) label for details. **PRECAUTIONS.** The surgeon should monitor the patient postoperatively for proper maintenance of IOP. Three out of 61 participants (4.9%) in the pivotal clinical trial were phakic. Therefore, there is insufficient evidence to determine whether the clinical performance of the device may be different in those who are phakic versus in those who are pseudophakic. **ADVERSE EVENTS.** The most common postoperative adverse events reported in the iStent infinite pivotal trial included IOP increase ≥ 10 mmHg vs. baseline IOP (8.2%), loss of BSCVA ≥ 2 lines (11.5%), ocular surface disease (11.5%), perioperative inflammation (6.6%) and visual field loss ≥ 2.5 dB (6.6%). **CAUTION:** Federal law restricts this device to sale by, or on the order of, a physician. Please see DFU for a complete list of contraindications, warnings, precautions, and adverse events.

PM-US-0909

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