Wills Eye Resident Series: A patient presents with a red eye and vision loss, *p. 70*

REVIEW of OPHTHALMOLOGY®

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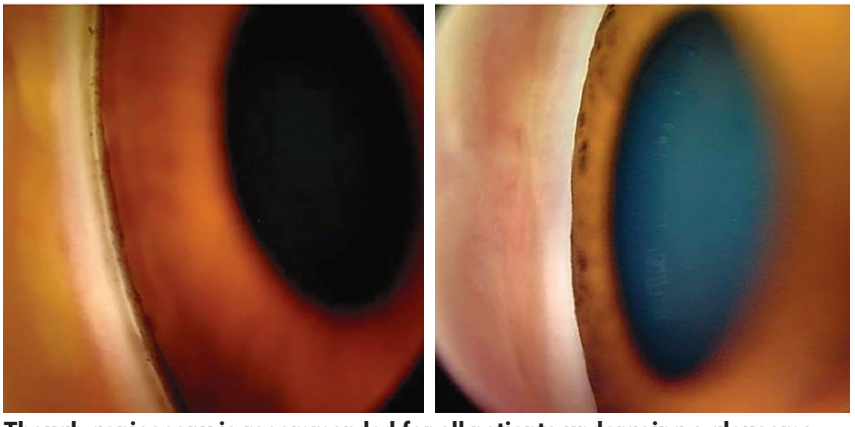
VOLUME XXXI • NO. 4

APRIL 2024

Study Finds Most Patients Who Need Gonioscopy Don't Get It

New research found that more than 70 percent of patients receiving an initial glaucoma evaluation in the United States do not have record of gonioscopy.[1]

In this retrospective, case-control study, researchers assessed patterns in gonioscopy during initial glaucoma evaluations in the United States. Subjects with a diagnosis of glaucoma suspect, anatomical narrow angle (ANA) or primary/secondary glaucoma were included. Among the 198,995 patients (56 percent female, 44 percent male) in this analysis, 20.4 percent had a recorded gonioscopy on the day of diagnosis and 29.5 percent within six months. There was no gender difference noted in gonioscopy rates.



Benjamin Xu, MD, PhD

Though gonioscopy is recommended for all patients undergoing a glaucoma evaluation, one study found only around 30 percent of these patients are receiving the exam. Shown here, an open (left) and a closed (right) angle.

"One thing that struck us as surprising was how low the rate of gonioscopy actually was," says one of the study's authors, Benjamin Xu, MD, PhD, of USC's Keck School of Medicine. "Previous studies had found it was probably closer to 50 percent, but those were in more academic settings. Another study looked at gonioscopy prior to doing glaucoma surgery, so it wasn't exactly at time of glaucoma evaluation. Those studies had found it was closer to 50 percent of those who should have received gonioscopy had a record of it. The fact that ours was actually lower was a bit surprising and concerning, as well. As the article mentions, the AAO really does recommend that all patients undergoing gluacoma evaluation receive gonioscopy.

"What was also surprising was that some of these patients who were being diagnosed with angle closure or anatomically narrow angles didn't have a record of gonioscopy," Dr. Xu continues. "So whether these providers are just assuming based on other exam techniques like van Herick, it's surprising and leads to the question: Are people just not billing for it? It doesn't pay a lot, about $20, but are people not aware to bill for it? I will say that most providers are pretty good about being aware of the in-office exam components that reimburse. So I'd find that to be surprising."

The researchers found several racial distinctions. Multivariate analysis revealed that the odds of recorded gonioscopy within six months of initial evaluation was lower among non-Hispanic white patients; however, it was similar for black and Hispanic patients when compared to their Asian counterparts. Among patients with primary angle closure glaucoma, only 56.6 percent of Asian subjects had a record of gonioscopy, whereas the other racial cohorts all had rates of at least 70 percent or more.

"Primary factors that influence a provider's decision to perform gonioscopy during glaucoma evaluation include perceived risk of angle closure based on patient demographics (e.g., Asian race or older age) or clinical findings associated with angle closure (e.g., shallow anterior chamber depth or hyperopic refractive error)," the researchers wrote in their recent *American Journal of Ophthalmology* paper on the work. "If the former was predominant, we should have

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†Out of 124 patients from the clinical study, 122 responded that they would have LASIK again.

References

1. Lobanoff M, Stonecipher K, Tooma T, et al. Clinical outcomes after topography-guided LASIK: comparing results based on a new topography analysis algorithm with those based on manifest refraction. *J Cataract Refract Surg*. 2020;46(6):814-819. doi:10.1097/j.jcrs.0000000000000176.

2. Stulting RD, Fant BS; T-CAT Study Group. Results of topography-guided laser in situ keratomileusis custom abalation treatment with a refractive excimer laser. *J Cataract Refract Surg*. 2016;42(1):11-18. Study description: Prospective, nonrandomized, multicenter study of 249 eyes with myopia (up to -9D) or myopic astigmatism of 6.0 D or less. Outcome measures included manifest refraction, UDVA, CDVA and visual symptoms up to 12 months.

For Important Product Information about Contoura® Vision, please refer to the adjacent page.

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WAVELIGHT® EXCIMER LASER SYSTEMS IMPORTANT PRODUCT INFORMATION

This information pertains to all WaveLight® Excimer Laser Systems, including the WaveLight® ALLEGRETTO WAVE®, the ALLEGRETTO WAVE® Eye-Q and the WaveLight® EX500. **Caution**: Federal (U.S.) law restricts the WaveLight® Excimer Laser Systems to sale by or on the order of a physician. Only practitioners who are experienced in the medical mangement and surgical treatment of the cornea, who have been trained in laser refractive surgery (including laser calibration and operation) should use a WaveLight® Excimer Laser System. **Indications**: FDA has approved the WaveLight® Excimer Laser systems for use in laser-assisted in situ keratomileusis (LASIK) treatments for: the reduction or elimination of myopia of up to - 12.00 D and up to 6.00 D of astigmatism at the spectacle plane; the reduction or elimination of hyperopia up to + 6.00 D with and without astigmatic refractive errors up to 5.00 D at the spectacle plane, with a maximum manifest refraction spherical equivalent of + 6.00 D; the reduction or elimination of naturally occurring mixed astigmatism of up to 6.00 D at the spectacle plane; and the wavefront-guided reduction or elimination of myopia of up to -7.00 D and up to 3.00 D of astigmatism at the spectacle plane. In addition, FDA has approved the WaveLight® ALLEGRETTO WAVE® Eye-Q Excimer Laser System, when used with the WaveLight® ALLEGRO Topolyzer® and topography-guided treatment planning software for topography-guided LASIK treatments for the reduction or elimination of up to -9.00 D of myopia, or for the reduction or elimination of myopia with astigmatism, with up to -8.00 D of myopia and up to 3.00 D of astigmatism. The WaveLight® Excimer Laser Systems are only indicated for use in patients who are 18 years of age or older (21 years of age or older for mixed astigmatism) with documentation of a stable manifest refraction defined as ≤ 0.50 D of preoperative spherical equivalent shift over one year prior to surgery, exclusive of changes due to unmasking latent hyperopia. **Contraindications**: The WaveLight® Excimer Laser Systems are contraindicated for use with patients who: are pregnant or nursing; have a diagnosed collagen vascular, autoimmune or immunodeficiency disease; have been diagnosed keratoconus or if there are any clinical pictures suggestive of keratoconus; are taking isotretinoin (Accutane*) and/or amiodarone hydrochloride (Cordarone*); have severe dry eye; have corneas too thin for LASIK; have recurrent corneal erosion; have advanced glaucoma; or have uncontrolled diabetes. **Warnings**: The WaveLight® Excimer Laser Systems are not recommended for use with patients who have: systemic diseases likely to affect wound healing, such as connective tissue disease, insulin dependent diabetes, severe atopic disease or an immunocompromised status; a history of Herpes simplex or Herpes zoster keratitis; significant dry eye that is unresponsive to treatment; severe allergies; a history of glaucoma; an unreliable preoperative wavefront examination that precludes wavefront-guided treatment; or a poor quality preoperative topography map that precludes topography-guided LASIK treatment. The wavefront-guided LASIK procedure requires accurate and reliable data from the wavefront examination. Every step of every wavefront measurement that may be used as the basis for a wavefront-guided LASIK procedure must be validated by the user. Inaccurate or unreliable data from the wavefront examination will lead to an inaccurate treatment. Topography-guided LASIK requires preoperative topography maps of sufficient quality to use for planning a topography-guided LASIK treatment. Poor quality topography maps may affect the accuracy of the topography-guided LASIK treatment and may result in poor vision after topography-guided LASIK. **Precautions**: The safety and effectiveness of the WaveLight® Excimer Laser Systems have not been established for patients with: progressive myopia, hyperopia, astigmatism and/or mixed astigmatism, ocular disease, previous corneal or intraocular surgery, or trauma in the ablation zone; corneal abnormalities including, but not limited to, scars, irregular astigmatism and corneal warpage; residual corneal thickness after ablation of less than 250 microns due to the increased risk for corneal ectasia; pupil size below 7.0 mm after mydriatics where applied for wavefront-guided ablation planning; history of glaucoma or ocular hypertension of > 23 mmHg; taking the medications sumatriptan succinate (Imitrex*); corneal, lens and/or vitreous opacities including, but not limited to cataract; iris problems including , but not limited to, coloboma and previous iris surgery compromising proper eye tracking; or taking medications likely to affect wound healing including (but not limited to) antimetabolites. In addition, safety and effectiveness of the WaveLight® Excimer Laser Systems have not been established for: treatments with an optical zone < 6.0 mm or > 6.5 mm in diameter, or an ablation zone > 9.0 mm in diameter; or wavefront-guided treatment targets different from emmetropia (plano) in which the wavefront calculated defocus (spherical term) has been adjusted; In the WaveLight® Excimer Laser System clinical studies, there were few subjects with cylinder amounts > 4 D and ≤ 6 D. Not all complications, adverse events, and levels of effectiveness may have been determined for this population. Pupil sizes should be evaluated under mesopic illumination conditions. Effects of treatment on vision under poor illumination cannot be predicted prior to surgery. **Adverse Events and Complications** Myopia: In the myopia clinical study, 0.2% (2/876) of the eyes had a lost, misplaced, or misaligned flap reported at the 1 month examination. The following complications were reported 6 months after LASIK: 0.9% (7/818) had ghosting or double images in the operative eye; 0.1% (1/818) of the eyes had a corneal epithelial defect. Hyperopia: In the hyperopia clinical study, 0.4% (1/276) of the eyes had a retinal detachment or retinal vascular accident reported at the 3 month examination. The following complications were reported 6 months after LASIK: 0.8% (2/262) of the eyes had a corneal epithelial defect and 0.8% (2/262) had any epithelium in the interface. Mixed Astigmatism: In the mixed astigmatism clinical study, two adverse events were reported. The first event involved a patient who postoperatively was subject to blunt trauma to the treatment eye 6 days after surgery. The patient was found to have an intact globe with no rupture, inflammation or any dislodgement of the flap. UCVA was decreased due to this event. The second event involved the treatment of an incorrect axis of astigmatism. The axis was treated at 60 degrees instead of 160 degrees. The following complications were reported 6 months after LASIK: 1.8% (2/111) of the eyes had ghosting or double images in the operative eye. Wavefront-Guided Myopia: The wavefront-guided myopia clinical study included 374 eyes treated; 188 with wavefront-guided LASIK (Study Cohort) and 186 with Wavefront Optimized® LASIK (Control Cohort). No adverse events occurred during the postoperative period of the wavefront-guided LASIK procedures. In the Control Cohort, one subject undergoing traditional LASIK had the axis of astigmatism programmed as 115 degrees instead of the actual 155 degree axis. This led to cylinder in the left eye. The following complications were reported 6 months after wavefront-guided LASIK in the Study Cohort: 1.2% (2/166) of the eyes had a corneal epithelial defect; 1.2% (2/166) had foreign body sensation; and 0.6% (1/166) had pain. No complications were reported in the Control Cohort. Topography-Guided Myopia: There were six adverse events reported in the topography-guided myopia study. Four of the eyes experienced transient or temporary decreases in vision prior to the final 12 month follow-up visit, all of which were resolved by the final follow-up visit. One subject suffered from decreased vision in the treated eye, following blunt force trauma 4 days after surgery. One subject experienced retinal detachment, which was concluded to be unrelated to the surgical procedure. **Clinical Data** Myopia: The myopia clinical study included 901 eyes treated, of which 813 of 866 eligible eyes were followed for 12 months. Accountability at 3 months was 93.8%, at 6 months was 91.9%, and at 12 months was 93.9%. Of the 782 eyes that were eligible for the uncorrected visual acuity (UCVA) analysis of effectiveness at the 6-month stability time point, 98.3% were corrected to 20/40 or better, and 87.7% were corrected to 20/20 or better. Subjects who responded to a patient satisfaction questionnaire before and after LASIK reported the following visual symptoms at a "moderate" or "severe" level at least 1% higher at 3 months post-treatment than at baseline: visual fluctuations (28.6% vs. 12.8% at baseline). Long term risks of LASIK for myopia with and without astigmatism have not been studied beyond 12 months. Hyperopia: The hyperopia clinical study included 290 eyes treated, of which 100 of 290 eligible eyes were followed for 12 months. Accountability at 3 months was 95.2%, at 6 months was 93.9%, and at 12 months was 69.9%. Of the 212 eyes that were eligible for the UCVA analysis of effectiveness at the 6-month stability time point, 95.3% were corrected to 20/40 or better, and 69.4% were corrected to 20/20 or better. Subjects who responded to a patient satisfaction questionnaire before and after LASIK reported the following visual symptoms as "much worse" at 6 months post-treatment: halos (6.4%); visual fluctuations (6.1%); light sensitivity (4.9%); night driving glare (4.2%); and glare from bright lights (3.0%). Long term risks of LASIK for hyperopia with and without astigmatism have not been studied beyond 12 months. Mixed Astigmatism: The mixed astigmatism clinical study included 162 eyes treated, of which 111 were eligible to be followed for 6 months. Accountability at 1 month was 99.4%, at 3 months was 96.0%, and at 6 months was 100.0%. Of the 142 eyes that were eligible for the UCVA analysis of effectiveness at the 6-month stability time point, 97.3% achieved acuity of 20/40 or better, and 69.4% achieved acuity of 20/20 or better. Subjects who responded to a patient satisfaction questionnaire before and after LASIK reported the following visual symptoms at a "moderate" or "severe" level at least 1% higher at 3 months post-treatment than at baseline: sensitivity to light (52.9% vs. 43.3% at baseline); visual fluctuations (43.0% vs. 32.1% at baseline); and halos (42.3% vs. 37.0% at baseline). Long term risks of LASIK for mixed astigmatism have not been studied beyond 6 months. Wavefront-Guided Myopia: The wavefront-guided myopia clinical study included 374 eyes treated; 188 with wavefront-guided LASIK (Study Cohort) and 186 with Wavefront Optimized® LASIK (Control Cohort). 166 of the Study Cohort and 166 of the Control Cohort were eligible to be followed at 6 months. In the Study Cohort, accountability at 1 month was 96.8%, at 3 months was 96.8%, and at 6 months was 93.3%. In the Control Cohort, accountability at 1 month was 94.6%, at 3 months was 94.6%, and at 6 months was 92.2%. Of the 166 eyes in the Study Cohort that were eligible for the UCVA analysis of effectiveness at the 6-month stability time point, 99.4% were corrected to 20/40 or better, and 93.4% were corrected to 20/20 or better. Of the 166 eyes in the Control Cohort eligible for the UCVA analysis of effectiveness at the 6-month stability time point, 99.4% were corrected to 20/40 or better, and 92.8% were corrected to 20/20. In the Study Cohort, subjects who responded to a patient satisfaction questionnaire before and after LASIK reported the following visual symptoms at a "moderate" or "severe" level at least 1% higher at 3 months post-treatment than at baseline: light sensitivity (47.8% vs. 37.2% at baseline) and visual fluctuations (20.0% vs. 13.8% at baseline). In the Control Cohort, the following visual symptoms were reported at a "moderate" or "severe" level at least 1% higher at 3 months post-treatment than at baseline: halos (45.4% vs. 36.6% at baseline) and visual fluctuations (21.9% vs. 18.3% at baseline). Long term risks of wavefront-guided LASIK for myopia with and without astigmatism have not been studied beyond 6 months. Topography-Guided Myopia: The topography-guided myopia clinical study included 249 eyes treated, of which 230 eyes were followed for 12 months. Accountability at 3 months was 99.2%, at 6 months was 98.0%, and at 12 months was 92.4%. Of the 247 eyes that were eligible for the UCVA analysis at the 3-month stability time point, 99.2% were corrected to 20/40 or better, and 92.7% were corrected to 20/20 or better. Subjects who responded to a patient satisfaction questionnaire before and after LASIK reported the following visual symptoms as "marked" or "severe" at an incidence greater than 5% at 1 month after surgery: dryness (7% vs. 4% at baseline) and light sensitivity (7% vs. 5% at baseline). Visual symptoms continued to improve with time, and none of the visual symptoms were rated as being "marked" or "severe" with an incidence of at least 5% at 3 months or later after surgery. Long term risks of topography-guided LASIK for myopia with and without astigmatism have not been studied beyond 12 months. **Information for Patients:** Prior to undergoing LASIK surgery with a WaveLight® Excimer Laser System, prospective patients must receive a copy of the relevant Patient Information Booklet, and must be informed of the alternatives for correcting their vision, including (but not limited to) eyeglasses, contact lenses, photorefractive keratectomy, and other refractive surgeries. **Attention:** Please refer to a current WaveLight® Excimer Laser System Procedure Manual for a complete listing of the indications, complications, warnings, precautions, and side effects.

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observed significantly higher rates of recorded gonioscopy among Asians, which we did not."

"We were happy to see that black and Hispanic patients were as likely to receive gonioscopy as Asians," says Dr. Xu. "It's widely known that Asians are at higher risk for angle closure and angle closure glaucoma. In a previous study we conducted, we found that black patients were unfortunately not receiving gonioscopy prior to developing glaucoma. But what this study shows, at least when they're evaluated for glaucoma, is that they appear as likely to receive gonioscopy.

"It's also not surprising that non-Hispanic whites are less likely to receive gonioscopy," Dr. Xu continues, "because they tend to have deeper anterior chambers, so they appear to be less likely to need gonioscopy. However, the recommendation for the first-time glaucoma evaluation is for everyone to receive gonioscopy. So this finding probably indicates that providers are doing gonioscopy selectively."

One of the reasons for the low rate of gonioscopy is potential anchoring bias, which involves hewing to the first piece of information you're given on a particular topic. "This has to do with what we're taught as trainees," says Dr. Xu. "As ophthalmology residents, the *Basic and Clinical Science* texts emphasize the importance of Asian race as a risk factor for narrow angles and narrow angle glaucoma. So, if you're taught that this disease is more prevalent in a subpopulation, you're more inclined to look for it in that subpopulation. However, by doing this, you're overlooking the fact that there are many people in other subpopulations that do have the disease. So, that's one of the challenges in teaching residents or trainees about the risk factors for disease because it creates these anchoring biases."

Dr. Xu was asked about the possibility that gonioscopy is skipped in some patients due to a combination of other exam factors, such as racial predisposition, in addition to a need to keep a clinic's patient flow moving.

"Gonioscopy takes time, takes expertise," Dr. Xu says. "And it can be hard to find time to do it in a busy clinical workflow. That's why our lab is developing new methods using technology like OCT to try to facilitate or simplify the clinical workflow. Another issue with gonioscopy is it typically has to be performed prior to dilation, so then you have to see them twice. So, it's true that gonioscopy isn't convenient for a streamlined clinical workflow, but it's a very important part of glaucoma evaluation."

Additionally, the study authors reported that the odds of recorded gonioscopy was also lower among patients over the age of 60, as well as those who lived outside of the Northeast region. "While it remains unclear whether this difference is related to practice or billing patterns, our results are consistent with prior studies that reported insured patients in the Northeast region are more likely to be detected with ANA prior to developing PACG."

Dr. Xu says they've seen this phenomenon before, and there are several possible explanations for it. "We see that diseases are detected more often and outcomes are better in the Northeast region," he says. "We think this might be due to the density of providers there: You're more likely to have access to a provider. There's also a high density of academic centers, so presumably doctors at those centers may

(Continued on p. 12)

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

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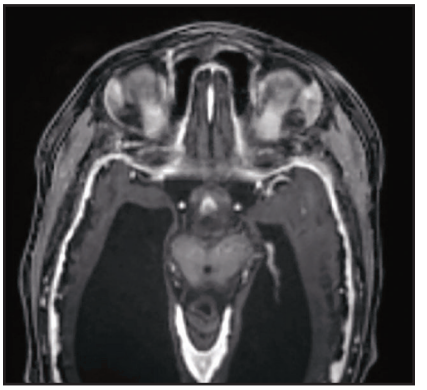
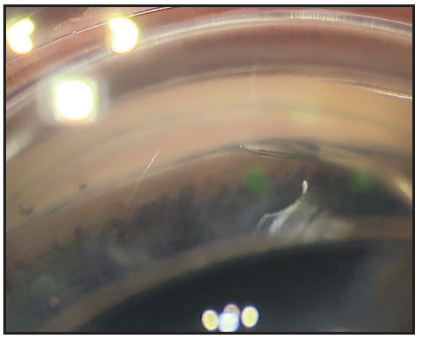
April 2024





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*Prescription market data, Dec. 2022 – S01K without cyclosporine.
†In a chronic dry eye patient usage study, participants from a variety of socioeconomic backgrounds answered questions about their experience with iVIZIA lubricant drops. In the study, 203 chronic dry eye patients, 28-80 years old, switched from their dry eye artificial tears to iVIZIA for a month.[1]
‡To limit blurriness when using contact lenses, remove contacts, apply drops, then insert contacts.

Reference: 1. Thea Data on File.

Thea
let's open our eyes

(Continued from p. 7)

be more up-to-date in terms of practice patterns and adhere to the standard of care. They are teaching residents as well, so that may have something to do with it too. There may also be exposure to a more diverse cohort of patients. There may be more specialists in the Northeast, as well."

When compared to patients with anatomical narrow angle glaucoma, data showed that angle closure glaucoma, secondary glaucoma or open angle glaucoma/suspect patients were less likely to have recorded gonioscopy.

Dr. Xu hopes that maybe the study will help get the word out about the importance of gonioscopy.

"The reason we wrote the article was to remind people that gonioscopy is a crucial element of the glaucoma evaluation," he says. "Not doing it can lead to misdiagnosis and mistreatment." He adds, however, that there seems to be some pushback on the importance of gonioscopy, even from trained glaucoma specialists. "One of the reviewers' comments—this is a top scientist—really shows the depth of this belief that perhaps gonioscopy is optional: 'What is the evidence of the need for gonioscopy when evaluating a glaucoma patient? Where preferred practice patterns may expect the collection of gonisocopy data, the underlying evidence regarding the need for such data for management of the patient is weak at best. Therefore, It's unclear to me why clinicians should collect this data in routine glaucoma patients.'

"This was a bit surprising," comments Dr. Xu, because clearly he's aware of the preferred practice patterns. Maybe we need more compelling evidence of why not doing gonioscopy could be problematic. But intuitively, the first fork in the glaucoma decision tree when making the diagnosis is: Is it open angle or angle closure? This is because the two are treated differently. And, you have to perform gonioscopy to make that determination. So, there's a very simple answer to this reviewer's objections: Gonioscopy is a fundamental aspect of managing the glaucoma. But, here's a very experienced clinician asking why we need to do it. Perhaps we need to make this point more clearly when either writing preferred practice patterns or teaching trainees. It's important to emphasize that the clinical management of glaucoma depends on the underlying mechanism and gonioscopy helps us understand that.

"Ultimately, some patients with narrow angles do develop narrow angle glaucoma, which is a higly blinding disease," Dr. Xu adds. "And, here in the U.S., even though we spend a lot of money on eye care, one out of eight patients is blind in at least one eye from this disease at first diagnosis. So we need to do better and in order to do so, we have to be better about adhering to these clinical guidelines."

1. Hui LJ, Kristy Y, Khristin I, et al. Patterns and disparities in recorded gonioscopy during initial glaucoma evaluations in the United States. American Journal of Ophthalmology. February 26, 2024 [Epub ahead of print].

RA Leads to Greater Cataract, Glaucoma Risk

Though seemingly unrelated, numerous studies have pointed to potential causal associations that exist between cataract, glaucoma and rheumatoid arthritis. However, it remains unclear whether RA is indeed a directly influencing underlying condition that raises risks for cataract or glaucoma. In a new genetic analysis, study researchers investigated the relationship of these conditions in European and East Asian populations.[1]

Genome-wide association study (GWAS) summary statistics were collected for cataract from 372,386 individuals and glaucoma from 377,277 individuals in the European population. RA summary data in this population was derived from a meta-analysis of 97,173 samples GWAS. The East Asian study population comprised 212,453 individuals for cataract and glaucoma and 22,515 individuals for RA.

Between eight and 56 single-nucleotide polymorphisms suited for investigation, depending on the condition. After analysis, the study researchers revealed that RA had an increased risk of cataract and glaucoma in the European population. RA only showed a positive association with cataract in the East Asian population. The authors "believe that oxidative stress and local inflammation are responsible for these causal associations," and they expand upon this statement in their discussion. It should be noted that reverse MR analyses suggested that cataract and glaucoma had no causal effect on RA.

Characterized by inflammatory changes in the synovial membrane of joints and erosive arthritis, RA has more recently gained increasing attention due to oxidative stress, which is thought to be a key player in development of the condition. Both the mitochondria and blood of RA patients have exhibited elevated levels of reac-

(Continued on p. 16)

CORRECTIONS

In the March feature "How to Succeed with the New Triple Procedure," Dr. Kourtney Houser's quote on page 40 should have read: "Any hydrophobic acrylic intraocular lens is safe to use, but I avoid hydrophilic acrylic lenses, as these can calcify and opacify with gas injection."

Dr. Sadeer Hannush's quote on page 43 should have read: "For example, I'll strip a diameter of 8.5 mm and I will graft a diameter of 7.75 to 8 mm, so I over-strip by 0.5 to 0.75 mm."

Dr. Hannush's complete title is "Attending surgeon at Wills Eye Hospital and professor of Ophthalmology at Thomas Jefferson University in Philadelphia."

Review regrets the errors.

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REFERENCES:
1. REF2022CT4107 Z311524E_A TECNIS Eyhance™ IOL with TECNIS SIMPLICITY™ Delivery System US DFU.
2. REF2021CT4007 Z311525E_A TECNIS Eyhance™ Toric II IOL with TECNIS SIMPLICITY™ Delivery System DFU.
3. DOF2021CT4002 - RUSH: TECNIS Eyhance™ IOL Monofocal Competitors MTF – US.

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REVIEW of OPHTHALMOLOGY

WALTER C. BETHKE, EDITOR IN CHIEF

EDITOR'S PAGE

Take a Bite Out of Reimbursement Cuts

We've all known that person—or maybe we've been that person—who avoids going to the dentist at all costs. When a molar on the right side of their mouth starts bothering them when they chew, they just take bites with the left side. Then, when a tooth on the left side starts to hurt, they start to chew in the middle with their front teet, like beavers. Finally, though, the pain becomes too much, and they drag themselves—or are dragged—kicking and screaming to the dentist's chair.

I bring this up because this may be the point we're at with drug prices in the United States. The obesity drug Wegovy might be that final, stabbing pain that forces the issue and makes drug companies sit down and negotiate prices with the government.

We've reached this point because last month the FDA approved Wegovy for the reduction of the risk for heart attacks, strokes and other cardiovascular events for overweight or obese adults. This broader approval, which skirts the ban on Medicare paying for obesity medication, sets the stage for the Centers for Medicare and Medicaid Services reimbursing for the use of the drug.

This could be a boon for patients, but a potential budget nightmare for the health-care system since, as it stands now, a prescription for Wegovy averages about $1,350 per month in the United States. If all of the adults with obesity (who, presumably, are also at risk for cardiovascular issues), were put on Wegovy, the cost would exceed the entire Medicare Part D budget.[1] As this column often does, we like to comment on how exorbitant spending in one aspect of the government and/or Medicare might ultimately impact ophthalmologists' reimbursement, since there's only so much of the budget to go around. In the case of Wegovy possibly getting CMS' coverage for this broader indication of cardiovascular risk, this could pose the threat of even deeper cuts to surgery in an effort to make up any shortfall.

It looks like this potential budget buster is what may bring the government and drugmakers to the table to try to agree on a lower price for the medication, to both allow patients to have access to the drug while also easing the economic burden. I'm hopeful that a lower price could work, since it seems very viable in Europe. There, a monthly dose of Wegovy is just $328 in Germany and only $296 in the Netherlands.[2] So, it is possible. Plus the drug manufacturers would still be making a good amount just based on the volume of patients in the United States.

The other potential positive in terms of curbing the cost of the drug is that, as one article points out, not all patients will need to be switched from their current statin medication if they're getting acceptable results.

Let's hope the drug manufacturers can see the wisdom in providing these drugs for more patients, at the cost of a bit less per case and are willing to negotiate. If they do, in the end, both they and the country can come out winners.

— Walter Bethke
Editor in Chief

1. Chen E. Covering new weight loss drugs could strain Medicare, policy experts warn. https://www.statnews.com/2023/03/11/new-weight-loss-drugs-wegovy-medicare/ Accessed March 18, 2024.
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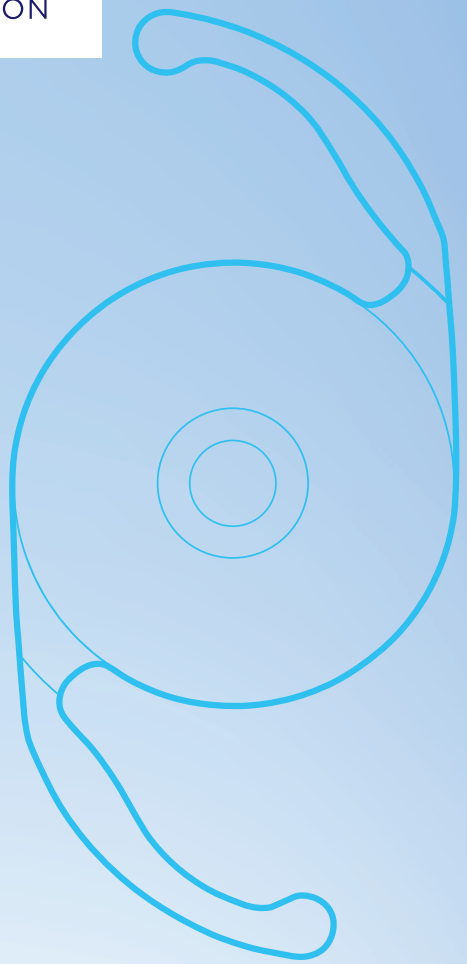

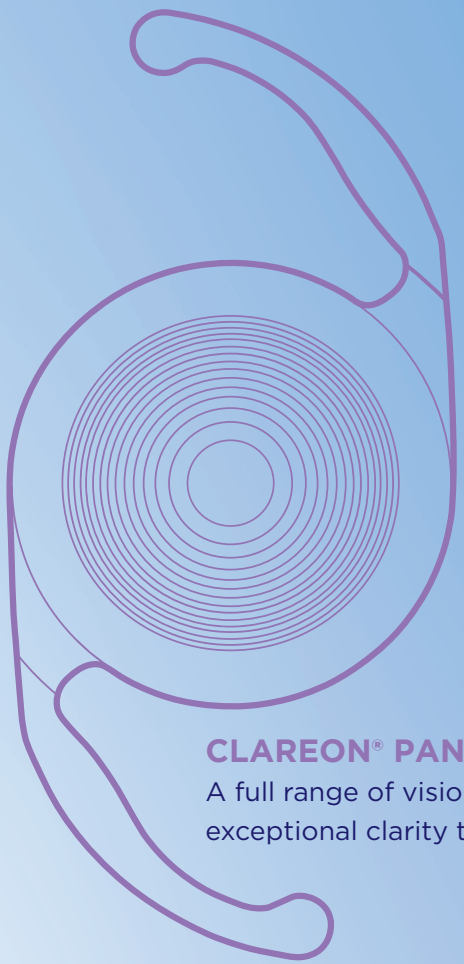

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‡ Snellen VA was converted from logMAR VA. A Snellen notation of 20/20-2 or better indicates a logMAR VA of 0.04 or better, which means 3 or more of the 5 ETDRS chart letters in the line were identified correctly.

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Alcon

(Continued from p. 12)

tive oxygen species, which is a prominent biomarker of oxidative stress. Subsequently, these species can cause damage to articular cartilage either directly or indirectly, leading to proteoglycan degradation and inhibition of their synthesis. Pathogenesis of cataract is also related to oxidative stress, with an imbalance in the lens' redox state driven by this stress and contributing to development. As well, oxidative stress accelerates lens epithelial cell loss, also a critical factor in cataract development.

Shifting to other aspects of the disease, RA also involves local inflammation as a central element in its development. Inflammatory factors and chemokines of tumor necrosis factor, interleukins and matrix metalloproteinase are all upregulated in synovial macrophages and dendritic cell subsets in RA patients. With this upregulation, the inflammatory mediators lead to cartilage degradation, bone erosion and accelerated RA development. Inflammation also plays a critical role in glaucoma pathogenesis. The same inflammatory factors of tumor necrosis factor, two different interleukins and matrix metalloproteinase can all promote retinal ganglion cell death—a hallmark of glaucoma development.

The authors are hopeful that their results may "offer guidance in the early prevention of cataract and glaucoma in RA patients and provide some evidence for the RA-induced inflammation on ophthalmic diseases."

1. Teng M, Wang J, Su X, et al. Causal associations between rheumatoid arthritis, cataract and glaucoma in European and East Asian populations: A bidirectional two-sample mendelian randomization study. PLoS ONE. 2024;19:3:e0299192.

Latest Victory for Ozempic?

Recent studies have demonstrated that a medication commonly prescribed for type 2 diabetes and obesity, glucagon-like peptide-1 receptor agonists (GLP-1RA), plays a role in facilitating retinal neuroprotection, which, in turn, may prevent glaucoma development and progression.

To further explore this hypothesis, researchers in Denmark performed a nationwide, nested case-control study comparing the risk of glaucoma development in individuals with type 2 diabetes being treated with GLP-1RA—a second-line antihyperglycemic medication—vs. those receiving alternative treatments.

Of 264,708 individuals in the Danish database, the researchers identified 1,737 incident glaucoma cases that were matched to 8,685 controls without glaucoma, all of whom were above 21 years old, had no history of glaucoma and were treated with metformin and a second-line antihyperglycemic drug formulation (a GLP-1RA).

Analysis of the data revealed that compared to individuals in the control group, who received treatments other than GLP-

(Continued on p. 27)

MARY PAT JOHNSON, COMT, CPC, COE, CPMA

MEDICARE Q&A

Use of the New "Complexity" Code

What you need to know about "complexity" code, which just went into effect in 2024.

You may have heard about Medicare's new "complexity" code, but haven't gotten many details on it. In this installment of Medicare Q&A, we'll answer providers' common questions about the new code.

Q What is the new 'complexity' code?

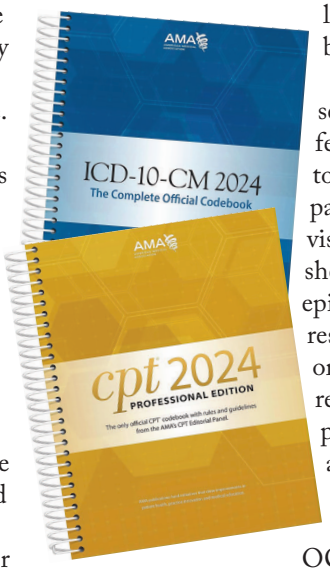
A HCPCS code +G2211 states: "Visit complexity inherent to evaluation and management associated with medical care services that serve as the continuing focal point for all needed health-care services and/or with medical care services that are part of ongoing care related to a patient's single, serious condition or a complex condition. (Add-on code, list separately in addition to office/outpatient evaluation and management visit, new or established)."[1]

Medicare introduced the code in 2021. However, it didn't go into effect until January 1, 2024. It's currently covered by CMS. The national, unadjusted allowed amount for HCPCS code +G2211 is $16.04. In terms of third party payors, private payors aren't required to cover and pay separately for +G2211. Policies vary.

The AMA and most surgical specialty societies opposed implementation of +G2211 due to the required statutory budget neutrality adjustment and resulting 2.18-percent reduction in the 2024 Medicare conversion factor.[2,3]

Q When does this code apply?

A According to the CMS Fact Sheet, "HCPCS code +G2211 includes services that enable practitioners to build longitudinal relationships with all patients (that is, not only those patients who have a chronic condition or single-high risk disease) and to address the majority of patients' health care needs with consistency and continuity over longer periods of time. This includes furnishing services to patients on an ongoing basis that result in care that is personalized to the patient. The services result in a comprehensive, longitudinal, and continuous relationship with the patient and involve delivery of team-based care that is accessible, coordinated with other practitioners and providers, and integrated with the broader health care landscape….In the context of specialty care, HCPCS code +G2211 could recognize the resources inherent in engaging the patient in a continuous and active collaborative plan of care related to an identified health condition the management of which requires the direction of a clinician with specialized clinical knowledge, skill and experience. Such collaborative care includes patient education, expectations and responsibilities, shared decision-making around therapeutic goals, and shared commitments to achieve those goals."[1]



Q Can ophthalmologists use this code?

A While there's nothing published that precludes ophthalmologists from reporting +G2211 in conjunction with an E/M code, it's unlikely that this will occur frequently. The code needs to be supported in the medical records by more than simply a long, time consuming encounter.

A particular case example can illustrate how the code may be used:

A neuro-ophthalmologist sees a 41-year-old, Hispanic female for a follow-up visit to review test results. The patient experienced dramatic vision loss three days ago; she experienced a similar episode 13 months prior that resolved with high-dose, oral steroids. At the most recent visit two days ago, the patient complained of headache and difficulty sleeping. A series of tests were ordered: blood tests; MRI; OCT; and VEP. At today's exam, her vision is light perception in both eyes. A diagnosis of bilateral retrobulbar optic neuritis secondary to multiple sclerosis is made. Based

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Mary Pat Johnson is a senior consultant at the Corcoran Consulting Group and is based in North Carolina. She can be reached at mpjohnson@corcoranccg.com.

on the Optic Neuritis Treatment Trial,[5][4] the neuro-ophthalmologist recommends intravenous steroids.

Immediately after the visit, a discussion occurs between the neuro-ophthalmologist and the patient's neurologist; interferon therapy is considered. The neurologist admitted the patient to the hospital later that day for IV steroid treatment.[5] The neuro-ophthalmologist will reassess the patient in the hospital frequently. The outpatient service of the neuro-ophthalmologist is billed with 99215 and +G2211. The admiszsion of the patient to the hospital by the neurologist is an inpatient service and ineligible to be billed with +G2211.

There's some similarity to care management services[6] in the description of +G2211, particularly where it refers to "plan of care" and "team-based care." CMS states, "…we do not believe the inherent complexity code would be duplicative of care management services since the inherent complexity better recognizes the professional work within the visit, while the care management codes recognize services that happen outside of the visit."[7]

The American Academy of Ophthalmology Fact Sheet cites several examples that don't support code +G2211:

- exam for ocular trauma, subconjunctival hemorrhage, seasonal allergies, viral conjunctivitis or other conditions that are time-limited in nature;
- exam that results in the decision for surgery to resolve a condition such as cataract or eyelid lesion; and
- exams where comorbidities are not present or not addressed, and/or when the billing practitioner has not taken responsibility for ongoing medical care for that patient with consistency and continuity over time, or does not plan to take responsibility for subsequent, ongoing medical care for that patient with consistency and continuity over time.[8]

TABLE 1. WHEN IS +G2211 SUPPORTED?

CPT 9920x, 99212 or higher
Ongoing, longitudinal, continuous care
E/M code unrelated to surgery
Complex medical (not surgical) care
Plan all or most of patient's health care
Team-based care, coordinated
Office or outpatient E/M only
Comprehensive, integrated care
Collaborative with other providers
Plan all/most of pt's health care

Q Which E/M services can be reported with +G2211?

A HCPCS contains an instruction for +G2211 that says, "Add-on code, list separately in addition to office/outpatient evaluation and management visit, new or established." It can't be combined with any other service such as inpatient E/M or eye codes (920xx). Also, it shouldn't be reported with 99211 or when an E/M service is reported with modifier -25.[9,10]

Q What providers can report code +G2211?

A All physicians may use +G2211, however CMS says it "…took into account the likelihood that primary care specialties will have a higher utilization of the add-on code than other specialties, surgical specialties will have the lowest utilization since they are less likely to establish longitudinal care relationships with patients, and other specialists are more likely to have longitudinal care relationships than surgical specialties but less likely than primary care specialists."[12] It's noteworthy that "primary care specialties" doesn't include ophthalmology or optometry according to CMS.[12]

Eye care providers' use of +G2211 should be rare. The characteristics that define this add-on code are not typically applicable in ophthalmology or optometry. The frequent use of it is only expected for primary care specialties. Post-payment audits commonly result from payor perception of inappropriate use. ◀

1. CMS Fact Sheet O/O E/M Visits, January 11, 2021. https://www.cms.gov/files/document/physician-fee-schedule-pfs-payment-officeoutpatient-evaluation-and-management-em-visits-fact-sheet.pdf. Accessed February 16, 2024.

2. CMS Fact Sheet. https://www.cms.gov/newsroom/fact-sheets/calendar-year-cy-2024-medicare-physician-fee-schedule-final-rule. Accessed February 16, 2024.

3. ASCRS. https://ascrs.org/news/washington-watch/ww-november-3-2023. Accessed February 16, 2024.

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APRIL 2024

THE VALUE OF REAL TEARS

Francis Mah, MD

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Viatris Inc., with oversight by Francis Mah, MD and Jessica Steen, OD, FAAO is responsible for the conception, design, and execution of the information presented in this article. Dr. Mah and Dr. Steen are paid consultants of Viatris and were compensated for their role in this article.

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The ocular surface is constantly undergoing desiccating stress but, under normal circumstances, is protected from damage by the production of a stable, homeostatic tear film.[1] Therefore, restoring tear film homeostasis is a major goal of dry eye management, and the patient's ability to produce real tears of sufficient quality and quantity should be taken into account when starting dry eye treatment.[2,3]

Tear film instability is a central driver of the complex cascade leading to clinical signs and symptoms of dry eye disease.

Jessica Steen, OD, FAAO

One of the reasons that a stable tear film is important is because it accounts for the majority of the refractive power of the eye, with tear film instability leading to reduced contrast sensitivity and increased optical aberrations.[3] A stable tear film also provides lubrication, protection, and nourishment to maintain a healthy ocular surface and has been a noticeable feature of many definitions of dry eye throughout the years (**Figure 1**).[4-7]

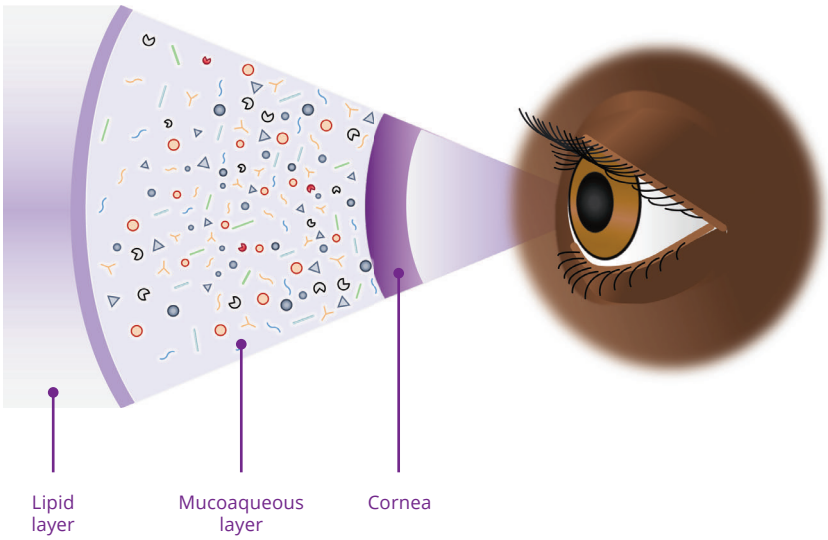

FIGURE 1:
A stable tear film accounts for the majority of the refractive power to the eye and the compounds found in the tear film provide lubrication, protection, and nourishment to the ocular surface.[3,4]

Almost all the definitions that have been proposed for dry eye, including those promulgated by TFOS DEWS II (2017) and the Global Consensus group (2020), have highlighted the idea that dry eye progression is driven by a cycle of tear film instability, hyperosmolarity, ocular surface damage, and inflammation.[7,8] Tear film stability can be compromised by decreased tear secretion, delayed tear clearance, and/or altered tear composition, which starts the cycle of dry eye and subsequently leads to the loss of homeostasis and ocular surface inflammation.[1,9,10]

GLOBAL CONSENSUS DEFINITION (2020)

"Dry eye is a multifactorial disease characterized by a persistently unstable and/or deficient tear film causing discomfort and/or visual impairment, accompanied by variable degrees of ocular surface epitheliopathy, inflammation, and neurosensory abnormalities."[7]

"

An unstable tear film is a critical initial step causing the downward spiral of the ocular surface leading to dry eye, tissue damage, and inflammation.

Francis Mah, MD

Tears are a complex mixture of elements and can come in four different types (basal, reflex, emotional, and closed-eye), each of which has a slightly different composition and function.[4-6,11,12] Basal tears are those that are present during the waking hours and are constantly being turned over. They are considered the primary tear that helps to maintain a healthy, functional ocular surface. Physical stimuli (eg, foreign bodies, trauma) to the eye produce a larger volume tear which is termed a reflex tear. Similarly, emotional stimuli (eg, sadness) also produce a larger volume tear called an emotional tear. The final tear type is the closed-eye tear that is produced when the eye is closed during a sleep cycle.[11,12]

Real tears, including basal tears, contain a complex milieu of over 2000 different components, each of which contributes to tear film stability and function (**Figure 2**). Among the many different components found in the tear film are proteins that protect the ocular surface and help it function (eg, growth factors, anti-inflammatory proteins), electrolytes and metabolites that play a role in basic cell metabolism, and mucins and lipids that help maintain tear film stability.[4-6]

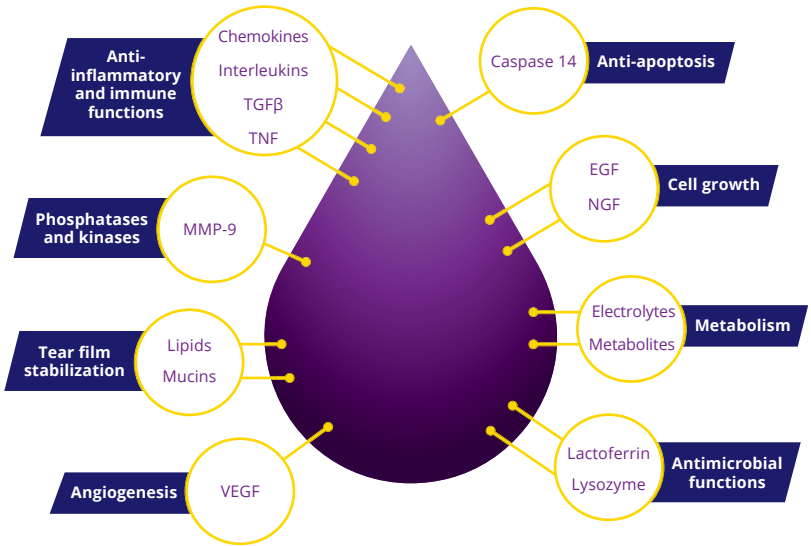

FIGURE 2:
Real tears, including basal tears, contain a complex milieu of over 2000 different components, each of which contribute to tear film stability and function.[4-6] This is just an example of some of the many components found in the tear film and their possible function.

With over 2000 components within a healthy human tear, treatment of dry eye should take into consideration the production of healthy, real tears.

Francis Mah, MD

The tear film and its many components are created and cleared by the lacrimal functional unit (LFU), which consists of the main and accessory lacrimal glands, meibomian glands, conjunctival goblet cells, and the lacrimal drainage system that is interconnected by sensory and motor nerves. The nerves of the LFU connect it to the central nervous system (CNS) via the trigeminal nerve and the trigeminal ganglion. Stimuli from either the ocular surface or the nose are transduced through the trigeminal nerve to the CNS (the afferent pathway) and then transmitted via efferent pathways to the secretory tissues (eg, main and accessory lacrimal glands, conjunctival goblet cells, and meibomian glands) and muscles that drive tear production and blinking (**Figure 3**). Stimulation of the LFU from intrinsic and extrinsic factors regulates tear production and helps produce a homeostatic tear.[1,3] For instance, normal, unlabored breathing and consistent airflow through the nasal passageways provide constant sensory stimuli to the LFU, which accounts for approximately 34% of basal tear production.[13]

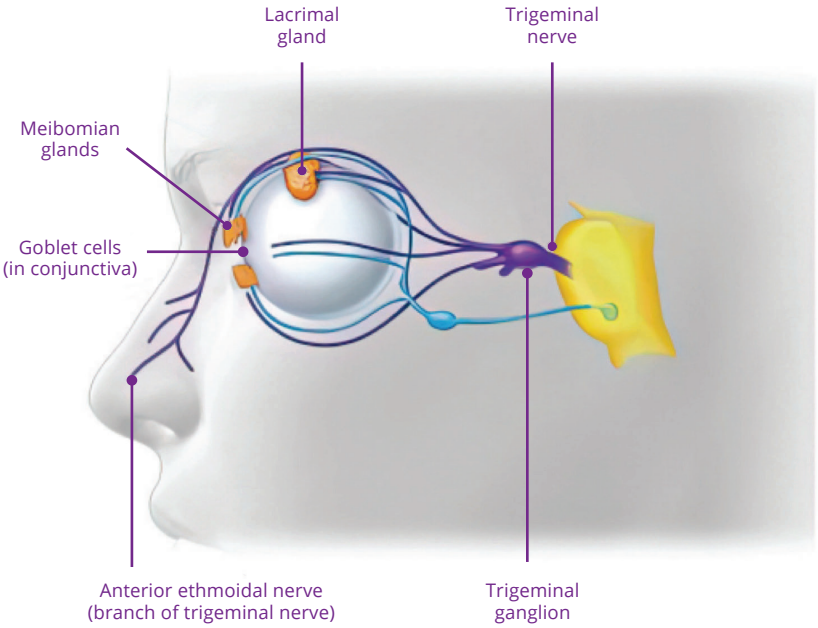

FIGURE 3:
Tears are created and cleared by the lacrimal functional unit (LFU), which consists of the main and accessory lacrimal glands, meibomian glands, conjunctival goblet cells, and the lacrimal drainage system that is interconnected by sensory and motor nerves. The nerves of the LFU connect it to the central nervous system via the trigeminal nerve and the trigeminal ganglion.[1,3] In this illustration, the afferent pathway is shown in purple, the efferent pathway is shown in blue.

It is widely acknowledged that dry eye is a multifactorial disease with many different etiologies. However, regardless of the etiology, the main goal of dry eye management is to break the cycle of dry eye by restoring tear film homeostasis, which can prevent the disease from either recurring or increasing in severity.[2,3] Dry eye treatment plans often start with environmental and behavioral modifications to reduce potential triggers and the implementation of lid hygiene regimens, as well as the use of artificial tears.[2] Artificial tears are considered a cornerstone of dry eye treatment and are formulated to mimic or supplement the mucoaqueous and lipid layers of the tear film.[2] However, they do not contain the biologically active components found in real tears and are temporary, palliative treatments that do not directly address the underlying etiology of dry eye.[2,14]

Furthermore, patients may encounter certain problems when using an eyedrop like an artificial tear. Depending on their age and dexterity, some patients may not be able to get a drop into their eyes or may have difficulties squeezing the bottle and others may dispense too many drops at a time.[15] Many patients initially choose to self-treat with artificial tears and may incorrectly use them.[16] Also, because each drop is a larger volume than that of the real tear film, they may induce reflex tearing and blinking and wash away natural components found in the tear film.[17]

Restoration of tear film homeostasis and disruption of the cycle of dry eye may be achieved by creating a real tear.

Jessica Steen, OD, FAAO

Additionally, artificial tears may contain anti-microbial preservatives that have been shown to harm the ocular surface and further exacerbate the signs and symptoms of dry eye. Benzalkonium chloride (BAK) is one of the most common anti-microbial preservatives used in eye drops and evidence suggests that BAK adversely effects the ocular surface by being toxic to corneal and conjunctival cells, including conjunctival goblet cells and corneal nerves, and delaying corneal wound healing.[2,18]

If patients have tried artificial tears and continue to have dry eye signs or symptoms, they are likely to be switched to a prescription eye drop, either an anti-inflammatory or a lipid layer enhancer.[2] While these prescription drops have been shown to treat dry eye, they may also have their difficulties. For instance, these eye drops need to be administered either twice or four times a day and are not compatible with contact lenses; for each administration, the patient must remove their contact lenses and keep them out for up to 30 minutes after instilling the drop.[19-24] Other approaches such as devices (eg, intense pulsed light therapy), tea tree oil, punctal occlusion, or therapeutic contact lenses may be used depending on the type of dry eye present and its severity.[2]

Nasal neurostimulation provides an alternative approach for the treatment of dry eye as it does not require patients to instill eye drops. Since part of the LFU can be accessed via the nasal cavities, it can be stimulated to induce the lacrimal glands, meibomian glands, conjunctival goblet cells, and other components of the LFU to produce basal tears.[1-3] Unlike artificial tears that mimic specific components of the tear film, nasal neurostimulation is thought to induce the production of a real tear.[13]

If the goal of dry eye therapy is to break the cycle of dry eye, then one key mechanism to doing so may be to stimulate the creation of real tears and restore tear film stability.[1-3] While artificial tears are a step in the right direction, they offer temporary, symptomatic relief without addressing the underlying causes of dry eye.[2,14] The other common treatment option, anti-inflammatories, specifically targets inflammation, which is downstream of tear film stability and does not directly restore tear film homeostasis.[2,9] Therefore, treatment for dry eye should begin by adequately addressing tear film instability as a distinct process, thereby breaking the cycle of dry eye.

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The Comfort of Routine

Musings on life, medicine and the practice of ophthalmology.

MARK H. BLECHER
CHIEF MEDICAL EDITOR

There's a lot you can learn from your dog. Unconditional love, live in the moment, patience. These are more apparent in a dog that has been well-trained and is calm. An anxious dog is a problematic dog. One thing I've learned from raising and training four Labs, is that if you are consistent and adhere to a routine, they're less anxious.

Tobey, my current Lab, is far and away my most chill, partly due to temperament, partly to environment. And, boy, does he love his routine. Deviate from it, and I hear about it. Like many dogs he has an amazing internal clock, especially for meals. Dinner at 4:00, cocktails and snacks to follow (my cocktail, his snacks) and his evening walk. He's on me for each step, reminding me if I'm late or forget. If you know what's coming next, you're less anxious, not on edge about the future. It's known and expected. And I've found I like routine as well. More so as I get older. Cycle of life, I guess. That isn't to say I don't appreciate something new and different, but on a day-to-day basis having a schedule that's predictable is reassuring. I think it's also partly a control issue. Well, its not an issue for me, because I like control. Ordering your life is very functional and for most of us, very necessary. Where it deviates into pathology is when it's taken to an extreme. For me, having guideposts in my day, establishing a routine, is sufficient. The details within can vary; I can be spontaneous.

During lockdown our lives were disrupted. Our pre-COVID routine disappeared. People stayed home and had to figure out how to conduct their day without the usual rhythm of work and friends. Some stayed in their pajamas, hung out, went with the flow. Others, such as myself, felt the need to quickly establish a new routine—something predictable and ordered. Even though at the beginning we weren't going anywhere, I insisted that by 4 p.m. you had to have had a shower and put on clean clothes. It was an effort to maintain civil behavior. I had a fear of life descending into the Lord of the Flies. That time was anxiety-provoking as it was and the loss of my previous routine made it more so.

There's a danger in order as well. It's easy to fall into the trap of predictability. You set up a routine and then disengage. You then don't have to think about it, about your life. Yes, it's well-ordered and perhaps comfortable, but boring and insular. And, if you're not careful, it becomes unsociable. You find yourself withdrawing from family, friends and life because they could disrupt your comfortable and known routine. I'm not a 'wild and crazy guy' in the classic Dan Akroyd and Steve Martin style from "Saturday Night Live," but I do like doing new things, going new places. As I said earlier, less so now at this point. And while I think I've crafted a routine that's both comfortable and reasonable, I find myself not wanting to disrupt it, and approaching new things—new travel—with less enthusiasm and with more angst. It's a strange feeling and I don't like it. I'm finding I have to exert conscious effort to leave my cocoon. I'm happy to have Tobey run my day, to execute the routine I taught him and which seems to serve him very well—although I'm jealous that he gets to sleep most of the day, I'm not ready to step back from life.

So, as with many things, I'll continue to try to find a balance, to keep a structure that's both reassuring and productive. I'm not ready to hang it up just yet. ◀

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

Cortical/Cerebral Visual Impairment

Expert discussion of the ins and outs of CVI diagnosis and work-up in children.

ALBERT YANG, BS, AND MELINDA Y. CHANG, MD
LOS ANGELES

Cortical/cerebral visual impairment is the leading cause of pediatric visual impairment in the United States and other developed economies.[1] CVI can be challenging to diagnose. In infants with visual impairment, the differential includes inherited retinal disorders, oculomotor apraxia, and delayed visual maturation. In older children, CVI can be confused with autism spectrum disorder or learning disabilities. Here, we'll break down the diagnostic cues and tests that can help you make a definitive CVI diagnosis in a young patient.

CVI Background

CVI has been defined broadly as a "verifiable visual dysfunction which cannot be attributed to disorders of the anterior visual pathways or any potentially co-occurring ocular impairment."[2] A stricter definition of CVI requires "bilateral visual acuity or visual field loss in the presence of a normal eye examination or vision loss that is greater than expected based on the degree of ocular pathology."[1] Though the exact definition of CVI varies in the literature, most diagnostic criteria require: 1) a demonstrable abnormality of vision; 2) no ocular findings sufficient to explain the visual abnormality; and 3) a neurologic condition that affects the developing visual pathways in the brain.

Risk Factors for CVI

CVI is heterogeneous in etiology. However, there are common causes to be aware of. They include:

- prematurity with periventricular leukomalacia;
- term birth with perinatal hypoxic-ischemic encephalopathy;
- hydrocephalus;
- seizures (particularly those that are associated with epileptic encephalopathy, such as infantile spasms);
- trauma;
- infections, including meningitis and encephalitis;
- structural brain abnormalities (such as schizencephaly and colpocephaly);
- metabolic conditions such as hypoglycemia; and
- genetic disorders.[1,3-6]

In many cases, CVI is multifactorial and it may not be possible to determine which underlying neurologic condition is responsible for the visual dysfunction *(Figure 1)*. Children with any of the aforementioned neurologic disorders should be considered at risk for CVI, and developmental pediatricians and neurologists may refer such patients for CVI evaluation.

Characteristics of CVI

CVI is also heterogeneous in its visual manifestations *(Table 1)*. Visual acuity may range from no light perception to age-normal, though the majority of patients evaluated by pediatric ophthalmologists have profoundly reduced visual acuity.[7] Other characteristics include visual field defects, reduced contrast sensitivity, relatively spared color discrimination, and a global motion processing deficit or, paradoxically, relatively preserved motion perception.[8-11] Visual behaviors associated with CVI include difficulty with visual search or using vision in crowded environments, highly variable visual function (visual behavior is often worse when the child is ill or fatigued), eccentric gaze preference (looking away while reaching), and light gazing or, paradoxically, photophobia.[8,12,13] In children with good visual

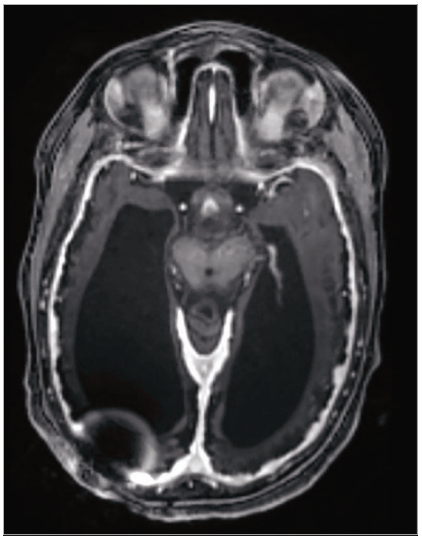

Figure 1. Brain magnetic resonance imaging scan of a 5-year-old child with cortical/cerebral visual impairment and multiple contributing etiologies, including hydrocephalus with a ventriculo-peritoneal shunt (artifact seen on the scan), hypoxic-ischemic encephalopathy with extensive cerebral volume loss, and seizures.

This article has no commercial sponsorship.

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TABLE 1. CHARACTERISTICS OBSERVED IN INDIVIDUALS WITH CORTICAL/CEREBRAL VISUAL IMPAIRMENT (CVI)

Lower-order visual deficits	Higher-order visual processing deficits	Behavioral characteristics	Oculomotor characteristics
Variably decreased visual acuity	Adverse effect of visual crowding	Fluctuating visual function	Increased saccadic latency
Reduced contrast sensitivity	Motion processing selectively spared or affected	Eccentric gaze preference	Abnormal vestibulo-ocular reflex
Visual field defects	Agnosias: simultanagnosia, prosopagnosia, topographic agnosia	Light gazing or photophobia	Fixation instability

acuity, higher-order visual processing abnormalities may be detected, including difficulties with recognition, orientation, depth perception and simultaneous perception.[14,15] Abnormal oculomotor behavior such as increased time to generate saccades when a visual stimulus is shown (latency), decreased or absent vestibulo-ocular reflexes, and fixation instability have also been described in CVI.[16,17]

Differential Diagnosis

The differential diagnosis of CVI depends on the age and presentation. In infants that are apparently blind, other diagnostic considerations include delayed visual maturation; oculomotor apraxia (prior to the development of neck control, which is required for head thrusting); and inherited retinal disorders. In older children with relatively good visual acuity, CVI may be confused with neurodevelopmental disorders such as autism spectrum disorder and learning disabilities, including dyslexia.

Evaluation and History

The evaluation of a child with suspected CVI should focus on elements that differentiate CVI from other conditions, and characterization of the severity of visual impairment in the affected child.

Structured history-taking questionnaires are available to elicit behaviors characteristic of CVI.[18-21] These questionnaires are particularly helpful in children with good visual acuity, suspected higher-order visual deficits and limited communication.

In all children with suspected CVI, important historical questions include:

Was the child born premature? Were there any birth complications? Was there a history of hypoxic-ischemic encephalopathy or cooling?

Is there a family history of neurologic or ophthalmologic conditions?

Was the child exposed to any drugs *in utero*?

Does the child have any known neurologic conditions? If so, are they controlled (e.g., seizure activity)?

Has the child undergone prior neuroimaging or genetic testing?

Examination

A complete pediatric ophthalmologic examination is critical to support the diagnosis of CVI and rule out other entities in the differential diagnosis above. Important components of the examination include:

• ***Visual acuity.*** In children with CVI who are unable to cooperate with optotype acuity testing, a 6-level scale of visual behavior may be used to grade visual acuity and monitor changes over time *(Table 2)*.[4,22]

• ***Pupils.*** In addition to assessing pupillary reactivity and presence of an afferent pupillary defect, it's important to evaluate the response to dark conditions in order to assess for paradoxical pupils. To check for paradoxical pupils in children, it's best to have a second person control the light switch while the child's attention is directed to a target in the distance (such as a toy or movie). The examiner uses a penlight for oblique illumination and observes the pupillary response when the light is turned off. In patients with paradoxical pupils, the pupils will initially constrict before dilating. The process may need to be repeated several times to observe a consistent response. Paradoxical pupils are a characteristic of inherited retinal disorders that may be mistaken for CVI.[23]

• ***Ocular motility.*** Children with CVI frequently have strabismus, which can change over time as their visual acuity improves.[24,25] The presence of nystagmus should raise the suspicion for an inherited retinal disorder, since nystagmus isn't typically a feature of CVI without anterior visual pathway dysfunction.

• ***Optokinetic nystagmus (OKN)***. In oculomotor apraxia, pursuit is intact whereas saccades are absent,[26] resulting in 'locking up' *(see referenced video[27] for example)*. Check horizontal and vertical OKN response, as vertical saccades are usually spared in congenital oculomotor apraxia. Children with CVI may have absent OKN responses both horizontally and vertically, particularly when visual acuity is poor.

• ***Fundus examination***. Subtle abnormalities suggestive of an inherited retinal disorder may be seen on careful fundus examination. Many children with CVI have optic nerve pathology, most commonly optic atrophy,[1] but the vision loss must be greater than expected based

TABLE 2. SIX-LEVEL SCALE OF VISUAL BEHAVIOR FOR GRADING VISUAL ACUITY IN CHILDREN WITH CORTICAL/CEREBRAL VISUAL IMPAIRMENT

1	Light perception only
2	Occasional fixation on large objects, faces or movement
3	Occasional fixation on small objects or reliable fixation on large objects (4-inch lighted toy at 1 foot) or faces, or optotype acuity worse than 20/400
4	Reliable fixation on small objects (2-inch toy at 1 foot), or optotype acuity between 20/400 to 20/200
5	Reliable fixation and pursuit of small objects (2-inch toy at 1 foot), or optotype acuity between 20/200 to 20/50
6	Reliable fixation and pursuit of smallest objects (1-inch toy at least 2 feet away), or optotype acuity between 20/50 to 20/20

on the optic nerve appearance in order to make a diagnosis of CVI.

• ***Cycloplegic refraction.*** High hyperopia or myopia may be a sign of an inherited retinal disorder,[28] although this is non-specific. CVI is also associated with a high rate of refractive errors, nearly equally divided between myopia and hyperopia.[29]

Table 3 provides a summary of examination findings that distinguish between CVI and the primary differential diagnoses in infants with apparently poor vision: inherited retinal disorders, oculomotor apraxia and delayed visual maturation.

In children with suspected CVI who have relatively good visual acuity, abnormalities of higher-order visual processing may not be identified on standard pediatric ophthalmologic examination, and specialized testing by allied health professionals may be required.

TABLE 3. OPHTHALMOLOGIC EXAMINATION FINDINGS IN INFANTS WITH VARIOUS DISORDERS

	Cortical/cerebral visual impairment (CVI)	Inherited retinal disorders (IRD)	Congenital oculomotor apraxia	Delayed visual maturation
Pupils	Normal, unless co-morbid optic nerve or retina disease	May exhibit paradoxical pupils	Normal	Normal
Ocular motility	High rate of strabismus. Nystagmus usually only present if co-morbid optic nerve or retina disease	Nystagmus usually present	Horizontal saccades absent, but vestibulo-ocular reflex is intact. Head thrusting present after approximately 6 months of age.	Normal
Optokinetic nystagmus (OKN) response	May be present or absent, depending on degree of visual impairment	Usually present	'Locking up' on horizontal OKN testing. Normal vertical OKN response is present.	May be present or absent, depending on degree of visual impairment
Fundus examination	Normal, unless co-morbid optic nerve or retina disease	Pigmentary changes of macula and retinal periphery may be difficult to visualize in young children	Normal	Normal
Cycloplegic refraction	No characteristic refractive error	High myopia and high hyperopia are features of certain IRDs (e.g., high hyperopia in Leber's congenital amaurosis)	No characteristic refractive error	No characteristic refractive error

Diagnostic work-up

While there is no single test to diagnose CVI, the following ancillary tests/imaging may be necessary to identify underlying neurologic conditions, rule out differential diagnoses and characterize the severity of CVI.

• ***Ophthalmic electrophysiology.*** Electroretinography and/or visual evoked potentials may be indicated in some children with suspected CVI. ERG is most useful to evaluate for an inherited retinal disorder in young children with poor vision and nystagmus. Flash VEP may have limited prognostic value. Sweep VEP has been used to assess grating acuity,[30] Vernier acuity,[31] and contrast sensitivity[10] in children with CVI, but obtaining reliable measurements in the most severely affected patients may be difficult or impossible. In general, electrophysiology isn't required in most cases to make a diagnosis of CVI.

• ***Neuroimaging.*** If not previously performed, children with suspected CVI should undergo brain magnetic resonance imaging to assess for structural abnormalities of the posterior visual pathway.

However, some children with CVI (especially those with genetic disorders) have normal structural brain MRI scans. Newer MRI techniques, such as diffuse tensor imaging, have demonstrated better structure-function correlation in some studies, but these are generally accessible only in the research setting.[32]

• ***Genetic testing.*** Genetic disorders are increasingly recognized as a cause of CVI. Diverse conditions including seizure disorders, leukodystrophies, congenital disorders of glycosylation and many others have been associated with CVI.[33] Genetic testing should be considered in children with CVI with syndromic features, especially when the etiology is unknown. Referral to medical genetics and a genetic counselor may be required to interpret the results. The American Board of Genetic Counseling maintains an online directory of certified genetic counselors at (https://abgc.learningbuilder.com/Search/Public/MemberRole/Verification).

• ***Functional vision assessments.*** Typically administered by teachers of the visually impaired or occupational therapists, tests of functional vision evaluate how a child uses his/her vision in everyday activities. This assessment is used to guide interventions, particularly in school, to allow the child to access educational material. The most widely used functional vision assessment is the CVI Range.[34] However, other assessments are being developed and validated. More information on CVI assessments may be found on the Perkins School for the Blind's "CVI Now" website (https://www.perkins.org/getting-started-with-cvi-assessments/).

• ***Neuropsychological assessments.*** Though the details are beyond the scope of this article and an ophthalmologist's practice, neuropsychological assessments may be particularly helpful to diagnose CVI in children with suspected higher-order visual perceptual deficits in the setting of good visual acuity and to evaluate them for neurodevelopmental disorders that may be mistaken for CVI, including autism spectrum disorder (ASD) and dyslexia. It's important to note that CVI may be co-morbid with these neurodevelopmental conditions, as vision is vital for both social interactions and reading text.[35] However, in order to diagnose CVI in the context of other neurodevelopmental disorders, children must have deficits specific to CVI that aren't explainable by the other diagnoses. Assessments for ASD and dyslexia are

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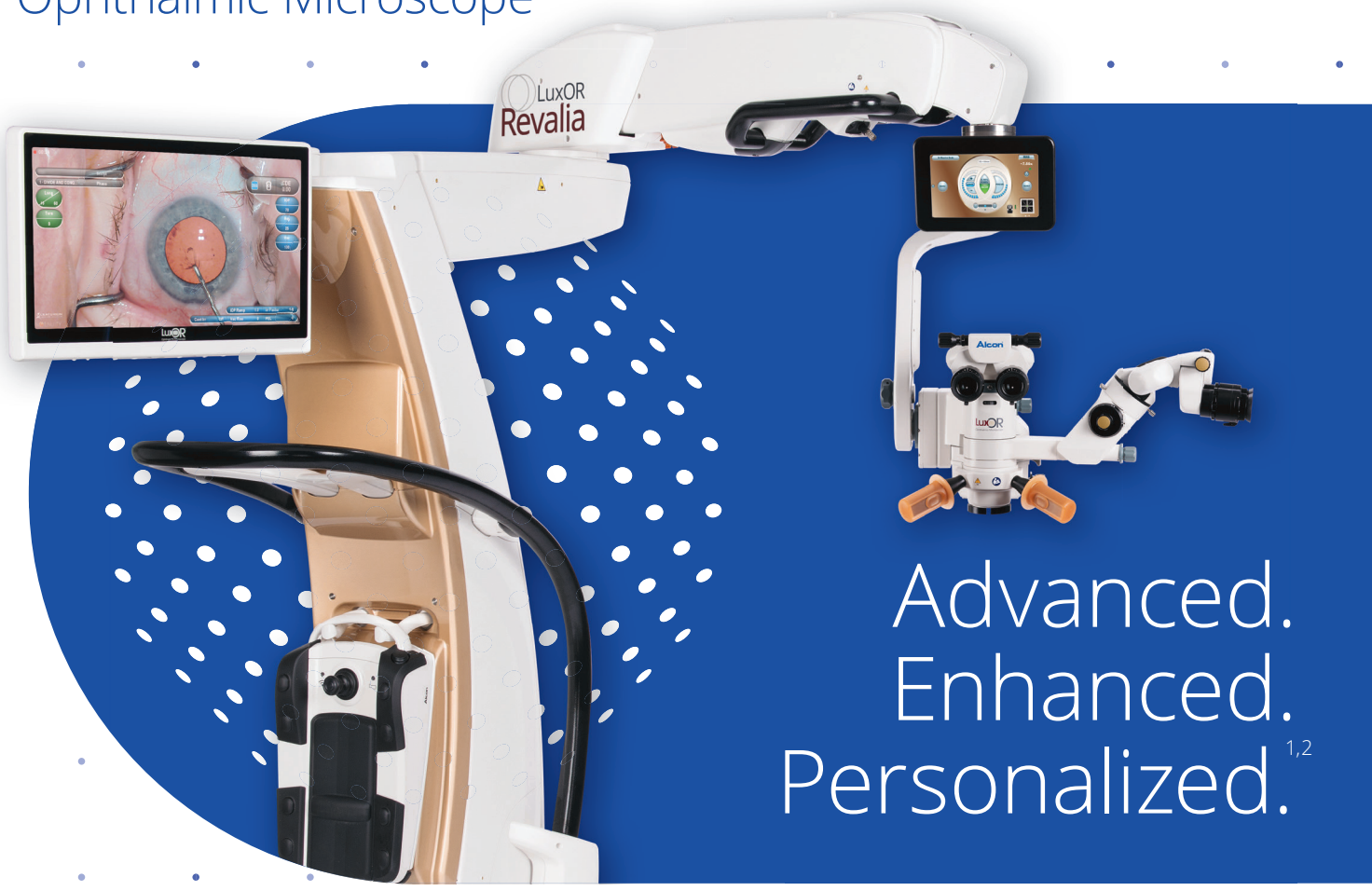

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usually provided by state-sponsored early intervention resources and school districts, although some parents may seek private evaluations.

In summary, CVI is a common and heterogeneous disorder that impacts functional vision. Pediatric ophthalmologists have an important role in suspecting CVI, guiding further diagnostic work-up, and ultimately providing the diagnosis. Recommendations for evaluating children with suspected CVI include:

- Consider incorporating CVI-specific questionnaires to identify higher-order visual perceptual deficits that are difficult to elicit in clinic.
- Conduct a thorough examination, paying careful attention to visual acuity (using the 6-level scale of visual behavior if needed), pupillary response to light and dark (particularly noting any paradoxical responses), presence of nystagmus and OKN response both horizontally and vertically, fundus examination (looking for subtle abnormalities of the retina and optic nerve) and cycloplegic refraction.
- ERG and VEP are generally not required for a CVI diagnosis, but ERG may be helpful to rule out an inherited retinal disorder in select patients (e.g. infants with poor vision and nystagmus, positive family history, and/or absence of risk factors for CVI).
- Consider brain MRI if not previously performed.
- Consider genetic evaluation in patients with syndromic features and no known risk factor for CVI.
- Obtain a functional vision assessment by a licensed professional, such as a teacher for the visually impaired or occupational therapist with expertise in CVI.
- Refer for neuropsychological evaluation if neurodevelopmental disorders (such as autism spectrum disorder) or learning disabilities (such as dyslexia) are suspected. ◀

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A Look at the Teneo Excimer Laser

Taking stock of the unique features of the newly FDA-approved Technolas Teneo Excimer Laser Platform.

LIZ HUNTER
SENIOR EDITOR

It's been over a decade since a new general-purpose excimer laser was approved by the U.S. Food and Drug Administration. Earlier this year, the drought came to an end with the approval of the Teneo Excimer Laser Platform (Bausch + Lomb) in January. Here, we'll take a look at the new machine.

Teneo's Background

The Technolas Teneo 317 Model 2 is indicated for myopia and myopic astigmatism LASIK, treating up to -10 D of myopic astigmatism, with sphere between -1 D and cylinder between zero and -3 D, according to the company.[1] The technology may offer updated levels of accuracy, efficiency and usability. The company says the laser is a "fast, small, technologically advanced machine."

The platform has been available in 50-plus countries for a number of years and now United States-based surgeons have their chance to access its features. We spoke with George Waring IV, MD, founder and medical director of Waring Vision Institute in Mt. Pleasant, South Carolina, and Y. Ralph Chu, MD, founder and medical director of Chu Vision Institute and Chu Surgery Center in Minneapolis, who were among the FDA trial participants. They say it's about time this technology made its way to the United States.

"As an industry, we haven't seen approval of a new excimer laser by the FDA in well over a decade," Dr. Waring says. "The recent FDA approval of the Teneo for myopia and myopic astigmatism is a landmark event representing positive energy around innovation in excimer laser technology in the United States."

Dr. Chu adds, "It's great now that we're able to access the same technologies that our colleagues overseas have. This technology is a pretty significant advancement to me in terms of speed of treatment and accuracy of treatment. As a surgeon, we want ease of use, ergonomics, speed, and safety—all of which provide great outcomes. That's what's been exciting about getting this new laser option."

Dr. Waring describes some of the new device's key features. "Number one, the form factor of the laser requires significantly less space and is streamlined and significantly smaller than the other lasers that are commercially available in the United States," he says. "That leads to improved space efficiency and

George Waring, IV, MD

George Waring, IV, MD, founder and medical director of Waring Vision Institute in Mt. Pleasant, South Carolina, performs a LASIK procedure with the newly FDA-approved Technolas Teneo 317 Model 2.

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.

Bausch + Lomb

Surgeons say the touchscreen interface is intuitive.

ergonomic flexibility."

According to the company, the Teneo is the smallest excimer laser unit currently available in the United States, clocking in at 6.8 sq. ft.

"Number two, the laser has an open, airy feel, and an advanced design, which is appreciated by our patients and staff alike," continues Dr. Waring. "It's a more comfortable procedure with an ergonomic bed as well." Not only does the patient bed swing out for easier access to patients of all sizes, but the surgical microscope also swivels 360 degrees to adapt to the surgeon's ergonomics. The microscope also includes five magnification settings with a 50-percent boost at each level.

The speed of the laser—500 Hz repetition rate and a truncated Gaussian beam profile—is "the fastest ablation time of all excimer lasers available in the United States at approximately 1.2 seconds per diopter," according to the company.

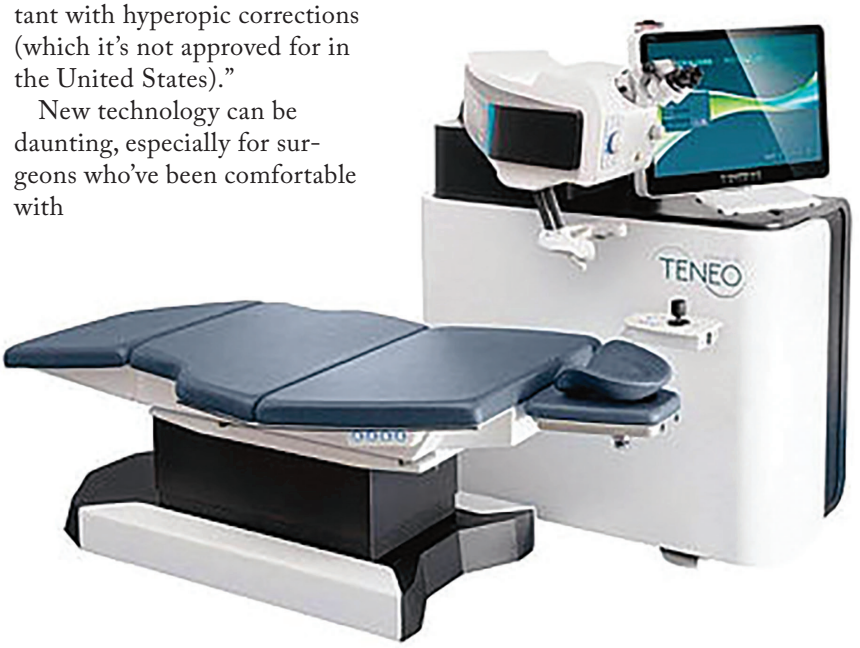
The Teneo's eye-tracking capability, which the company says operates at 1,740 Hz and has "iris-recognition illumination and digital coaxial camera for real-time active z-tracking," are among its most unique features highlighted by Dr. Chu and Dr. Waring.

"I love that the tracker has x, y and z directions, which is terrific," Dr. Chu says. "You can center the treatment on the visual axis vs. the pupillary center. This is very important with hyperopic corrections (which it's not approved for in the United States)."

New technology can be daunting, especially for surgeons who've been comfortable with their current laser platform, but the surgeons we spoke with say the Teneo is user-friendly. "One of the most exciting things about it is the intuitive user interface," says Dr. Waring of Teneo's customizable graphical interface with a touchscreen. "The Teneo platform is much more like an Apple computer or a Tesla and it's an intuitive and simple user interface that's easy for staff to use. The efficiency of treatments leads to a more enjoyable experience for staff and patients, and we think potentially quicker recovery as well because there's less time for the stromal bed and LASIK flap to be exposed during these treatments."

"Technologically it feels very advanced," Dr. Chu says. "In terms of the surgeon interface, it has a cockpit feel to it. I think the eye-tracking system, the speed of the laser and the results are the most impressive things. It's a big step forward."

To further save time, it comes with an internal nomogram. "It still allows for physician adjustments, but it doesn't require external adjustments through the use of external nomograms or physician adjust-



According to Bausch + Lomb, the Teneo is the smallest excimer laser available in the United States at 6.8 sq. ft.

ments," Dr. Waring says. "That tremendously streamlines the workflow, where you simply plug in the manifest refraction and treat off of that. This is how the FDA studies were designed and it provided exceptional results." (Results have been submitted for peer review and are forthcoming.)

> **Technologically, it feels very advanced. I think the eye-tracking system, the speed of the laser and the results are the most impressive things.**
>
> **– Y. Ralph Chu, MD**

Some studies have been conducted and published in other countries, including a retrospective study[2] of 135 eyes in 80 patients who underwent PRK for high astigmatism (-8 D or higher) with the Teneo 317 Model 2 excimer laser. Researchers examined the clinical results after six months. Spherical power averaged from -8.04 ± 0.90 D before surgery to -0.18 ± 0.55 D six months after surgery. Cylinder averaged from 1.74 ± 0.93 D preop to 0.51 ± 0.29 D six months postop. The average corneal thickness was measured at 543.67 ± 22.14 µm before surgery and 457.19 ± 26.34 µm six months postop.

Surgeons are looking forward to learning more about this laser's potential for hyperopic patients as well. "Given the beam profile and the efficiencies, the studies for hyperopia are ongoing and appear very promising," Dr. Waring says. "We're highly optimistic about the indications that are being pursued across the refractive spectrum.

"It's never been a better time to be a refractive surgeon or a refractive patient because we now have really notable improvements across a full spectrum of vision-correction procedures," Dr. Waring continues. "We're encouraged to see the advancements in excimer laser vision technology to continue to be able to provide visual freedom to more and more individuals in a safe and effective manner." ◀

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DISCLOSURES

Dr. Chu and **Dr. Waring** are consultants for Bausch + Lomb.

REVIEW NEWS

(Continued from p. 16)

1RA, those treated with GLP-1RAs had a lower risk of incident glaucoma (hazard ratio: 0.81). This risk was reduced even further in cases of prolonged treatment extending beyond three years (HR: 0.71), though GLP-1RA treatment for zero to one years (HR: 0.89) and one to three years (HR: 0.85) weren't significant.

In their paper for *Ophthalmology*, the study authors explained that their work accomplished two things. "First," they wrote, "the use of GLP-1RA was associated with a 19-percent decrease in risk of glaucoma. Second, increased exposure to GLP-1RA, especially over extended durations, accentuated this protective association with a duration-response pattern. Notably, with a significant 29-percent risk reduction when looking at three or more years exposure to GLP-1RA." They added, "Our sensitivity analysis supported the finding of risk reduction when looking at users of GLP-1RA."

These findings support the possibility of GLP-1RA being an adjunctive therapy to IOP-reducing eye drops in glaucoma management, the authors argue. They advised in their paper, "The lower risk of developing glaucoma among individuals with type 2 diabetes on GLP-1RA warrants further investigation to establish if there is an effect beyond improved glycemic control."

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ChatGPT Tries Its Hand at Evaluating Images

Researchers recently explored the use of the AI program ChatGPT to assess ophthalmic photos.

The investigators used a publicly available dataset of clinical photos from ophthalmic cases from OCTCases—a medical education platform based from the Department of Ophthalmology and Vision Sciences at University of Toronto—along with clinical multimodal imaging and multiple-choice questions. Of the 137 cases, 136 had multiple-choice questions.

Included in the analysis alongside the 136 cases were 429 total multiple-choice questions and 448 images. The questions were answered at an accuracy of 70 percent overall (n=299). Performance of the chatbot was best on retina questions (77 percent correct) and worst on neuro-ophthalmology questions (58 percent correct). Intermediate performance was seen in categories of ocular oncology (72 percent correct), pediatric ophthalmology (68 percent correct), uveitis (67 percent correct) and glaucoma (61 percent correct). Additionally, ChatGPT was significantly better at answering questions that were non-image based (82 percent) vs. image-based (65 percent).

(Continued on p. 68)

THE JOURNEY TO TRUE ACCOMMODATION

Various companies have been working for years to develop intraocular lenses that achieve true accommodation.

ANDREW BEERS
ASSOCIATE EDITOR

Though intraocular lenses have been around a long time, the market continues to grow and improve each year as new innovations are made. Patients who undergo cataract surgery are offered a host of IOLs for implantation, such as monofocal, multifocal and extended depth-of-focus lenses. But what if there was an IOL that could precisely mimic the human crystalline lens? Here, we take a look at several of the accommodative IOL concepts in development.

Accommodation: The Elusive Target

There have been many theories in the past that explained how the eye can be restored after surgery with accommodative effort. To create a truly accommodative IOL, researchers and pharmaceutical companies have been developing lenses using hypotheses from these accommodative theories. One of the first and best-known theories to propose accommodation in the eye was that of Hermann von Helmholtz.

In von Helmholtz's hypothesis, he suggests that during distance vision, the ciliary muscle is relaxed and the zonules are in a state of "resting" tension. When an accommodative IOL (A-IOL) is introduced into the eye, the ciliary muscle can contract and release the tension of the zonules. When this occurs, the accommodative power of the lens increases.[1] This theory provides a basic blueprint on how A-IOLs can be developed and used in surgery, but the road to true accommodation isn't easy.

"The promise of accommodation continues to be attractive although it has been challenging to mimic true human accommodation, which is far more complex than [von] Helmholtz originally predicted," says George Waring IV, MD, the founder and medical director of the Waring Vision Institute in South Carolina. "However, this hasn't held back innovation, and in recent years there have been numerous accommodative IOLs in development."

When will an A-IOL meet true accommodation and gain market approval from the FDA? "Proving accommodation is tricky because there's no gold standard as to what the FDA wants with respect to an endpoint for accommodation, and how do you actually prove accommodation as the mechanism?" asks Sumit Garg, MD, a cataract surgeon at UCI Health in Irvine, California. "The FDA is in the process of updating their requirements on what's required to designate an IOL as 'accommodating,'" Lenses currently undergoing development are being held back by this, but it doesn't mean the future of A-IOLs isn't bright.

"I think the future is bright for IOL technology in general, particularly accommodative technology," comments Dr. Waring. "I don't believe we'll be able to reproduce the young human crystalline lens, but we'll get to the next best thing. But, like all technologies, this takes time to develop and will continue to evolve and improve overtime."

A-IOLs in Development

There's an incredible amount of A-IOLs in development all over the world, and some particularly promising devices are pushing to begin trials for market approval in the United States. Juvene (LensGen), OmniVu (Atia Vision), FluidVision

This article has no commercial sponsorship.

Dr. Waring is an investigator for Atia Vision. **Dr. Garg** is an investigator for LensGen. **Dr. Werner** is an investigator for Alcon/PowerVision, LensGen, Atia Vision, Adaptilens and Ocumetics.

(Alcon), Opira (ForSight Vision6), Lumina (AkkoLens) and JelliSee (JelliSee Ophthalmics) are all under investigation and development with the hope of one day seeing the ophthalmology market. Here are the latest findings and information on each A-IOL.

• ***Juvene (LensGen).*** One novel device on its way to FDA trials is LensGen's Juvene A-IOL. "They have a modular IOL that has shown the ability to achieve accommodation," says Dr. Garg. "The question is: Is it going to meet what the FDA requires to be called accommodation versus some other designation which would have an equivalent refractive effect?

"LensGen has shown best corrected distance corresponding intermediate and near vision without diffractive optics," continues Dr. Garg. "But, to actually prove that's happening is more difficult because there's no real guideline on how to show that and, typically, the movements required to give this range of vision are really small and therefore hard to capture."

Dr. Garg presented the 36-month visual outcomes after implantation of the Juvene A-IOL at the 2023 ASCRS meeting in San Diego. The data presented focused on 10 eyes with seven various diopter points examined between the 24-month follow-up and the 36-month follow-up visits. Researchers observed the means of best-corrected distance visual acuity (-0.06 logMAR [slightly better than 20/20]), distance corrected intermediate (0.09 logMAR [slightly worse than 20/20]) and near visual acuities (0.21 logMAR [around 20/32]), as well as binocular measures for intermediate (-0.02 logMAR [around 20/20]) and near (0.12 logMAR [a little worse than 20/25]).[2]

Also presented at the meeting were monocular defocus curves that showed that visual acuity was better than 20/40 from +1.5 D through -2.5 D of defocus. Binocular defocus curves increased the diopter range from +2 D through -2.5 D. Additionally, contrast sensitivity curves were reported to be "virtually identical" to a monofocal lens.

"We haven't seen any safety signals that said that this isn't going to be a very safe lens inside the eye," says Dr. Garg. At the ASCRS presentation, he reported that the Juvene A-IOL didn't show any device-related adverse events during follow-up visits after a three-year period. He adds, "We have toxicology studies to satisfy FDA requirements, so there's no issues with biocompatibility with the material."

The Juvene lens is developed using a two-part system. "It has a fixed optic in the base that fills the whole capsular bag and then it has a fluid lens optic that fits within that base to give you that actual change in refraction needed to give you continuous vision from distance, intermediate and near," explains Dr. Garg. "So, you put the base lens in first and then you put in the fluid lens, and then you have to tab it into place inside the eye. It's not as simple as putting it in the eye and then you're done. There's a little bit more to it than a standard lens. That being said, I've done a handful of them outside the U.S. and it's not a very difficult thing to do.

"Because it's a two-part lens, there's some modularity to it," continues Dr. Garg. "So, you can always exchange or upgrade the optic, if you needed to, depending on if a patient's vision requirements change."

Dr. Garg mentioned that the Juvene lens is implanted using an off-the-shelf injector but didn't disclose precisely what injector system he's used in the past. However, he did add that the incision for implanting the A-IOL is much larger than a typical incision needed for other lenses. "It's a little over a 3-mm incision for the injection into the capsular bag," he says.

Currently, LensGen is preparing their lens for their Phase I FDA trial. "The hope is that everything will go well there to move towards commercialization in a few years assuming no major hiccups," comments Dr. Garg.

JelliSee Ophthalmics

JelliSee Ophthalmic's A-IOL is a two-piece, silicone-based IOL implanted into the capsular bag.

• ***OmniVu (Atia Vision)***. "The OmniVu is a modular shape-changing lens system that's composed of a fixed power front optic and a fluid-filled shape changing base," explains Dr. Waring. "The fixed power front optic is a hydrophobic acrylic and the shape changing base is fluid-filled. This is designed to restore a continuous full range of vision binocularly across more than four diopters of defocus while promoting contrast sensitivity and without unwanted dysphotopsias or other photopic side effects.

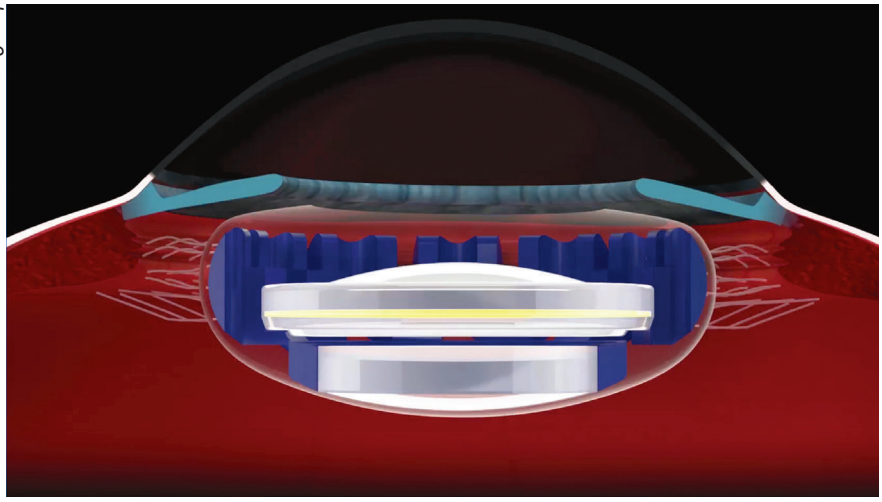
"Six months and one year in-human trials have been presented," adds Dr. Waring. "The six-month data showed that 95 percent

of eyes were within a half a diopter of plano and maintained greater than 20/32 visual acuity over four diopters of defocus binocularly. It will come in a power range of +12 to +28 in half-diopter increments and recently, 12-month data has also been presented at AAO by Daniel Chang, [MD]."

Dr. Chang's presentation at AAO 2023 provided one-year follow-up results from 13 eyes (monocular) and four patients (binocular) with the OmniVu implanted. He reported that after one year, 92 percent of eyes were within a 0.5 D of plano. Additionally, he reported that monocular CDVA, DCIVA and DCNVA were −0.06 ± 0.08 [better than 20/20], 0.01 ± 0.10 [around 20/20] and 0.19 ± 0.12 [around 20/32]. Furthermore, binocular CDVA, DCIVA and DCNVA were −0.15 ± 0.10 [better than 20/16], −0.02 ± 0.07 [better than 20/20] and 0.15 ± 0.12 [a little worse than 20/25]. In the presentation, Dr. Chang reported that the mean monocular defocus curves showed visual acuity better than 20/32 from +1.25 D through -1.75 D, and binocular defocus curves showed the same visual acuity from +1.75 D through -2.75 D of defocus. Further data was reported at the AAO meeting.[3]

Dr. Waring goes on to explain the OmniVu's surgical technique. "This is done with a standard phaco technique," he says. "The lens does require a 3.5-mm incision and a 5.5-mm capsulotomy. The base lens is inserted into the capsular bag after standard phacoemulsification and the fixed power front optic is then injected also into the capsular bag and is docked with the docking tabs into the base.

"This lens is designed to provide a continuous range of vision and [Atia Vision] believes that the unique features of the capsule-filling technology may provide additional beneficial characteristics such as stabilization of effective lens position with the bag-filling technology, as well as potentially minimizing posterior capsule opacification," continues Dr. Waring. "Even though the lens appears to provide a full range of vision, there's always the possibility of requiring magnification, such as a small amount of magnification for reading details and low-light conditions."



LensGen

A simulated image of the Juvene lens implanted into the eye. The dioptric power of Juvene is adjusted through the curvature change influenced by the ciliary muscle. This A-IOL is implanted into the capsular bag.

There are other developments for the OmniVu planned as well. "The toric option is planned for the future and another unique attribute of this technology is the fact that the front optic can be changed if needed for refractive purposes or other enhancements in the future," says Dr. Waring.

• ***FluidVision (Alcon/PowerVision)***. In 2018, Louis Nichamin, MD, an ophthalmologist from Brookville, Pennsylvania, presented the results from a six-month pilot study on the FluidVision A-IOL.[4] During the presentation, Dr. Nichamin explained that the FluidVision A-IOL is developed with a refractive-index-matched, silicone fluid-filled optic which is connected by channels to two fluid-filled haptics. It achieves accommodation by forcing fluid from the haptics into the optic, which increases the thickness of the lens as well as the optical power. To reverse the accommodation, fluid flows back into the haptics.

Dr. Nichamin mentioned that the pilot study focused on monocular results in 28 subjects. Only one subject wasn't included for the six-month follow-up visit. Each subject had a FluidVision A-IOL implanted through a 3.5-mm incision and their visual acuities along with contrast sensitivity were assessed. The mean CDVA at six months was -0.05 logMAR [a bit better than 20/20], the mean DCIVA was 0.05 logMAR [a little worse than 20/20], and the mean DCNVA was 0.14 logMAR [a little worse than 20/25], respectively. Also, he mentioned that the subjects achieved contrast sensitivity equivalent to a monofocal lens.

In 2019, Alcon announced that it would be acquiring PowerVision to develop the FluidVision A-IOL. According to PowerVision, future planned developments include introducing a toric platform and improving post-implant adjustment. They also believe the incision can be smaller, and PowerVision is looking into reducing the size to 2.8 mm.[5]

• ***Opira (ForSight Vision6).*** According to the company, the Opira A-IOL is a silicone, ciliary muscle driven, capsule-fixated, dynamic shape-changing device. It's attached to the capsule using the A-IOLs haptics.[6]

David F. Chang, MD, a cataract surgeon in Los Altos, California, provided the latest trial results for the Opira A-IOL at Hawaiian Eye 2024. During the six-month study, a total of 32 sub-

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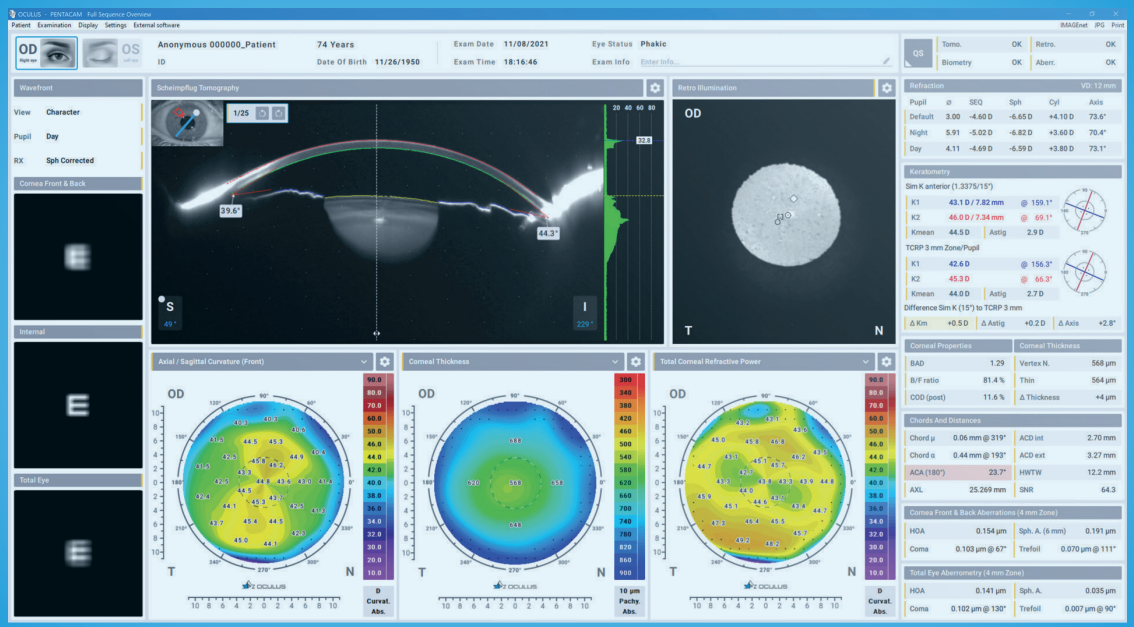

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jects had the Opira implanted bilaterally through a 3.75-mm incision. Only two subjects weren't included in the results. In logMAR notation, monocular visual acuity at distance, intermediate and near were -0.02 (a little better than 20/20), -0.07 and 0.04 (a little worse than 20/20). Binocular visual acuity at distance, intermediate and near were -0.06, -0.11 (a little better than 20/16) and -0.01 logMAR. Uncorrected visual acuity at distance, intermediate and near were -0.04, -0.11 and -0.02 logMAR with 97 percent of subjects becoming spectacle-free.

Then, subjects were asked to note any adverse outcomes in a questionnaire following the study. Dr. Chang reported that adverse effects such as glare, starbursts, hazy vision, distortion, focusing difficulties, depth perception issues, as well as fluctuations in vision, were all lower in comparison to monofocal and trifocal counterparts. It was reported that a total of 275 eyes have been implanted with the Opira A-IOL over the last five years, with no cases of uveitis-glaucoma-hyphema syndrome, IOL dislocation or IOL explantation.

Dr. Chang reported in his presentation that while the A-IOL is fixated to the capsule, the mechanism for accommodation is independent of the capsular fibrosis which allows for more predictable performance. A future plan for Opira is to reduce the incision size for implantation to 3 mm.

• ***Lumina (AkkoLens)***. According to AkkoLens, the Lumina is a two-piece A-IOL consisting of an anterior element and a lens. This lens is implanted within the sulcus to promote accommodation. Research has suggested that the design of the Lumina A-IOL can provide approximately 4 D of accommodative power. It requires a 2.8 mm incision, which makes the procedure suture-free.[6]

In a study to analyze the accommodative performance of Lumina, researchers compared the lens to a monofocal IOL.[7] A total of 25 eyes were implanted with Lumina and 18 eyes received a monofocal lens as a control. After a one-year follow-up, researchers observed that Lumina subjects had better visual acuity results than subjects in the control group over a defocus range of -0.5 to -5 D. The study showed that Lumina had similar UDVA results to the control group. However, Lumina showed significantly better UNVA of 0.91 ± 0.11 (20/22 Snellen) compared to the control group.

• ***JelliSee (JelliSee Ophthalmics)***. JelliSee is currently undergoing human pilot studies. According to their website, the A-IOL's design is foldable and offers 7 D or more of accommodation. When the ciliary muscle in the eye relaxes, a force is applied by the zonules to the lens. Only <0.2 mm of diameter change in the eye is needed to gain full range of accommodation. The haptics of the A-IOL are fixated to the fibrotic peripheral lens capsule to allow the natural accommodation mechanism to work effectively, the company says.

During the 2021 Winning Pitch Challenge presented at ASCRS, representatives for JelliSee explained that the lens is liquid-filled with a relatively flat anterior surface. Due to the haptics, a radial outward force is applied to the anterior surface.

Other A-IOLs

Not all A-IOLs are undergoing human trials. There are some lenses in development that are currently going through biocompatibility studies. Liliana Werner, MD, PhD, a researcher and director of the Intermountain Ocular Research Center at the University of Utah, provided *Review* with information about the latest devices undergoing biocompatibility studies using rabbit models.

"The company Adaptilens is developing what they call a biomimetic accommodating lens," informs Dr. Werner. "The design was conceived to imitate the elastic, young natural crystalline lens, and it's composed of a membrane filled with a proprietary high molecular weight polymer engineered with specific chemical, optical and mechanical properties to mimic human crystalline lens properties. The lens has been tested in cadaver eyes with capsular bags of varying sizes, demonstrating at least 4 D of accommodation. It uses the natural mechanism of accommodation of the eye. Current pre-clinical studies performed in the rabbit model in our laboratory are demonstrating biocompatibility and safety.

"The company Ocumetics is developing the Bionic lens," continues Dr. Werner. "This is a one-piece, silicone, air-filled shape-changing lens. There's an air-filled space between the optical elements; there's no fluid such as silicone oil within the lens. It can be inserted through a 3-mm incision, and it's fixated within the capsular bag; it was designed to deliver 3.25 D of accom-

AkkoLens

According to AkkoLens, the Lumina can provide patients with continuous "sharp" vision from 25 to 40 cm.

modation. The processes of accommodation and dis-accommodation happen fast, in less than a second. Biocompatibility is being evaluated in our lab in rabbit studies. During accommodation, with ciliary body contraction and zonular relaxation, there's an increase in the anterior-posterior dimension of the lens, increasing IOL power. And, during dis-accommodation, with ciliary body relaxation and increase in zonular tension, the anterior-posterior dimension decreases, decreasing the IOL power."

Future of A-IOLs

Once accommodation of a sort can be achieved in these lenses, the market is going to begin opening up. Unfortunately, there are several lenses in development and only a few researchers have had the opportunity to study and work with them. Should young ophthalmologist be worried about learning the particular implantation techniques for these lenses? Probably not, since both Dr. Waring and Dr. Garg agree that there'll only be a small learning curve when implanting these lenses.

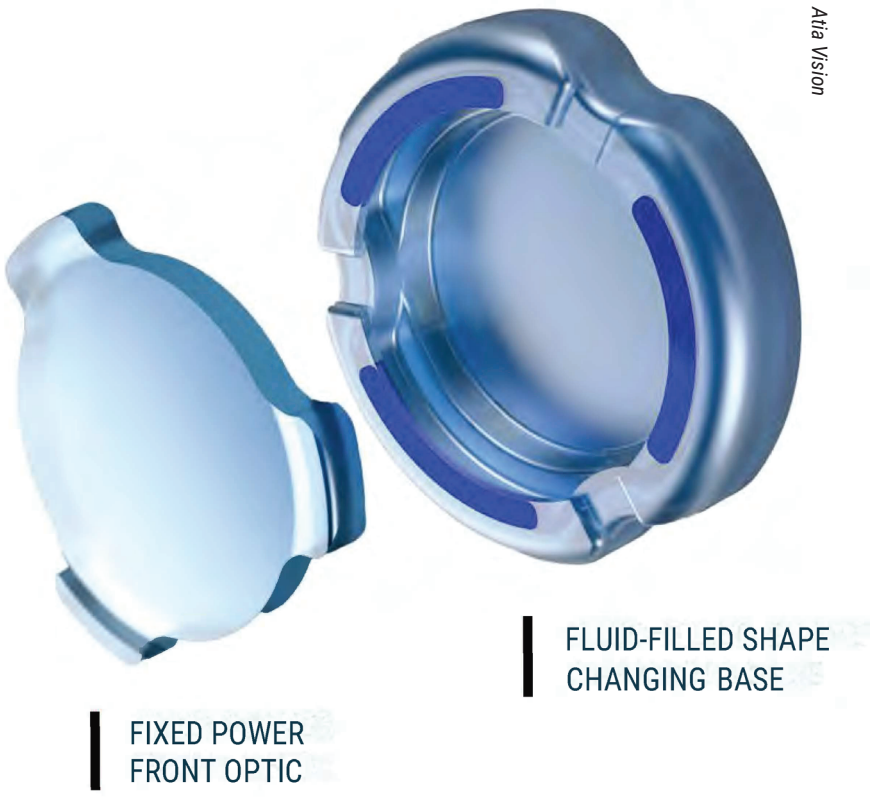
"I think time will tell what will happen as we get further into trials to figure out what actual learnings there are for the particular lenses, and I'm sure there'll be nuances for each lens depending on if it's one-piece or two-piece, where you have to place it and how it gets assembled," explains Dr. Garg. "So, certainly it will be something that'll require some training, like any new technology does. We learned that with MIGS and we learned that with other intraocular surgeries such as secondary lens implantation. There's aways new skillsets that we're learning. I don't anticipate this being any different than that.

"Do I think that it'll be a very high bar to achieve? I don't," continues Dr. Garg. "I think most of these lenses are going to be fairly straightforward, but I don't think it's going to be the same as just implanting a one-piece into the capsular bag."

Dr. Waring adds, "I think the learning curve will be modest. It's part of the innovation cycle where we optimize techniques. The first-generation technology inevitably has enhancements over time for ease of use and increased efficacy. So, yes, we do anticipate a modest adoption period and optimization process over time which is in line with new technology employment."

Eventually, these devices will undergo FDA trials with market approval in their sights. It seems that ophthalmologists have been anticipating this technology since it was first theorized. "As they are essentially monofocal lenses, accommodating IOLs are still considered the holy grail of presbyopia correction," says Dr. Werner.

Surgeons are hopeful for the future of lens replacement surgery as more accommodating IOLs begin development. "Our hope is that different lenses make it to market that can build one on top of the other to give us options for our patients," says Dr. Garg. "Our goal as a surgeon is to have choices for our patients so that we can tailor the best lens to meet their needs." ◀



Atia Vision

OmniVu's fluid-filled shape changing base is inserted first into the capsular bag followed by the fixed power front optic, which docks into the base.

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FIRST-LINE TREATMENT: SLT OR MEDICATION?

Medication has historically been the gold standard, but recent success with SLT is giving surgeons more options.

MICHELLE STEPHENSON
CONTRIBUTING EDITOR

Traditionally, glaucoma treatment has consisted of medication, then laser if needed, and then, if it were necessary, surgery. However, laser proponents say that, due to medication's drawbacks—such as non-compliance—and the safety and efficacy of selective laser trabeculoplasty being demonstrated in recent studies, SLT should be considered the first-line treatment. Of course, this is an opinion not shared by all. Here, glaucoma specialists review the pros and cons of laser as a first-line option.

The Medical Route

One of the disadvantages of glaucoma medication is patient non-compliance. "Like any other medication, it doesn't work unless you take it. There are very few ocular medications that are used less than once a day. We know that our patients aren't compliant in some cases. In other cases, they are extremely compliant because they're very worried about losing their vision, if they've had good information as far as the necessity for treatment," says Richard Lehrer, MD, who's in practice in Canton, Ohio.

Overland Park, Kansas, physician Michael Stiles says one of the benefits of going the medication route is the fact that the effects are reversible. "If patients don't like the medication, they can just simply stop taking it, go on to something else, or then consider laser," he says. "In the real-world, we're not bound to randomized trials. After hearing the pros and cons of both, some patients will just feel more comfortable trying medication. The reversibility of it, as compared to a one-time procedure, gives patients some comfort. Additionally, most medications don't lose their efficacy over time, so it is something that can be used for a long period of time."

Dr. Stiles adds, however, that one of the downsides to medications is the potential for side effects. "We're finding more and more evidence that preservatives, like benzalkonium chloride, have an effect on the ocular surface, both short- and long-term, as far as quality of life is concerned," he says. "For example, contrast sensitivity is less in patients who are on eye drops, and there can be long-term cosmetic side effects with the prostaglandins. Laser treatment has none of these issues. This is a concern because, if you need subsequent incisional filtration surgery, medication use can set you up for failure because of the beating the ocular surface has taken over the years with medications."

SLT

For proponents, SLT has several benefits over medication. According to Dr. Lehrer, "one pro of SLT is that it's effective for a decent period of time, meaning at least one year. I've seen it last up to 20 years. In patients who have mild glaucoma and don't require further therapy, that may be the only thing they need, and, therefore, they aren't required to take daily eye drops or do other further treatment," he says. "A con is that it sometimes doesn't work. In my hands, the success rate is about 85 percent. Fifteen percent of the time, it won't do anything, and very rarely, it may cause some inflammation or a transient rise in intraocular pressure."

Dr. Stiles adds that SLT has been found in clinical trials to be as safe as medications, and has a good success rate. "Initial treatment is equal to at least one medication and, long-term, the

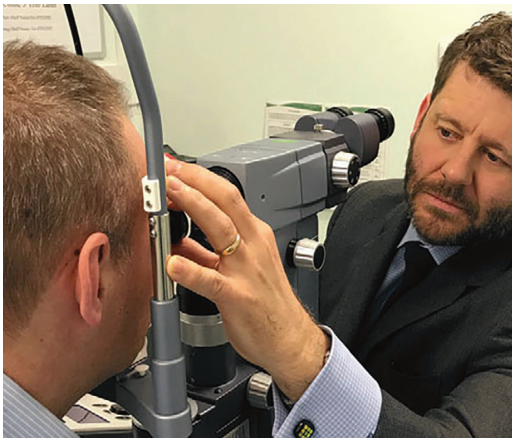
This article has no commercial sponsorship. **Drs. Harasymowycz, Lehrer** and **Stiles** have no financial interests to disclose.

visual field stability has been found to be superior to medications," he says. "The downside is that it doesn't work in all patients, and it doesn't last forever. Additionally, it's a 'procedure,' which gives some patients pause, but, to counteract that, we can safely say that it's no more dangerous than starting medications."

In an extension of the Laser in Glaucoma and Ocular Hypertension (LiGHT) Trial,[1] SLT was found to be safe for the treatment of open-angle glaucoma and ocular hypertension, providing better long-term disease control than initial drop therapy, with reduced need for incisional glaucoma and cataract surgery over six years of follow-up.

The LiGHT Trial showed that SLT is clinically effective and cost-effective as a primary treatment of both open-angle glaucoma and ocular hypertension at three years. A prospective, randomized, multicenter extension of the study examined health-related quality of life (HRQoL) and clinical effectiveness of initial treatment with SLT compared with IOP-lowering eye drops after six years of treatment. The study included treatment-naive eyes with open-angle glaucoma or ocular hypertension. Patients were randomly assigned to initial treatment with SLT or IOP-lowering drops. After the initial three years of the trial, patients in the SLT group were allowed a third SLT if needed, while patients in the drops group were allowed SLT as a treatment switch or escalation.

Of the 692 patients completing three years in the LiGHT Trial, 633 patients entered the extension, and 524 patients completed six years in the trial. At six years, no significant differences were found for the EuroQol EQ-5D 5 Levels, Glaucoma Utility Index, and Glaucoma Quality of Life-15. The SLT group had better Glaucoma Symptom Scale scores than the drops group (83.6 ± 18.1 vs. 81.3 ± 17.3, respectively). Of eyes that were initially treated with SLT, 69.8 percent remained at or less than the target IOP without the need for medical or surgical treatment. More eyes in the drops group experienced disease progression (26.8 percent vs. 19.6 percent, respectively). Trabeculectomy was required in 32 eyes in the drops group compared with 13 eyes in the SLT group, and more cataract surgeries occurred in the drops group (95 compared with 57 eyes). No serious laser-related adverse events occurred.



Prof. Gus Gazzard

For patients with mild glaucoma, SLT may be all they need for years, proponents say.

According to Paul Harasymowycz, MD, who's in practice in Montreal, "the LiGHT Trial results have demonstrated that first-line SLT treatment may actually be beneficial for patients over a medical treatment, as well as being cost-effective. One should always remember, however, that SLT is not without potential complications itself," he says. "Although very rare, someone did refer a case to me recently where a -9 myope who had bilateral SLT ended up with a hypermetropization, so the refraction changed to -4 in one eye and -5 in the other—a large shift. It seems to happen in patients who have pre-existing inflammatory conditions. If too much fluorescein is left in the eye, I'm concerned that the fluorescein on the surface of the eye may be up taken by the light, and that perhaps may be contributing to that process. When we're checking the pressure before the SLT, we definitely make sure that there's not too much fluorescein used, and we wash it out with artificial tears. You must weigh the pros and cons of both."

Another study examining the results of eight trials found that SLT is safe and has a low incidence of ocular side effects.[2] The researchers concluded that SLT can be the first-line choice of therapy for open-angle glaucoma.

This review article included randomized controlled trials conducted before August 2019 that compared the efficacy of SLT and medication only for open-angle glaucoma. Studies were selected using PubMed, Embase, Cochrane Library and Web of Science. Grading of Recommendations, Assessment, Development and Evaluations (GRADE) methodology was used to rate the quality of the body of evidence.

The eight trials comprised 1,229 total patients. Overall results revealed no significant differences between SLT and medication-only treatments regarding IOP reduction and the success rate of IOP control. The SLT group required significantly fewer medications compared with the medication-only group.

Which to Choose?

Both medication and SLT are great options for first-line therapy, so physicians say it can be difficult to choose between the two. Dr. Lehrer gives patients the option to choose. "If a patient has never been treated and has an IOP in the mid-20s, I think SLT is a very reasonable first-line option for them. Obviously, if they come into the office and their pressure is 45 or 50, they're going to start on medication right away. But, for patients with mild to moderate glaucoma who have never been treated, I think SLT is a very good first-line option. I give patients all of the statistics. I tell them that the chance of the laser harming their eye is very low. I tell them that the chance of the laser working for at least a year is extremely good. Many of them do not want to take a medicine every day," he says.

Dr. Stiles agrees and says he presents both medication and SLT to patients as options for first-line treatment. "I'm very honest with them about the LiGHT trial. With this evidence, I can safely say that I prefer laser first. But, they're not bound to a trial. If they want to try the medications first, they can, but I do go

over all of the pros and cons. I think the pros heavily favor laser first as opposed to medications first. That's the way I lay it out, and the majority will pick laser first," Dr. Stiles says.

Dr. Harasymowycz considers target pressure when recommending a treatment. "I would love for patients' pressures to be 12 or lower with no side effects. Studies have suggested that the longer we follow our glaucoma patients, the more often we see some degree of progression, depending on the intraocular pressure," he says.

For example, the Canadian Glaucoma Study identified four independent predictive factors for glaucomatous field progression in addition to intraocular pressure.[3] This multicenter prospective longitudinal study included 258 patients (131 men and 127 women), with a median age of 65 years. Baseline systemic measures included assessment of peripheral vasospasm and markers for hematopathology, coagulopathy and immunopathology. Patients were followed up at four-month intervals with perimetry, optic disc imaging and a standardized interventional protocol for IOP control.

Patients were followed for a median of 5.3 years, with 167 patients (64.7 percent) being followed for five or more years and 67 patients (26 percent) being followed for seven years or more. Four factors were associated with progression: abnormal baseline anticardiolipin antibody levels; older age at baseline; female sex; and higher mean follow-up IOP before progression.

"If I have a newly diagnosed glaucoma patient, we really want to reach more aggressive IOP targets. It would be rare for SLT or prostaglandins to lower the pressure more than 30 to 35 percent. So, if someone comes in with a pressure of 30, he or she may not necessarily reach the target pressure that we want with only one treatment," Dr. Harasymowycz explains.

He often prefers to start patients on a prostaglandin analog and reserve laser therapy for later. "After two months, we know the efficacy of that drop, and if we still haven't achieved our target pressure, then we might add SLT as a second-line. However, if someone comes in with very little damage and doesn't have a very high starting IOP, then SLT is definitely something worth trying first-line. The Canadian Glaucoma Study backs that," Dr. Harasymowycz says.

He also considers SLT first if patients cannot afford medication or if they have been non-compliant in the past. "I think it's important with both treatment options for patients to understand that this isn't a curative treatment, and that they will have to be followed up. As long as they know the pros and cons of each, I think we can help guide them to choose the treatment that's best for them," he concludes. ◀

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MAXIMIZING VISION AFTER CATARACT SURGERY

Most surgeries are successful, but there are some patients who aren't happy with their vision for no obvious reason, and surgeons have to delve deeper.

CATLIN NALLEY
CONTRIBUTING EDITOR

With more than three million Americans undergoing cataract surgery each year, it is one of the most common—and safest—procedures performed in the United States. And ongoing advancements in surgical techniques and intraocular lens technology support the efforts of ophthalmologists who continuously strive to ensure their patients have the best possible visual outcomes.

Maximizing outcomes depends on a number of factors and doesn't end with the removal of the cataract and the implantation of an IOL. "The key aspects of patient satisfaction after cataract surgery today include a meticulous preoperative evaluation, judicious patient selection and a comprehensive patient education to set the appropriate postoperative expectations," says Garden City, New York's Eric Donnenfeld, MD, while noting that postoperative management also plays a crucial role in successful cataract surgery outcomes, and part of that is addressing patient concerns and complaints.

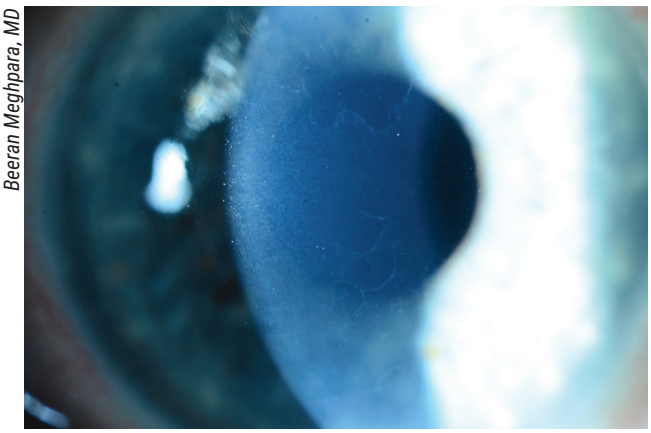
However, what do you do if you have run the appropriate tests and everything (i.e., the macula, IOL, cornea) looks normal yet the patient is still having an issue with their vision? In this article, we'll explore various strategies to maximize vision after cataract surgery and IOL implantation as well as how to help their patients navigate the process.

Clinical Pearls for Surgeons

When the standard exams all come back normal, taking a step back and carefully considering how best to proceed can help ophthalmologists uncover the underlying issue and appropriate intervention. Below ophthalmologists offer advice on how they approach these cases.

If a patient isn't satisfied with their visual outcome post-surgery, Daniel Chang, MD, of Empire & Laser in Bakersfield, California, begins by making sure he has a clear understanding of the issue. Is it quality of vision? Range of vision? Dysphotopsia?

To determine next steps, it's important to get as much detail from the patients as possible. Dr. Chang will often ask questions like, "What specific thing are you doing and when does it specifically bother you?" This allows you to get a detailed picture of the problem and from there you can figure out the cause and best



Beeran Meghpara, MD

A slit lamp photo of subtle epithelial basement membrane dystrophy.

This article has no commercial sponsorship.

Dr. Chang consults for Johnson & Johnson Vision and Carl Zeiss. **Dr. Davidson** consults for Zeiss, Johnson & Johnson Vision, Alcon and Centricity Vision. **Dr. Donnenfeld** consults for Allergan, Alcon, Bausch & Lomb and Johnson & Johnson Vision. **Dr. Meghpara** reports no relevant disclosures.

treatment approach.

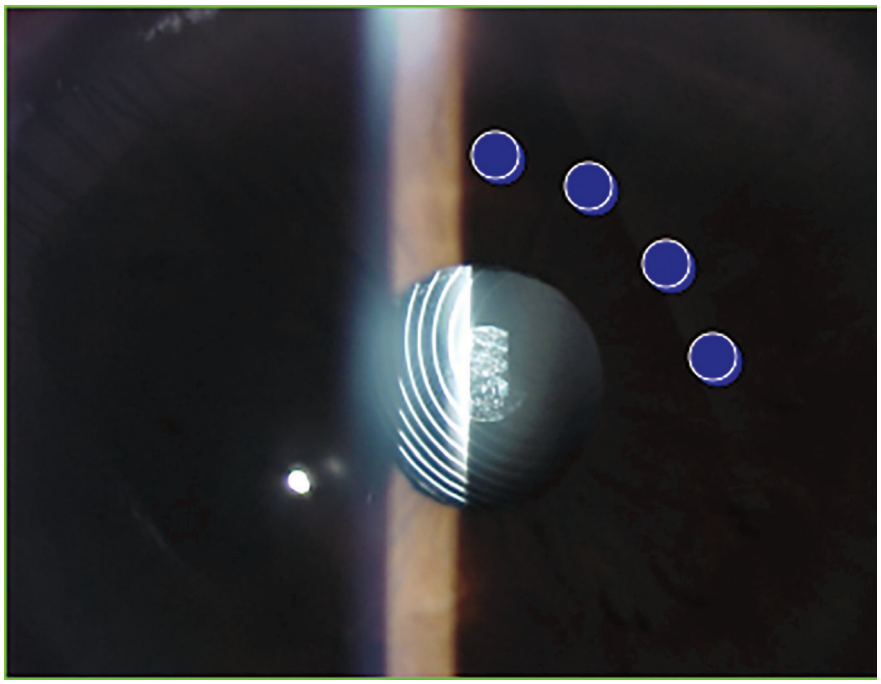
Don't overlook dry eye, advises Dr. Donnenfeld. "Even if the patient's cornea looks normal, very commonly you will find irregularities that explain the vision, and I look for a history of visual fluctuation. Any time the vision fluctuates, I consider ocular surface disease," he explains. "In addition to a visual inspection of the ocular surface, I add lissamine green to highlight any staining irregularities in the conjunctiva and provide a more in-depth evaluation of the ocular surface."

Additionally, Dr. Donnenfeld will use topography to find slight irregularities that may be compromising a patient's vision. "When I see these problems, I will often take a more aggressive approach to manage the ocular surface." This includes perfluorohexyloctane (Meibo), which he has found stabilizes the surface and is a good refractive solution. Punctal plugs can also have a role as well as some low-dose steroids, he notes. "Even the mildest tear film abnormalities, which can be very easily missed, can cause significant patient dissatisfaction."

Wills Eye's Beeran Meghpara, MD, reiterated the value of a corneal topography for these cases. "It's very easy to miss subtle changes, especially if you're a doctor who doesn't specialize in the cornea. Therefore, I always perform a corneal topography on these patients, which can help pick up issues such as subtle epithelial basement membrane dystrophy that you may not be able to see or subtle areas of irregular astigmatism," he says, noting the importance of looking at the Placido ring image when using this tool.

Dr. Meghpara will also get an OCT of the macula when trying to determine the reason behind a patient's vision complaints. "Even if the retina appears normal, there are some changes, such as a subtle epiretinal membrane, that you can't see when using a slit lamp," he explains.

A very commonly overlooked problem, according to Dr. Donnenfeld, is



Eric Donnenfeld, MD

For patients whose pupil isn't coincident with the center of the lens, Eric Donnenfeld, MD, says laser iridoplasty can help pull the pupil over the center of the lens. He places four or five spots where he wants to move the pupil, with a setting of 500-milliwatts, 500 microseconds, 500 millijoules.

one that wasn't always on his checklist either. "In the past I didn't always include the vitreous in my standard workup, but what we're seeing now is that a lot of patients, particularly those with multifocal lenses, who have even mild vitreous opacification can have significant loss of quality of vision," he says, while emphasizing the need for a dilated eye exam.

"Vitreous floaters are an often underdiagnosed reason for patient dissatisfaction after multifocal IOL surgery," adds Dr. Meghpara. "In our practice, we'll refer patients to a retinal surgeon for vitrectomy. Afterwards, patients are very grateful and happy with the results. Some ophthalmologists may opt to address floaters with an office-based approach, such as a YAG laser."

When addressing visual concerns post-surgery, Dr. Meghpara suggests tools like iTrace can be helpful. "This diagnostic tool performs both corneal topography and wavefront aberrometry," he says. "If you conduct this test on a patient after cataract surgery, the image quality should be excellent (9 or 10 on a scale of 10). However, if that image quality is low, say a 5 or 6, but everything looks crystal clear then you are missing something. Oftentimes, that is the vitreous."

Another easily missed abnormality, notes Dr. Donnenfeld, is related to the angle kappa—the angle between the pupillary axis and the visual axis. "When the pupils aren't coincident with the central lens that will induce coma, glare and some halo as well."

In those cases, when other options have been exhausted, Dr. Donnenfeld will perform an argon-laser iridoplasty. "I can actually put laser spots onto the iris and pull the pupil over the center of the lens to make the lens more productive. Using a 500-milliwatt, 500 microsecond and 500 millijoule procedure, I place four or five spots in the area of the iris where I want to move the pupil. So, if the pupil is decentered temporally, I place the spots nasally and you can move the pupil very effectively into the area."

Refraction is another key component, notes Richard Davidson, MD,

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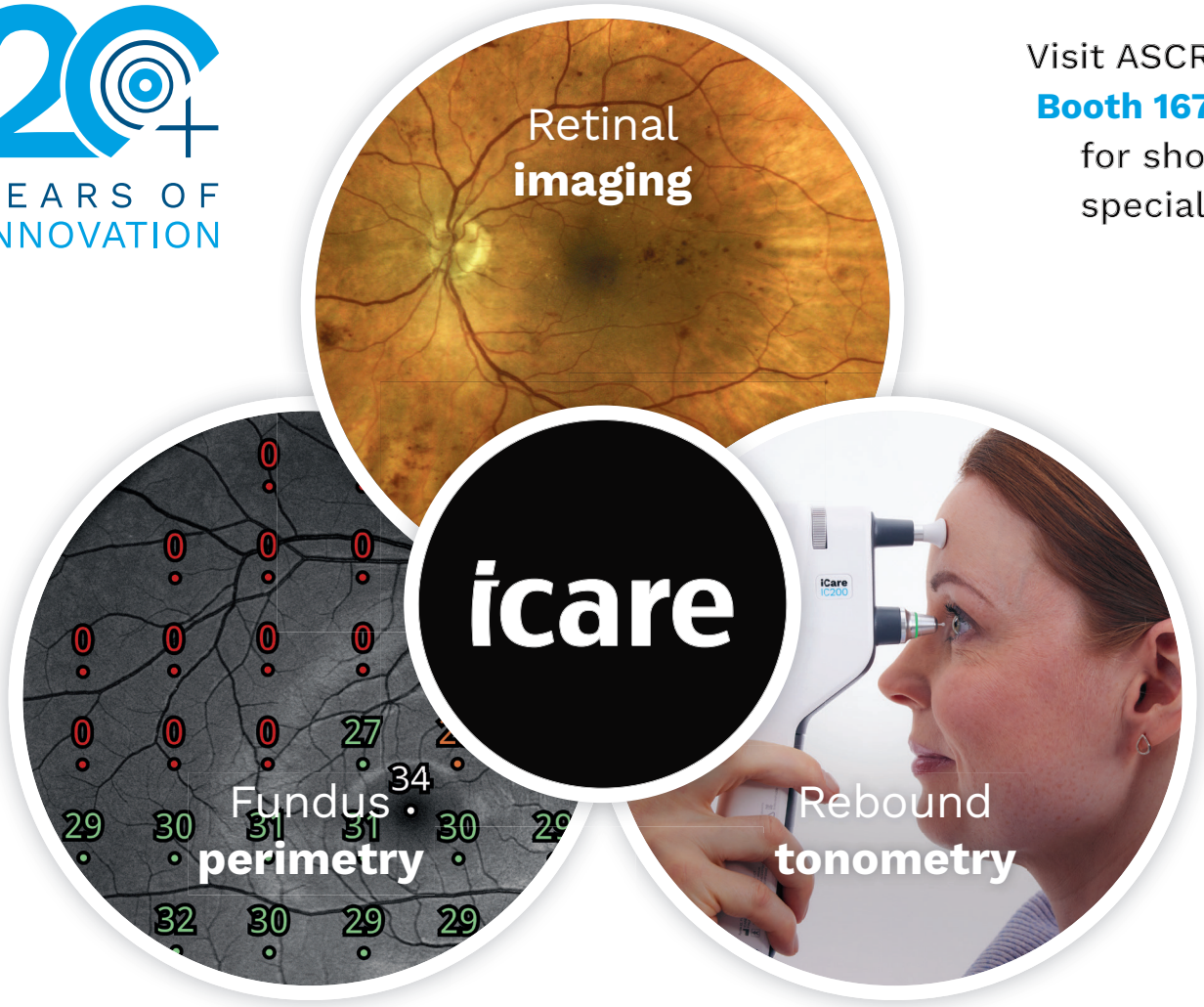

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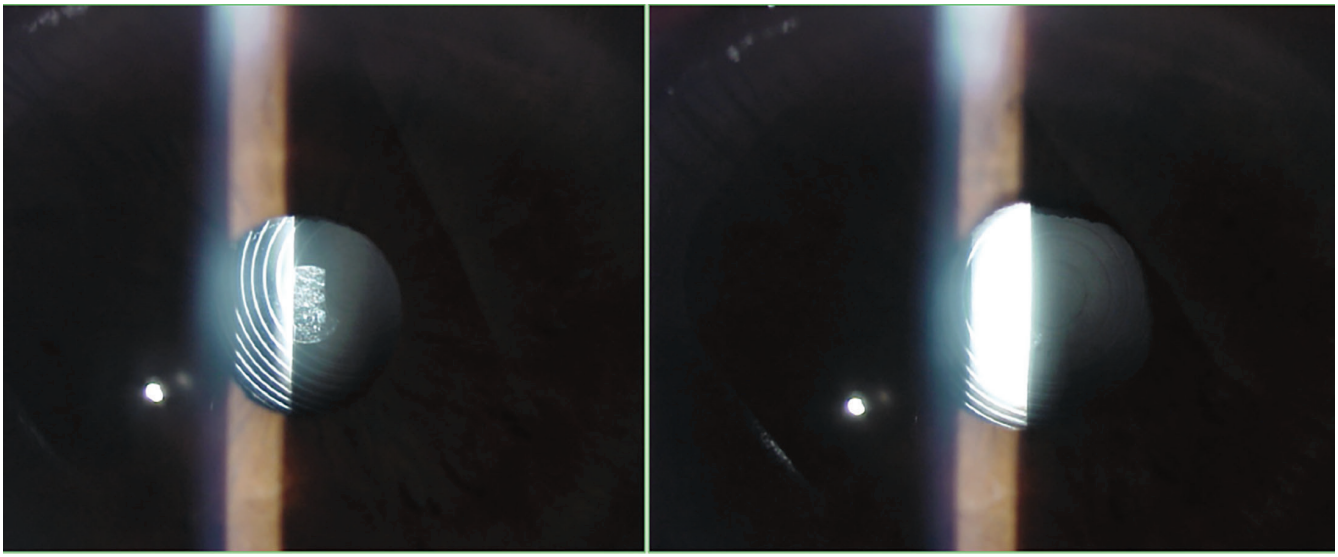


Eric Donnenfeld, MD

The eye in the previous figure before laser iridoplasty (left) and after (right) showing the pupil has moved to a position that allows the center of the lens to be more coincident with the center of the pupil.

of Aurora, Colorado. "Our team will always conduct a thorough eye exam. This includes visual acuity and refraction. We will refract every one of these patients and really try to nail down a good refraction because even if someone is '20/20,' they still may have a little residual astigmatism, for instance, and that may be enough to bother them."

Another consideration for surgeons is when additional procedures, such as a YAG laser capsulotomy or PRK enhancement, are warranted. For example, Dr. Davidson recently saw a patient who was one-week postop in her right eye and three-weeks postop in her left eye. She has multifocal lenses and was happy with the vision in her right eye but was complaining of blurriness in her left.

"Based on our discussion, this was not a lens adaptation issue," he says. "We refracted the left eye and even with refraction the vision quality wasn't as good as she wants it to be.

"I know she doesn't have any macular edema," he continues. "So, I looked at her capsule and she's got a little wrinkling. It's not a lot but enough that it can drop her vision enough, especially compared to the other eye. Therefore, I recommended a YAG laser capsulotomy. We know that with patients who have multifocal lenses there's going to be a lower threshold to do a YAG compared to someone with a monofocal lens."

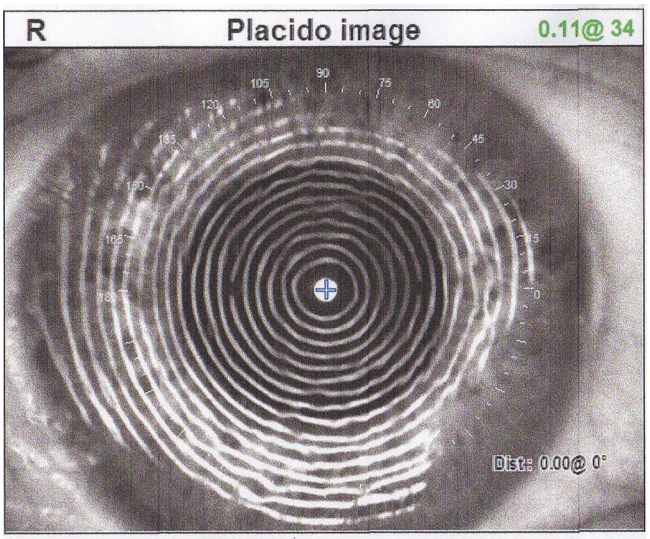
Dr. Davidson notes that it can be challenging to determine if, and when, these types of interventions are necessary. This is particularly true when they have only had surgery in the first eye. Are they unhappy with the lens? Are they unhappy because they have a cataract in the other eye? Are they unhappy because they have posterior capsule opacification and need a YAG?

"This is always one of the surgeon's most frustrating and challenging dilemmas," says Dr. Davidson, while adding that there is no one-size-fits-all approach. "It really comes down to a variety of factors, including how the patient did immediately postop, how bad the cataract is in the other eye, do they have a lot of anisometropia, etc. If the patient is happy with the type of lens and I've done everything else, I'd consider a YAG capsulotomy."

When it comes to PRK enhancement, Dr. Davidson waits a minimum of six weeks before considering it. "I want to see how they're functioning as well as make sure that the lens has settled in and that they have consistent refractive error," he explains. "If we're going to move forward to a PRK enhancement, I want to have a complete picture to ensure we're providing our patients with the approach that best fits their individual needs."

Determining if a lens exchange is

(Continued on p. 68)



Beeran Meghpara, MD

A Placido ring image on topography can help pick up subtle changes on the cornea.

INTO THE WEEDS OF REFRACTIVE SCREENING

Experts share how they decide whether or not a cornea-based procedure is appropriate for a potential candidate.

CHRISTINE YUE LEONARD
SENIOR ASSOCIATE EDITOR

Holding safety paramount to efficacy is the overarching principle for determining whether a patient is a candidate for corneal-based refractive surgery, according to Gaurav Prakash, MD, an assistant professor of ophthalmology at the University of Pittsburgh School of Medicine. "You will have some patients who are borderline, and you may have to say 'no' or offer something else," he says. "That said, if I randomly see 100 patients, about 60 to 70 percent will probably fit into some sort of refractive surgery, corneal-based or otherwise."

Here, veteran surgeons discuss the steps they take and the red flags they look for when evaluating prospective corneal refractive surgery patients.

Communicating Expectations

"Giving patients very realistic expectations early on is important," says Dr. Prakash. "I always tell patients that the aim is to make them less dependent on glasses, but that might mean they still need glasses for challenging tasks, and they'll eventually need glasses for reading as they grow older. If the patient tells me they definitely want to be free of glasses, then refractive surgery and especially corneal refractive surgery is probably not for them. There's always an amount of variation in outcome that we have to be mindful of.

"Additionally, I mention that healing can vary from person to person," he adds. "There are risks with corneal refractive surgery as well as certain side effects. Patients should expect some amount of dryness, for which we give them drops, and may have some halos and glare in the night when driving. LASIK flap dislocation is a potential risk."

Helen K. Wu, MD, of the New England Eye Center at Tufts Medical Center in Boston, notes that setting patient expectations further down the line is also important. She educates patients about cataract formation and about the eventual need for cataract surgery. "I tell them what to expect over years' time, so they understand that laser vision correction doesn't induce early cataracts. I also mention that laser vision correction changes the shape of the cornea, necessitating alternative methods of calculating lens implant power for cataract surgery to get the best refractive outcome."

Ascertaining Visual Goals

Part of the screening process involves trying to understand what the patient's goals are and how to meet those goals. The first thing Dr. Wu asks patients is why they want to have LASIK done. "Occasionally, these goals stem from vocational requirements. However, certain professions, like first responders such as firefighters, face scenarios where LASIK flaps might not be ideal—entering smoke-filled buildings, for instance. Similarly, individuals in the military or involved in contact sports are susceptible to facial impact, making them less suitable candidates for LASIK."

Correcting both eyes for distance is a common strategy for young patients in their 20s, but this approach might not meet the visual goals of some older patients, says Dr. Wu. "When we see patients in their 40s, I don't automatically correct

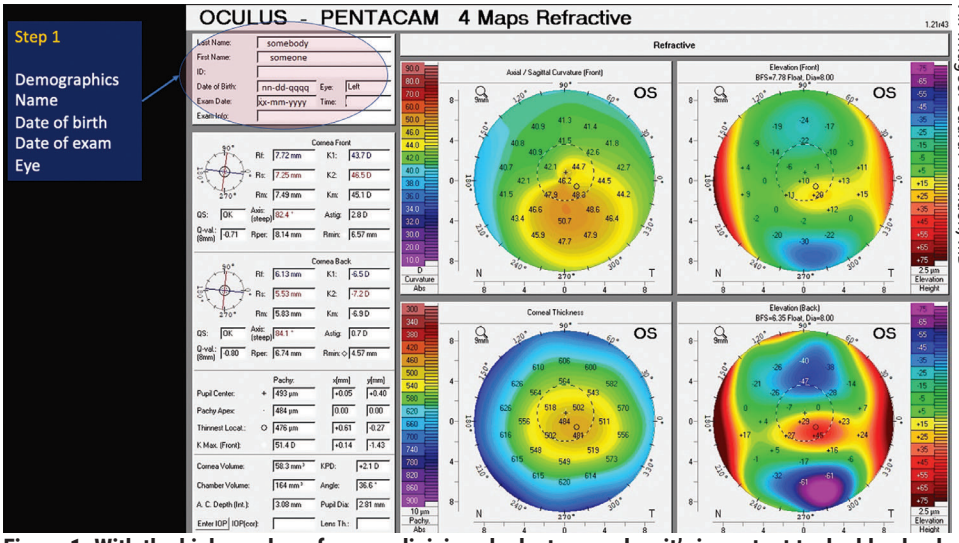
This article has no commercial sponsorship. **Dr. Wu, Dr. Weikert** and **Dr. Prakash** have no related financial disclosures.

both eyes for distance," she says. "Their aim may be to eliminate the need for glasses entirely, but given their age, they'll soon require reading glasses as natural accommodation diminishes. It's crucial for them to comprehend this. I prefer to present blended vision as an alternative."

A trial with disposable contact lenses can help determine candidacy for blended vision (monovision). "I work side-by-side with my optometry colleague when I'm seeing refractive surgery consultations," Dr. Wu says. "She might provide trial lenses to achieve plano in their dominant eye and, for example, -1 D, -1.25 D, or -1.5 D in their non-dominant eye, depending on their age. Then we assess their tolerance to this setup."

She says that while a five-day trial is often done, it may take more time than that to get completely used to blended vision. "If they tell me they're happy with it right away, that's a good sign," she says. "If patients experience difficulty adapting, we can assist by allowing them to wear their contacts for a bit longer to see if their brain adjusts. It's important to convey to highly motivated patients seeking freedom from glasses that complete elimination of glasses for reading fine print or in dim lighting may not be achievable."

Sometimes holding off on surgery is the best option. Young patients in their mid-20s interested in LASIK may need counseling about the potential for a myopic shift, especially if they're going to graduate school. "We call it graduate school myopia, or medical/law school myopia," Dr. Wu says. "Patients may experience a myopic shift after LASIK due to extensive reading or screen usage, or simply because they're in their mid-20s. If this isn't acceptable to them, they may opt to continue wearing contact lenses until they've completed graduate school and then reconsider. Over the years, I've observed patients, perhaps initially at -2 D, undergo treatment in their early 20s, only to return to -1 D after graduate school. This could be attributed to a normal myopic shift for them, but it's not uncommon. Refractive stability in your early 20s may vary depending on your activities."



All images: Gaurav Prakash, MD

Figure 1. With the high number of scans clinicians look at every day, it's important to double check that the topography matches the right patient in the EMR. In the upper left corner, review key demographics, including the patient's name, date of birth, date of exam and eye.

Dr. Prakash notes that the candidacy criteria for SMILE is similar to that of LASIK. "Any patient who isn't a good candidate for LASIK won't be a good candidate for SMILE," he says. "This new procedure might offer some advantages [over LASIK] because it doesn't have a flap, but it's not at the same point we're at with LASIK right now. Down the line, it might be a good treatment to consider but it's still a bit far away from the accuracy of treatment we're getting with LASIK."

Objective Screening

"Potential refractive patients will undergo a comprehensive eye exam to evaluate uncorrected and best-corrected vision at distance and near," explains Dr. Wu. This includes manifest refraction and cycloplegic refraction with cyclopentolate. Additionally, it's important to check intraocular pressures and do fluorescein staining to screen for ocular surface disease.

"Always look carefully at the lids and lashes," she advises. "Check for blepharitis and ensure the lids close properly, especially if the patient has a history of blepharoplasty. In some cases, the lids may not fully close after aggressive blepharoplasty, leading to potential exposure issues." Other key evaluations include dim-light and bright-light pupil size, eye dominance and checking the patient's current glasses prescription.

Mitchell P. Weikert, MD, of Baylor College of Medicine in Houston, says that dry eye and ocular surface disease are at the forefront of surgeons' minds when screening patients. He says that a careful history can help create a picture of a patient's subjective dryness while a slit lamp exam with fluorescein and/or lissamine green staining and tests such as tear breakup time can paint an objective picture. "We like to see a TBUT of seven to 10 seconds or more," he says. "When you start to get below seven seconds, it's not a deal-breaker, but we'll look more closely.

"Dry eye can masquerade as other things, such as forme fruste keratoconus, so before making any final judgments on corneal shape, be sure

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that the ocular surface is healthy," he continues. "On Placido topography, we'll look for blurring or smudging of the mires and potential reasons behind that. Distorted mires could be a sign of dry eye or ocular surface disease, but it can also reveal epithelial basement membrane dystrophy that might otherwise go unnoticed. There are indices for dry eye [on topography], but I find them more useful when managing a dry-eye patient over time to monitor treatment response. [For refractive screening], we're getting more of the gestalt by looking at the mires."

On Placido-based topography, Dr. Weikert says the old-school but still valid I-S value showing the average dioptric power difference between the inferior and superior hemispheres is a good early indicator of inferior steepening. "The I-S value should be below 1.2 to 1.4," he says. "You can visualize [inferior steepening] when you're looking at the topography."

Scheimpflug tomography is the gold standard for corneal evaluation today, says Dr. Prakash. "When trying to determine whether a patient will be a good candidate for corneal-based refractive surgery, we have to map the entire cornea," he says. "The earlier testing modalities using keratometry or surface topography were limited by the amount of cornea they could cover. If there were pathology in the periphery of the cornea, you might miss it. That's why Scheimpflug imaging has been revolutionary. Scheimpflug instruments such as Pentacam, Galilei and Sirius have a camera that rotates around the corneal curvature, resulting in a much better, parallax-free image of the periphery, which gives us much more information."

For ectasia risk assessment, many surgeons refer to the Belin/Ambrósio Enhanced Ectasia Display on Pentacam, an AI-based method for predicting ectasia susceptibility that provides a global view of the cornea. Dr. Prakash explains that this tool analyzes multiple factors, including how the cornea changes in terms of pachymetry from the center to the periphery, the steepest point, the relational thickness (how the cornea changes from point to point) and the overall posterior and anterior surfaces of the cornea, among other metrics.

"It results in a composite algorithm to see whether a cornea is at risk for developing ectasia or not," Dr. Prakash says. "The D-score has a range of normal, and anything outside of the normal range falls in the yellow zone—where you might think of [doing] a different procedure than LASIK, such as PRK or an ICL—or in the red zone, which is a red flag."

"On the elevation maps, the posterior surface is compared to a reference surface, which is usually a sphere," Dr. Weikert says. "When you see it deviate from that standard pattern, that will raise your suspicions. You can also use a toric reference surface and do a best-fit sphere or best-fit toric asphere, which will cancel out the normal, regular astigmatism on the elevation maps and reveal irregular, asymmetric astigmatism or foci of abnormal elevation. Other indices such as the posterior asphericity asymmetry index (PAAI), which looks at the difference between the lowest and highest points on the posterior elevation map fit with a toric asphere, can be helpful. If the PAAI is more than 21.5 µm, that's another red flag."

Other instruments such as Galilei and Anterion AS-OCT have their own ectasia analysis systems, and the Corvis ST's air-puff tonometry paired with Pentacam can also supplement analysis. However, there's no single index or analysis that will flag every patient, Dr. Weikert cautions. "Some may flag one individual and not another," he says. "If a patient has a small ectasia risk, you're never going to be able to totally rule someone out with just one device at this point. The more [data] you can get, the better, but you at least need to have the tomography, which gives you [data on] the front and back of the cornea, and the pachymetry across its surface."

How do you reconcile data from different devices? "If I use five devices and one shows a suspicious index, I'll have to weigh it by how much faith I have in that particular index versus the others," Dr. Weikert says. "But, if I see different indices lighting up on more than one device, then that will obviously

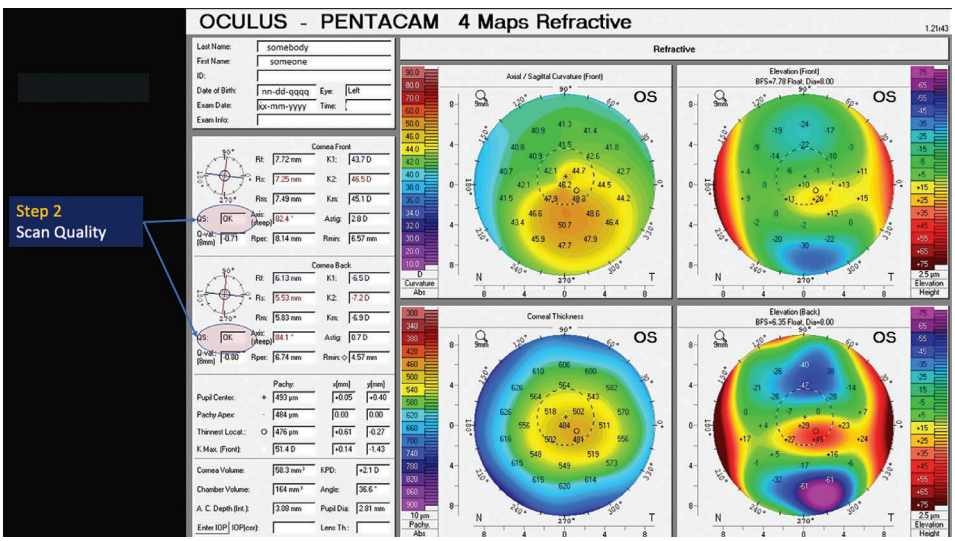

Figure 2. Most topographers include information on scan quality. Referring to the quality score can help rule out bad-quality scans and artifacts, but experts caution against relying solely on this indicator when evaluating scan quality.

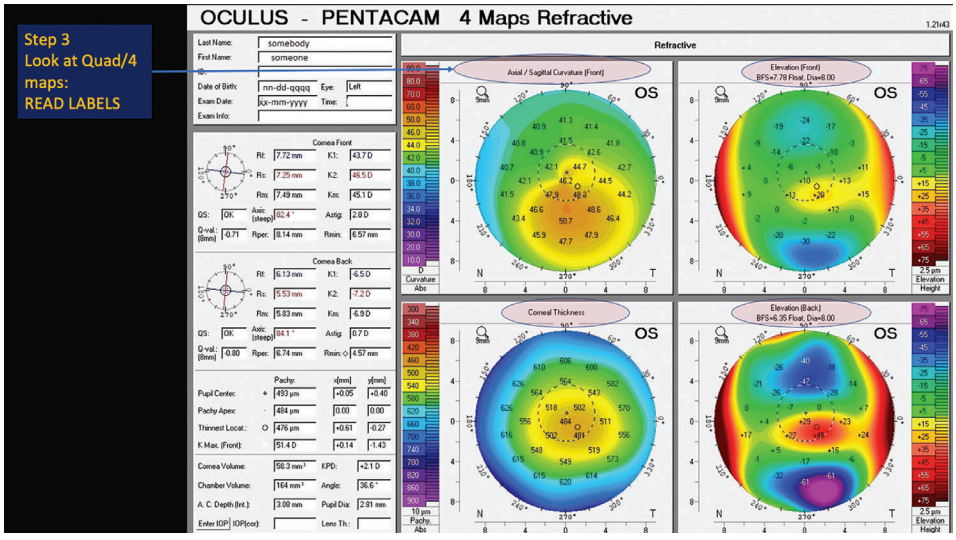

Figure 3. Double check the labels of each map to ensure you're looking at the correct one.

raise suspicions. A single index on a single device means you need to look a bit deeper, and it may not be a deal breaker."

He adds that most analysis systems judge whether the patient's cornea is safe for LASIK. "The indices are developed for post-LASIK ectasia," he says. "PRK can often still be a safe option since you're not going as deep into the cornea or creating a flap. That's not to say ectasia can't happen after PRK, but it's less likely."

Another of many corneal criteria that surgeons consider is percentage tissue altered, or the sum of the flap thickness and ablation depth, divided by the preoperative central corneal thickness. A value ≥40 percent thickness indicates a high risk for post-surgical ectasia.

"I generally don't do LASIK [on corneas] under 500 µm," Dr. Wu says. "I typically opt for PRK unless there's an abnormality in the corneal topography. Depending on the specific abnormality, or if the patient experiences severe dryness, I may refrain from proceeding with either LASIK or PRK. In such cases, addressing the dry eye first and ensuring the cornea is free from fluorescein staining before considering a corneal-based procedure is essential."

Dr. Wu says that in addition to pachymetry and Scheimpflug and Placido-based imaging, patients also undergo a dilated fundus exam and anterior segment OCT for epithelial thickness mapping. "We typically don't conduct macular OCT or nerve fiber layer OCT imaging unless there's a specific indication to do so. For example, if the patient's vision is inconsistent with the clinical exam, or if there's uncertainty regarding amblyopia or subtle retinal pathology, we may then opt for additional testing in such instances."

To mitigate potential false positives from the BAD-D scores, surgeons frequently cross-reference the results with epithelial thickness maps. "We often observe posterior elevation on Pentacam," notes Dr. Wu. "However, if epithelial mapping reveals a 'donut sign'—indicating an area of epithelial thinning overlying the area of posterior elevation seen on Pentacam, surrounded by epithelial thickening—it strengthens the likelihood that the posterior elevation seen on Pentacam is genuine. This significantly reduces the probability of proceeding with a corneal-based procedure for that patient."

Quick Tips for Scans

When evaluating scans, surgeons say to keep these points in mind:

• ***Check the quality.*** "It's simple 'garbage in, garbage out,' and if the quality isn't good—the patient may have been moving or the tester may be new or not have focused the instrument well—then the data is of no value," Dr. Prakash says. "It's easy to look at the scan and determine the quality. There are metrics for that, but obviously common sense is important too. If you don't feel that the scan looks good, do it again."

• ***Confirm the patient data.*** "Double check the EMR, especially when looking at multiple scans throughout the day," Dr. Prakash says. "Be sure to verify you're getting the correct patient, the correct eye and the correct date."

• ***Double check the scale.*** "Look at the scale of the scan," Dr. Prakash says. "Each device has its own criteria because they're proprietary. Many surgeons are used to a 0.5-D scale and a certain color pattern, but the colors and their corresponding ranges vary slightly from device to device. That said, it's better to stick to the same device and do the scan a couple of times."

Determining whether a scan is good or bad takes time. "Especially for surgeons just starting out with refractive surgery, the more scans you see, the more you learn," Dr. Prakash says. "There's a finite learning curve, and a bit of an art to assessing a good scan. It's more than just pure science. You may look at a scan and say, 'Oh, this looks abnormal,' even though it looks clinically okay. What do you do? You might offer a slightly safer option or a procedure more suited to that patient. For example, let's say a patient comes in with a borderline scan for even PRK. You could still do PRK in that patient, but you might want to offer an ICL because it's a safer option. It's that overarching principle of safety first."

"I don't think you can beat a visual interpretation of corneal topographic maps," Dr. Weikert says, agreeing that scan interpretation is more than

looking at the numbers. "Looking for symmetric bowties, asymmetric bowties, 'crab claws' or other patterns—that pattern recognition is very useful."

Red Flags

What other circumstances should give surgeons pause before deciding whether or not to proceed with a corneal-based refractive procedure? Here are a few key contraindications and some conditions that may warrant additional attention prior to surgery:

• ***Contact lens overwear or dry eye***. Patients in soft contact lenses are instructed to discontinue wear for a week, while those in rigid gas-permeable lenses are advised to wait two weeks at minimum. "If there's any suspicion of topographic irregularity due to dry eye or contact lens overwear, then we'll keep the patient out of their contact lenses longer—the longer, the better," Dr. Wu says. "If irregularities persist, we may schedule the patient for sequential corneal topography and tomography to monitor normalization. If normalization doesn't occur, we may discuss topo-guided procedures or potentially no procedure at all with the patient. If there are concerns about forme fruste keratoconus or if we're unsure about the shape and thickness of their cornea, we may explore options such as ICLs or other lens-based procedures."

• ***Epithelial basement membrane dystrophy***. In EBMD, the upper layer of epithelium is a bit loose and doesn't stick as well to the rest of the cornea, Dr. Prakash says. "These patients might not be good candidates for LASIK, but you can do PRK."

• ***Certain skin conditions***. "We perform an external examination of the patient's face to check for conditions such as rosacea or eczema or any other skin disorder that might affect the results of the laser vision correction," says Dr. Wu. "Atopic dermatitis, for example, can harbor gram-positive bacteria. If patients exhibit eczema around the lids or on the face, we may want to either treat that ourselves or have a dermatologist address it prior to the refractive procedure."

Another condition to inquire about is keloids. "A keloid is a pathological skin condition," Dr. Wu explains. "Keloids tend to be more prevalent in people of color, although this is not always the case, so I avoid making assumptions. I ask patients about any surgical scars or other scars they may have. While this association hasn't been firmly established in the literature, there are numerous anecdotal instances and several published case reports of individuals with keloids experiencing excessive haze after laser vision correction. Therefore, although I have performed LASIK on patients with keloids, I don't recommend surface ablation for them."

• ***Sensitivities and allergies***. Managing patients' allergies beforehand is an important part of the initial screening process. "Patients with uncontrolled allergies may rub their eyes quite a lot," Dr. Prakash says. "I definitely want to take care of that first."

He says he once had a patient with papillae who had been referred for refractive surgery due to contact lens intolerance. "The contact lenses were causing the papillae," he says. "We put her on olopatadine for a few months to control the papillae and then once it was resolved we did the surgery. If patients have active allergies or other triggers we shouldn't do refractive surgery at that point. Refractive surgery is an elective, planned procedure that should be done only when the eye is most optimized."

• ***Previous eye surgery or trauma***. "Eye trauma causing a rupture in a cornea unfortunately happens, and any refractive surgery will become very challenging on that eye," Dr. Prakash says. "In these patients we have bigger issues than to get them out of glasses, so refractive surgery is probably not a good idea.

"For a previous surgery, it depends on what's been done," he continues. "Say a patient had cataract surgery done when they were young and unfortunately had a pretty big refractive error left, -4 or -5 D. Or they had cataract surgery when they were young and as they've grown, the eye has changed and now they have glasses which are very thick. Refractive surgery is definitely an option provided they have a normal cornea with a stable refractive error.

"Patients with significant, deep

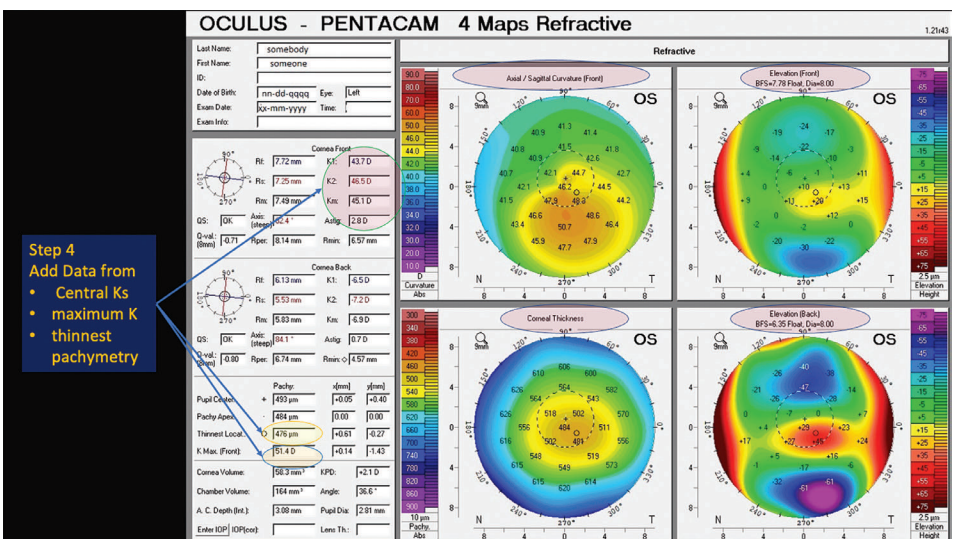

Figure 4. Add the data from central Ks, maximum K and thinnest pachymetry.

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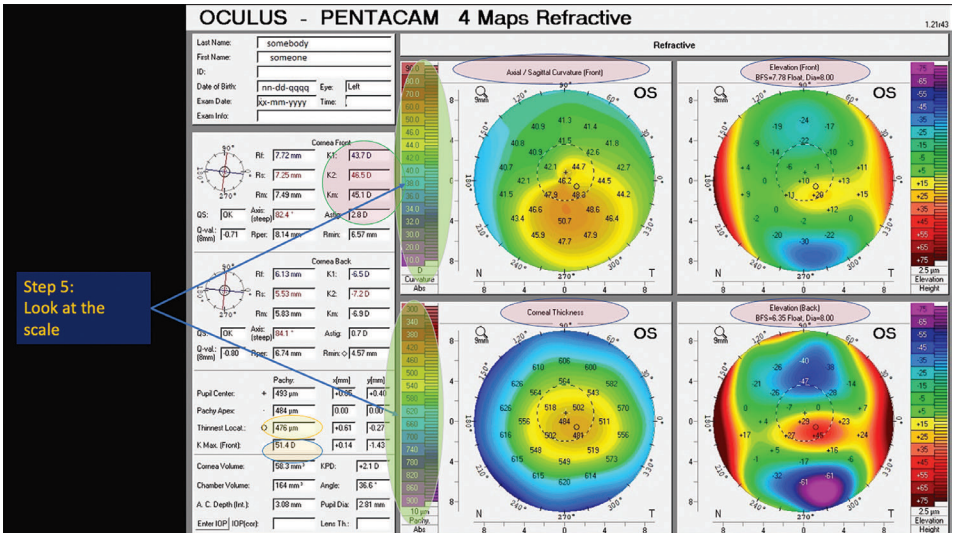

Figure 5. Always double check the scan's scale, especially if looking at scans from multiple devices since each device has its own proprietary criteria. The corresponding colors and ranges may differ slightly among devices.

scarring on the cornea from, say, a corneal ulcer, may not be good candidates," he says. "You could do PTK for a faint scar to clean up the cornea and then do PRK."

Previous retina surgery may require some more planning. "These patients can get refractive surgery, but we'd run it by a retina specialist to make sure there's nothing else happening in the eye," Dr. Prakash says. "There's always a small probability of pushing on the back of the eye, making it weaker, when doing LASIK. That risk is less with PRK, so that's an option. If a patient who had retinal detachment surgery wants to be less dependent on glasses down the line, we can do PRK but not LASIK."

• ***Autoimmune diseases.*** Performing a comprehensive medical history review can help identify conditions that may indicate poor candidacy for laser vision correction. Dr. Wu explains that she's less inclined to proceed with a laser vision correction procedure in patients with autoimmune diseases like rheumatoid arthritis or systemic lupus erythematosus, or in those with a family history of autoimmune diseases, due to concerns regarding potential disruption in wound healing or corneal melting. "Studies[1] indicate that patients who are well-controlled and don't have dry eye can achieve good results, and I certainly concur with that," Dr. Wu adds. "However, as a general practice, I would likely recommend lens-based procedures for such patients."

She says ICLs are a great option for young patients with autoimmune diseases. "I often prescribe perioperative oral steroids to modulate their wound-healing," she says. "Generally, the dry eye resulting from a lens-based procedure is more manageable and shorter-lived than a corneal-based procedure." Similarly, Dr. Wu says she exercises an extra degree of caution in patients with diabetes and diabetic retinopathy. "These patients may experience poor epithelial wound healing and an increased risk for infection, making them less suitable for PRK, and I may lean toward LASIK instead. If their disease is poorly controlled, they have diabetic retinopathy and they're young, then then they may not be the most suitable candidate for any sort of procedure."

• ***Neurologic conditions.*** "It's important to ask about systemic conditions that may be associated with nerve abnormalities, such as multiple sclerosis, diabetes, autoimmune disease, small fiber neuropathy or fibromyalgia," Dr. Wu says. "Damage to the corneal nerves from trauma, surgery, dry eye or underlying systemic conditions can cause the nerves to regenerate abnormally, resulting in their sending off pain signals without a stimulus or with a subthreshold stimulus. Individuals

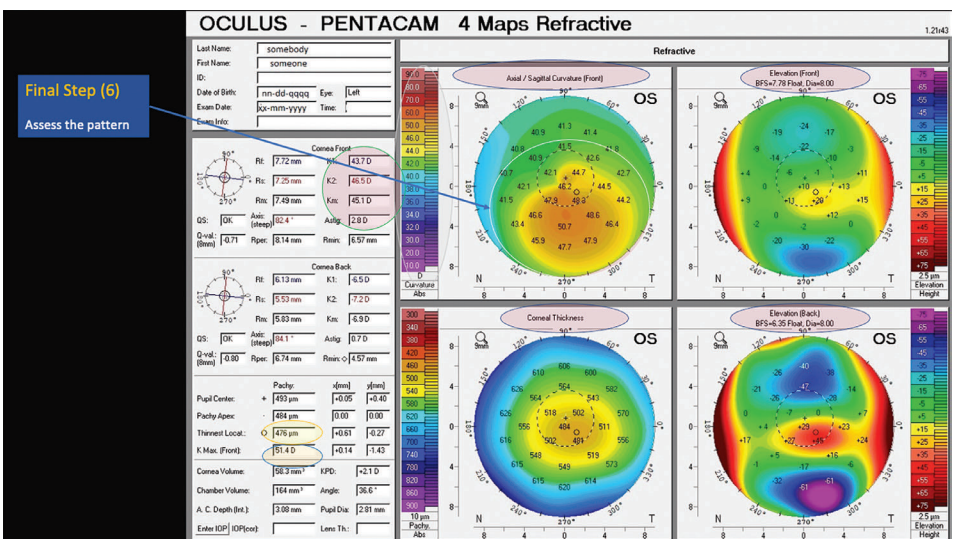

Figure 6. Finally, assess the pattern. Visual interpretation of topography goes hand-in-hand with the numbers. Experts say to look for patterns such as symmetric bowties, asymmetric bowties, crab claws and other patterns.

may, for example, be oversensitive to light or wind hitting their eyes. Some cases of corneal neuropathic pain have resulted in suicide. While it's a very rare condition that occurs in perhaps 1 in 10,000 cases or less, it's a devastating outcome that can occur after ocular surgery.

"The most significant associations with corneal neuropathic pain are anxiety, depression, PTSD and migraine headaches," Dr. Wu explains further. "When patients mention having any of these conditions, I inquire about the duration, medications they use to manage symptoms, and whether they've ever been hospitalized for them. I discuss neuropathic pain with every patient, informing them about what's considered normal after laser vision correction—typically a few days of discomfort after PRK and perhaps a day or less after LASIK—so they have realistic expectations. I emphasize that we don't expect prolonged eye pain beyond these periods and encourage them to inform us if they experience symptoms. If necessary, we can use confocal microscopy at our center to image their nerves and assess if any abnormality is present in terms of nerve regeneration."

Dr. Wu says corneal neuropathic pain is more manageable if it remains localized to the peripheral nervous system. "If it's early and it stays within the cornea, treatment is relatively straightforward. However, if it evolves into centralized pain, management can be more challenging. In these cases, patients may require agents such as gabapentin, pregabalin or other tricyclic antidepressants such as nortriptyline or low-dose naltrexone, which target the central nervous system.

"Patients with a history of fibromyalgia or existing neuropathic pain elsewhere in the body from conditions like diabetes, especially if they're already on medications like gabapentin, may be at higher risk for this outcome," she continues. "While this doesn't necessarily rule out refractive surgery, I may advise against corneal-based procedures in these cases. However, it's important to note that neuropathic pain can also occur after lens-based surgery, so open communication about potential risks and expectations is essential—not to alarm patients, but to prepare them for what may occur and what constitutes abnormal symptoms."

> **"I discuss neuropathic pain with every patient, informing them about what's considered normal after LVC—typically a few days of discomfort after PRK and perhaps a day or less after LASIK—so they have realistic expectations."**
>
> ***— Helen K. Wu, MD***

Dr. Wu explains that patients at greater risk for this outcome may have what's called "pain without stain," experiencing symptoms of dry eye without the typical signs. "Everybody has seen these patients in their clinic if they've been in practice long enough," she says. "They may mistakenly attribute their symptoms to psychiatric causes due to the overlap with anxiety and depression."

• ***A history of herpes***. "I inquire about any history of fever blisters or cold sores," says Dr. Wu. "Typically, it's necessary to inquire whether patients had cold sores during childhood, as they may not associate herpes with their condition if they haven't experienced a cold sore in a long time. If there's a history of herpetic infection, I usually prescribe valacyclovir or another oral antiviral around the time of their laser vision correction. Procedures such as cataract surgery or those involving excimer lasers can activate herpes in the cornea due to UV light exposure or the trauma of surgery itself. Therefore, patients need not have a prior history of ocular herpes for concern. However, I do consider a history of ocular herpes a contraindication for laser vision correction."

Dr. Wu gives patients with oral or skin herpes either a maintenance or a treatment dose of antiviral medication. "The full treatment dose for herpes simplex virus is valacyclovir 500 mg three times a day or famciclovir 250 mg three times a day. You can also give acyclovir 200 mg five times a day, but I usually give 800 mg three times a day for convenience. For herpes zoster treatment, it's double the simplex dosage—valacyclovir 1 g three times a day, famciclovir 500 mg three times a day and oral acyclovir 400 mg five times a day."

• ***Medications.*** Patients who are taking or have taken medications that are known to cause dry eye, such as Accutane or multiple glaucoma medications, often are not considered ideal candidates for corneal-based procedures.

When examining potential surgical candidates, Dr. Wu examines the meibomian gland structure and expresses the glands to evaluate for meibomian gland dysfunction. "If they have significant meibomian gland dysfunction, I inquire about Accutane usage," she says. "Sometimes these patients may exhibit severe meibomian gland dysfunction, making PRK less suitable for them. They may achieve better outcomes with LASIK or alternatively, if they have moderate to severe dry eye—which is common after Accutane use—a lens-based procedure may be more appropriate." ◀

1. Schallhorn JM, Schallhorn SC, Hettinger KA, et al. Outcomes and complications of excimer laser surgery in patients with collagen vascular and other immune-mediated inflammatory diseases. Journal of Cataract and Refractive Surgery 2016;42:12:1742-1752.

HOW PRACTICES ARE MAKING PRIVATE EQUITY WORK

Any partnership can have its ups and downs, but so far, ophthalmologists seem to say it's working out.

CHRISTINE YUE LEONARD
SENIOR ASSOCIATE EDITOR

Private equity acquisitions of physician practices have grown rapidly in the last decade. Ophthalmology in particular is an attractive medical specialty for its high procedural volume and the high demand for ophthalmic care among the aging population. In the year leading up to the COVID-19 emergency, monthly acquisitions of ophthalmology and optometry practices averaged 5.71 per month and increased to 8.78 per month from January to September 2021, following vaccine availability.[1]

For many ophthalmologists, private equity partnerships have helped their practices realize their dreams of expansion while offering quality business expertise. These advantages don't come without some measure of change, however. Here, doctors who've gone through a private equity sale share their experiences and discuss the compromises that come with the territory.

Physicians' Experiences

Private equity investment in medical practices seeks to increase the value of purchased practices through consolidation, streamlining of operations and increasing revenue before reselling at a profit to another private equity company.

Richard L. Lindstrom, MD, and his colleagues at Minnesota Eye Consultants, co-founded Unifeye Vision Partners with Chicago-based private equity firm Waud Capital about seven years ago. "We wanted to open a large office in St. Paul, but the cost was significant," he says. Because partner bank debt guarantees would challenge some younger partners, they began investigating private equity opportunities.

The decision to join with private equity didn't come about lightly. "We spent nearly three years making the decision, and then we did it," Dr. Lindstrom says. "The ten partners in our group all chose to join. We had several votes along the way, all of which were unanimous to proceed. We had all the partners check with their own personal financial advisors to see if this venture seemed like a good idea for them, and interestingly enough, the younger doctors had even greater positive input from their financial advisors than the older doctors, because they of course have more opportunities in the future with recapitalization and the like."

Over the last seven years, Unifeye Vision Partners has acquired 25 practices in Minnesota, other parts of the Midwest and in Southern California and Texas. "We've just begun in the Dallas-Fort Worth, Texas, area," Dr. Lindstrom adds. "We've grown meaningfully, and we're still with our first [private equity] partner. During the worst of COVID-19, we consolidated what we had and kind of stopped doing acquisitions, but since that time, we've continued to grow."

Dr. Lindstrom says that the way he and his partners practice hasn't been affected by the private equity partnership. "They're not in the clinic with us, so to speak. They're certainly reviewing our productivity and overhead, but we always had our business associates doing that in the past as well, so that really hasn't changed. We run our clinics the way we've always run them."

David M. Brown, MD, of Retina Consultants of Texas, says that initially, his practice didn't intend to go

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Drs. Lindstrom, Brown and **Grayson** are participants in private equity operations.

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into private equity. "We were happy with our practice, and we were making a good living," he says. "We didn't see how it would be beneficial. But we decided that we ought to do our due diligence and make sure we were correct that we shouldn't [go into private equity]."

Dr. Brown's practice created a private equity committee of doctors to look into it. "When you first approach private equity, one of the first things you need to do is find an investment banker," he says. "We wanted to make sure we had the right investment banker for us, so our committee interviewed 17 different investment bankers and narrowed it down to five and then did five live interviews. We eventually chose Wyatt Ritchie of Cain Brothers & Company."

He says the next step in their process was determining their goals. "When we started our practice in Houston in the 90s, we were 17 retina doctors, and everyone was within about a mile of each other," Dr. Brown says. "The business plan was to put world-class retina in West Houston, North Houston and South Houston and at the same time to create research centers. What we were essentially looking for in a private equity transaction was ways to increase what we've already done and grow from Houston to Greater Houston to Texas and then to the United States. We wanted a company that was willing to help us expand our reach to patients so we could improve patient care and build our research empire. We also determined that we would remain retina-only. It didn't make sense to us to engage in a private equity venture that involved buying up our referring entities."

Dr. Brown says his group's investment banker pitched their practice to several of the biggest private equity firms in the medical field that were known to be hands-off. "He pitched us to 30 different firms, and 17 said 'It'll never work, no thank you,' but 13 said, 'That's interesting. Let's talk.' Our private equity committee went to New York and speed dated 11 firms over two days, an hour and a half each. Then, we invited two of them to Houston.

"We created Retina Consultants of America," Dr. Brown says. "It's a pretty unique private equity venture in that 44 percent is owned by the retina doctors. Our private equity sponsor owns 14 percent and the rest are limited partners. Retina Consultants of America is run by a medical leadership board that's composed entirely of retina doctors."

Douglas K. Grayson, MD, of Omni Eye Services in Iselin, New Jersey, and the New York Metro Area, joined with private equity in 2017. "We were four partners—two optometrists and two ophthalmologists," he says. "None of us were planning on retiring, but we wanted to try to expand because we felt we were doing pretty well, and we could grow. We'd already looked at some neighboring practices that we wanted to either merge with or acquire. So, the concept of private equity seemed a very good prospect. It would give us the cash to be able to acquire these practices and it would give us the expertise of people who were used to integrating EMR systems, billing systems, HR systems, etc. to reduce redundancy and hopefully improve our efficiency.

"In a four-way partnership, there are always issues that come up," he continues. "Going forward with a private equity entity, a single check would be split four ways, and we'd be minority partners. The majority partner, the private equity entity, would have the final say in any disputes. So, for all of these reasons, private equity seemed like a good choice for us.

"They made our accounting system more efficient, and we acquired a few neighboring practices," he says. "They appointed leadership, marketing and brought in a host of officers who laid out an infrastructure for us to be able to acquire more practices and grow much bigger. They were mostly hands-off, so they didn't interfere much with the day-to-day operations or patient care. They mainly focused on trying to merge all the cultures of the different practices they acquired and lower overhead."

Considerations for Private Equity

Experts say that private equity partnership has a lot to offer practices, but compromise is necessary. Here are some of the changes that accompany a private equity deal:

• ***Added business acumen.*** "Most doctors want a hands-off [private equity partner] because if you're already running a great business, why would you want somebody to do it differently?" Dr. Brown says. "That being said, there are many economies of scale. While most of us don't want to be told what we should do with an individual patient or how to treat patients, there are probably ways in which billing, for example, could be improved. We were amenable to changing some business and back-office operations."

"Anytime you're in a group setting, there are differences of opinion and challenges along the way," Dr. Lindstrom notes. "When you bring in a private equity partner, you're bringing a very meaningful additional partner to the table. Today we spend more time looking at the financial ramifications of purchases and acquisitions and growth opportunities than we did before.

"I see this as an asset," he continues. "We do an analysis of whether a purchase makes sense from a patient-care perspective and from a return-on-investment perspective. Our private equity partner hasn't interfered with our practice style or our ability to provide high-quality care. They also haven't interfered with our partners' ability to consult with industry or our ability to do clinical trials."

Dr. Lindstrom says that before the private equity partnership, while the managing partner led the practice in most ways, the practice administrator brought business savvy and outside consultants Bruce Maller & Associates brought business acumen as well.

"Prior to helping found Unifeye Vision Partners, it was challenging and relatively complex management, with four ASCs, five offices, 10 partners, 30 doctors and over 300 employees," he says. "Now, we have the input of many highly educated MBAs who help analyze our decision making. In some cases, it's led to increasing investment in some areas. We've enhanced our offices and improved our internal and external marketing by being able to hire high quality experts and spend more in those areas."

Richard L. Lindstrom, MD

At Minnesota Eye Consultants, teaching the next generation of doctors is an integral part of the practice. Experts say it's important to find a private equity partner who wants to support your practice's values.

• ***The decision-making process.*** Adding a business-minded partner to the mix has its advantages, but this entails giving up some measure of control. "We've moved more toward the way in which corporations would manage their decision making," Dr. Lindstrom says. "Some ophthalmologists would find this undesirable or even unacceptable. I think you have to be a little insightful as to whether or not you're willing to give up some control. You're in a group practice when you join private equity, you're not a solo practitioner. It's a more corporate decision-making process with a board of directors and leadership team."

Dr. Grayson says that private equity partnerships may struggle when business leaders fail to incorporate doctors' advice. "There are a tremendous number of subtleties in taking care of ophthalmology patients," he says. "We've got different subspecialties with completely separate procedures—retina, cornea, pediatrics, oculoplastics and cataracts. We have an integrated blend of MDs and ODs. It's a very complex arena. The managers hired by private equity are well-intentioned and want the best for patients, but they aren't always able to completely understand all the subtleties of a medical practice.

"Medicine isn't the same as traditional business," he continues. "Every patient needs to be treated as an individual with individual needs. A business-focused manager, for the most part, has the viewpoint that if the practice is running well as a business, then there shouldn't be emergencies or fires to put out. But there will always be emergencies despite structured plans and a need for rapid change to address them. In the past, the partners would get together to make those changes happen quickly. Now, the required business meetings often delay action."

• ***Strength in numbers.*** Dr. Brown says that "most retina practices on their own aren't big enough to be able to get economies of scale in terms of contracting abilities to negotiate with vendors on EMR, for example. A practice of 10 or 12 doctors is small in the grand scheme of things, statewide and nationwide. A 265-doctor retina practice [like Retina Consultants of America] is definitely stronger."

In a related vein to decision making, more doctors can mean more collaborative challenges. "The biggest challenge is when we acquire a smaller group practice with one to four doctors," Dr. Brown says. "Those groups haven't necessarily had to figure out the best way to work together. Certainly, if the doctors are all owners in the entity, then I think they're more likely to see the benefit of doing things together, as opposed to if the doctors are employees."

• ***Recruiting young doctors.*** Bringing in the best of the next generation is always a goal for growing practices. "Most of the next generation of doctors are going to be employee doctors," Dr. Lindstrom points out. "They're not going to be practice owners in a major

way, which was the way it was when I started out. If you join a university medical center or any large consortium of doctors, you're an employee doctor. If you join a private equity group, you're an employee doctor.

"Some private equity companies have made it possible for younger doctors to acquire equity," Dr. Lindstrom continues. "Just like any corporation, when they want to recruit and retain people they'll find a way to equity-integrate their most talented individuals. That's the corporate world. But many doctors coming out now are going to find the opportunities for ownership to be less than they were when I started in practice almost 50 years ago. Then, it was very common. Now, sometimes equity ownership is good and bad. There are practices today that are struggling and having capital calls or even failing. It isn't always fun to own equity and be responsible for the challenges that arise—like COVID-19, where all of a sudden, we weren't seeing patients and there was no income.

"So, it's not always great to be equity-integrated, but there are individuals who want to be, and I'd say the numbers of opportunities for that are going down," Dr. Lindstrom says. "There's probably only 30 percent of practices today that are totally independent, where you can 'buy in' in the classical way, buy a meaningful share of the practice. Now, for most doctors, it's a little like going to work for a corporation. We've been able to recruit many talented, high-quality doctors at Minnesota Eye Consultants and Unifeye Vision Partners, and I think the way we're set up allows for us to do that. But there are some doctors who want to own a third, a half or even all of a practice, and that's not going to happen in our setting, just like it's not going to happen in a university or VA system."

"Recruitment was one of our biggest worries initially," Dr. Brown says. "Would we be able to continue to recruit top talent? We have. We've got some great fellows coming out of top programs. They've been excited to join because they actually make more money starting than they would have starting before private equity. They're all given equity without a buy-in. In other words, before private equity, doctors were paid less and then would pay with cash post-tax dollars to get ownership of the equipment, etc. Now there's no buy-in. The doctors make more and they become a partner sooner. There are also more opportunities across the country to participate in research and join collaborative projects that go to Retina Society, Macula Society, AAO and other major meetings. It's been a pleasant surprise that recruitment hasn't been the problem we thought it would have been."

> **"I think you have to be a little insightful as to whether or not you're willing to give up some control. You're in a group practice when you join private equity, you're not a solo practitioner."**
>
> **— *Richard L. Lindstrom, MD***

• ***Compensation.*** Dr. Brown says that the individual practices within Retina Consultants of America continue to get their compensation as they had, or as they want. "My group splits the pool, but other practices that were 'eat what you kill' before have remained that way," he says.

"One difference between private equity practice and private practice retina is that in private practice retina, if you decide to buy a piece of expensive equipment, then you all take home less money," Dr. Brown notes. "With private equity, there's more capital and you can buy that piece of equipment and it doesn't hurt your income because you work on EBITDA—earnings before interest, taxes, depreciation and amortization. Hard assets are a capital expense, so they depreciate over time. If you think a piece of equipment is going to make your practice better or is going to help improve patient care, then there are more resources and incentive to buy the equipment as opposed to saying, 'we'll get by with this 10-year-old OCT that's a bit behind the times.' I think that's a big difference that really helps patient care."

• ***Overhead trade-offs.*** The overhead put in place by private equity may help to alleviate the burden of day-to-day practice management, but too much overhead can weigh a practice down. "During COVID-19, it became more challenging to maintain the overhead with markedly decreased patient care visits," Dr. Grayson says.

"As we started to emerge [from the pandemic restrictions] and get our volume up almost to where we were before, everyone got slammed with interest rate hikes, which effectively caused our debt service to the bank to increase substantially," he continues, adding that as a well-run, efficient practice before the private equity expansion, there wasn't much room to increase revenue. "We were stuck with all this infrastructure and a higher debt service on interest rates, and that's when things became more difficult."

Dr. Grayson explains that one of the initial attractions of private equity was the ability to create value through efficiencies and consolidation, and then sell the new entity to another buyer at an even higher multiple than the initial purchase price, therefore increasing the value of retained ownership. This sale, of course, depends on the practice's financial health and integration with all the other acquired practices. The resale outlook was clouded by increased interest rates, higher debt and decreased profitability.

"Many cost-saving maneuvers including outsourced billing, call

centers and prior authorization and decreasing personnel were implemented, which put a strain on the overall functionality of the practice in the short term," Dr. Grayson says. "However, as the managers learned to control the new outsourced entities better, the practice is back in growth mode and doing well."

• ***Practice growth.*** It isn't as simple as just selling to private equity when you want to as a private ophthalmologist. "Private equity does its due diligence as well," Dr. Lindstrom points out. "There are a lot of practices that think, 'When I'm ready, I'll just join private equity,' but there are a lot of practices that private equity doesn't want. Private equity is for the most part interested in practices that can grow at 10 to 12 percent per year, not those that will grow at only 2 to 3 percent per year. Some practices are happy the way they are and don't want to grow, but that doesn't work in private equity."

• ***Navigating state laws.*** Multistate private equity groups must consider individual state laws. "We spend a lot more money on lawyers and compliance than we ever did before," Dr. Brown says. "Before, it was really just learning about what you did in your own state."

Overall, he says it hasn't been an obstacle. "It hasn't affected us much. Some things are more of a Retina Consultants of America problem vs. Retina Consultants of Texas or California," he says. "Certainly, it makes you think more about these things when an issue is multistate."

• ***Standardizing data protocols.*** "Another challenge with a conglomeration of retina doctors is ensuring that each local group remains what it was before (i.e., the top group) while also getting them to realize that some things are going to have to change," Dr. Brown continues. "We have to consolidate our data and have similar OCT scanning protocols, for example. A group might be used to the way they did it before, but some change has to happen when you're getting together the power of a large group.

"We partnered with an artificial intelligence company called Retina AI that can do automated reading of OCTs," he says. "Some people get 16 lines of OCT scanning, others get 32 or 120. It's not that [the number of scans] changes the way you treat patients but certainly if you want to consolidate data, your data is stronger if everyone's acquiring it in the same way. We haven't mandated this, but we've worked together so that the majority of people realize it's not too big a deal to change the way they do OCT scanning."

The Right Culture

"We're big believers that culture is critically important," Dr. Lindstrom says. "Our culture was an 'academic' private practice, where we provide the highest quality patient care and surgical care, teach, do clinical research and work with industry in developing the next generation of drugs, devices and diagnostics. We wanted to be able to continue to do that, so we needed to find a partner who also valued those things.

"We were initially founding a Midwestern group, so we were looking for a Midwestern partner," he continues. "Though we're all Americans, our culture is a little different from that of the East or the West or the Southeast, Southwest or the South Central. We wanted a quality partner with an upper Midwest culture. We found our partner in Chicago—a family-owned private equity company with similar values.

"I think it's really important to take a look at what you're doing today and what you want to do going forward," he says. "We have two MD fellows and two OD fellows in our system, and we do a lot of teaching in the local community, nationally and internationally. Many of our doctors are KOLs. We would've been really unhappy if we brought in a private equity company that said, 'We just need you to see patients all day, as many of them as you can, and we don't want you to teach, do clinical research or consult with industry.'"

Many of the doctors in Dr. Lindstrom's practice were engaged in the business of the practice prior to the private equity partnership and wanted to continue to have a voice. "We made sure they had that voice," he says. "There are four MDs on the Board of Directors at Unifeye Vision Partners. Our doctors' voices are heard—we prioritized that.

"We continue to operate our own clinics and ORs in the way we think is best, with one caveat: We do business decisions together [with our private equity partner]," Dr. Lindstrom says. "We wanted to open a new office in outstate Minnesota, but when we did the business analysis our business partners didn't think it was a good idea. So together, we decided instead to consolidate from five to four offices and remain focused on Minneapolis and St. Paul, because one office wasn't very productive. Everyone's happier now, and the doctors are happier because they're now in a setting where they're busier and more efficient.

"When it comes to opening any new office, we do a very careful analysis," he continues. "Where should we put it? How big should it be? How many doctors are going to work there? It's very helpful to have smart businesspeople helping us make that decision. I don't think that we, as a group of doctors, would have done it as well on our own, although we would have hired consultants to help us. Having an equity-integrated partner, where the outcome is as important to them as it is to us, definitely helps." ◀

1. Patil SA, Vail DG, Cox JT. Private equity in ophthalmology and optometry: A time series analysis from 2012 to 2021. Digit J Ophthalmol 2013;29:1.

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†Tyrvaya was evaluated across 3 randomized, vehicle-controlled, double-masked studies in which adults aged ≥22 years diagnosed with dry eye disease received 1 spray of either active drug or vehicle in each nostril twice daily. Primary endpoint: % of patients with mean change from baseline in STS of ≥10 mm at week 4 in ONSET-1: 52% with Tyrvaya (n=48) vs 14% with vehicle (n=43) and in ONSET-2: 47% with Tyrvaya (n=260) vs 28% with vehicle (n=252). Onset of action: mean change from baseline in STS ~5 minutes after first dose (not a prespecified endpoint) in ONSET-1 was 17.2 mm with Tyrvaya (n=48) vs 4.0 mm with vehicle (n=43) and in ONSET-2 was 16.5 mm with Tyrvaya (n=260) vs 6.9 mm with vehicle (n=251). Observed data. On Day 1 in clinical studies, a baseline anesthetized Schirmer's test was performed. Tyrvaya was then administered concurrently with Schirmer's test. Schirmer's test results were measured at ~5 minutes. Mean change from baseline in STS at week 12 in the MYSTIC study was 10.8 mm with Tyrvaya vs 6.0 mm with vehicle. Limitations: Ex-US, single-center study. All subjects were Hispanic or Latino. Tyrvaya group mean baseline STS 5.5 mm (n=41); vehicle group mean baseline STS 5.3 mm (n=41). All randomized and treated patients were included in the analysis and missing data were imputed using last-available data. [2-8]
See references on next page.

Indication
Tyrvaya® (varenicline solution) nasal spray is indicated for the treatment of the signs and symptoms of dry eye disease.

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.

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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.

References: 1. Jones L, Downie LE, Korb D, et al. *Ocul Surf.* 2017;15(3):575-628. **2.** Tyrvaya. Prescribing Information. Oyster Point Pharma; 2021. **3.** Oyster Point Pharma. Data on file. OPP-002 (ONSET-1) Clinical Study Report. August 4, 2019. **4.** Oyster Point Pharma. Data on file. OPP-101 (ONSET-2) Interim Clinical Study Report. October 13, 2020. **5.** Quiroz-Mercado H, Hernandez-Quintela E, Chiu KH, Henry E, Nau JA. *Ocul Surf.* 2022;24:15-21. **6.** Wirta D, Torkildsen GL, Boehmer B, et al. *Cornea.* 2022;4(10):1207-1216. **7.** Wirta D, Vollmer P, Paauw J, et al. *Ophthalmology.* 2021;0(0):379-387. **8.** Oyster Point Pharma. Data on file. OPP-004 (MYSTIC) Clinical Study Report. March 19, 2020.

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Can LASIK Lead to Earlier Cataract Surgery?

Researchers say there may be a connection between undergoing LASIK and needing cataract surgery at an earlier age than patients who didn't have the refractive surgery.

The investigators conducted a matched, case-control study. Cases were otherwise healthy adults with a history of LASIK. Groups were paired according to corrected-distance visual acuity, axial length and cataract grade.

A total of 213 patients were included; 85 patients were classified as post-LASIK group, and 128 were identified as controls. Here are some of the findings:

- The mean age at the time of LASIK was 42.32 ±9.24 years.
- The mean CDVA before phaco was 0.29 ±0.19 logMAR in the post-LASIK group and 0.34 ±0.22 logMAR in controls (p=0.07).
- The mean axial length was 23.99 ±1.78 mm in the post-LASIK group and 23.62 ±0.98 mm in controls (p=0.085).
- The mean nuclear cataract grading was 1.36 in the post-LASIK group and 1.47 in controls (p=0.34).
- The mean age at the time of phaco was 60.18 ±7.46 years in the post-LASIK group and 67.35 ±9.28 in controls (p<0.0005).
- The difference between the mean age of LASIK and the mean age of phaco was 17.85 ±5.72 years.
- Scientists found a positive association between the post-LASIK group and the age of phaco ≤55 years (OR: 4.917; CI, 2.21 to 10.90; p<0.001).

Scientists concluded that LASIK was associated with early phacoemulsification surgery. Patients with LASIK had a seven-year earlier phacoemulsification surgery vs. the matched control group.

Int Ophthalmol 2024;3;44:1:125.
Ortiz-Morales G, Ramos-Davila EM, Elizondo-Fernández B, et al.

Risk for Impairments in Wet AMD Patients

Investigators assessed the prevalence and correlates of impaired activities of daily living (ADLs) in patients with neovascular age-related macular degeneration (nAMD) who present for anti-vascular endothelial growth factor therapy.

In a clinic-based cohort of 437 patients with nAMD who presented for anti-VEGF therapy, the Older American Resources and Services Scale (OARS) was administered to assess for impairments in basic, instrumental and total ADL. Logistic regression analyses were conducted to determine odds ratios (OR) and 95 percent confidence intervals for factors associated with ADL impairment.

Here are some of the findings:

- The prevalence of impaired basic, instrumental and total ADL was 37.76, 67.82 and 39.59 percent, respectively.
- In multivariate-adjusted models, moderate visual impairment (OR: 5.65; CI, 2.31 to 13.83) and blindness (OR: 5.43; CI, 2.09 to 14.12) were associated with greater odds of impaired total ADL.
- Depressive symptoms (OR: 2.08; CI, 1.08 to 4.00), the presence of any disability (OR: 3.16; CI, 1.64 to 0.07) and never driving (OR: 4.00; CI, 1.60 to 10.00) were also positively associated with total ADL impairment.
- Better vision-related quality of life was inversely associated with impaired instrumental ADL while higher health-related QoL scores were associated with decreased odds of total ADL impairment.

In one study, depressive symptoms were associated with total impairment of activities of daily living in wet AMD patients.

Investigators found a high prevalence rate of activities of daily living impairment among neovascular age-related macular degeneration patients presenting for therapy. They found that visual impairment, never driving, and poor physical and mental health increased the odds of experiencing activities of daily living impairment while better vision- and health-related quality of life reduced the odds of impairment.

Eye (Lond) 2024; Feb 19. [Epub ahead of print].
Van Vu K, Mitchell P, Detaram HD, et al.

Could Nanothin be "In"?

Scientists aimed to describe a method to achieve a high success rate for nanothin (NT, ≤50 µm) Descemet's stripping automated endothelial keratoplasty graft preparation using an anterior chamber pressurizer (ACP)

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A prospective cohort (study group) of 24 patients with corneal endothelial dysfunction was consecutively enrolled and received DSAEK grafts using the modified ACP method from December 2021 to May 2022. The control group included 24 historical patients who received DSAEK grafts using a conventional ACP procedure. Central graft thickness (CGT), graft regularity (3-mm and 5-mm diameter zones), best spectacle-corrected visual acuity and endothelial cell density were compared between the two groups.

Here are some of the findings from the study:

- A 100 percent ultrathin (UT, ≤100 µm) DSAEK rate and 62.5 percent NT-DSAEK rate was achieved at three months post-surgery in the study group, with a 51.3 ±14.8 µm CGT, while a 70.8 percent UT-DSAEK rate and 4.2 percent NT-DSAEK rate was achieved in the control group, with an 89 ±15.4 µm CGT (p<0.001).
- At three-month postoperative follow-up, the regularity of graft thickness was significantly better in the study group:
  — central-to-peripheral thickness difference: p=0.044 and 0.014 for 3 mm and 5 mm diameter zones, respectively; and
  — graft thickness uniformity: p<0.001 and 0.012, respectively.
- No statistical difference was reported in the best spectacle-corrected visual acuity (p=0.170) or ECD (p=0.833) between the two groups at the three-month postoperative follow-up time point.

The researchers determined that Descemet's stripping automated endothelial keratoplasty grafts harvested using a modified anterior chamber pressurizer method were thinner and more regular compared with the conventional anterior chamber pressurizer method.

Cornea 2024; Feb 21. [Epub ahead of print].
Zhao Z, Lin L, Zhou W, et al.

Long-term Results of Treat and Extend with Faricimab

Researchers evaluated the two-year efficacy, durability and safety of the bispecific antibody, faricimab, which inhibits both angiopoietin-2 and vascular endothelial growth factor-A, as part of the TENAYA and LUCERNE identically designed, randomized, double-masked, active comparator-controlled Phase III noninferiority trials across 271 sites worldwide.

Participants included treatment-naïve patients with neovascular age-related macular degeneration (nAMD) ages ≥50 years randomized (1:1) to intravitreal faricimab 6 mg up to every 16 weeks (Q16W) or aflibercept 2 mg every eight weeks (Q8W).

Faricimab fixed dosing was based on protocol-defined disease activity at weeks 20 and 24 up to week 60, followed up to week 108 by a treat-and-extend–based personalized treatment interval regimen.

Efficacy analyses included change in best-corrected visual acuity (BCVA) from baseline at two years (averaged over weeks 104, 108 and 112) and proportion of patients on Q16W, every 12 weeks (Q12W) and Q8W dosing at week 112 in the intention-to-treat population. Safety analyses included ocular adverse events (AEs) in the study eye through study end at week 112 in patients who received ≥ one dose of study treatment.

Of 1,326 patients treated across the trials, 1,113 (83.9 percent) completed study treatment (n=555 faricimab and n=558 aflibercept). Here are some of the findings:

- BCVA change from baseline at two years was comparable between faricimab and aflibercept in the trials, as demonstrated by the following findings:
  — TENAYA adjusted mean change: +3.7 letters; CI, +2.1 to +5.4 with faricimab and +3.3 letters; CI, +1.7 to +4.9 with aflibercept; mean difference: 0.4 letters; CI, -1.9 to +2.8; and
  — LUCERNE adjusted mean change: +5 letters; CI, +3.4 to +6.6 with faricimab and +5.2; CI, +3.6 to +6.8 with aflibercept; mean difference: -0.2 letters; CI, -2.4 to +2.1.
- At week 112 in TENAYA and LUCERNE 59 percent with faricimab and 66.9 percent with aflibercept achieved Q16W faricimab dosing, increasing from year one; and 74.1 with faricimab and 81.2 percent with aflibercept achieved ≥Q12W dosing.
- Ocular AEs in the study eye were comparable between faricimab and aflibercept in TENAYA (55 and 56.5 percent, respectively, of patients) and LUCERNE (52.9 and 47.5 percent, respectively, of patients) through week 112.

Researchers wrote that treat-and-extend-based faricimab treatment based on neovascular age-related macular degeneration disease activity maintained vision gains through year two with most patients achieving extended dosing intervals.

Ophthalmology 2024; Feb 19. [Epub ahead of print].
Khanani AM, Kotecha A, Chang A, et al.

Optic Disc Hemorrhage Size And Glaucoma Progression

Researchers investigated the correlation between optic disc hemorrhage size and glaucoma progression, as part of a retrospective observational cohort study at a tertiary hospital in South Korea.

A total of 250 open-angle glaucoma patients with DH were included. Participants were followed for five years or longer, with a minimum of five visual field tests.

The DH area was calculated by comparing the pixel numbers of the DH area with the disc area based on optical coherence tomography. For recurrent DH cases, researchers calculated the average DH area. DH size was classified as large or small based on the median value. Rates of mean deviation (MD) loss were determined using Guided Progression Analysis. Univariable and

To treat ocular inflammation and pain following ophthalmic surgery or ocular itching associated with allergic conjunctivitis.

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INDICATIONS

DEXTENZA is a corticosteroid indicated for:

- The treatment of ocular inflammation and pain following ophthalmic surgery.
- The treatment of ocular itching associated with allergic conjunctivitis.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

DEXTENZA is contraindicated in patients with active corneal, conjunctival or canalicular infections, including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella; mycobacterial infections; fungal diseases of the eye, and dacryocystitis.

WARNINGS AND PRECAUTIONS

Intraocular Pressure Increase - Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. Intraocular pressure should be monitored during treatment.

Bacterial Infections - Corticosteroids may suppress the host response and thus increase the hazard for secondary ocular infections. In acute purulent conditions, steroids may mask infection and enhance existing infection.

Viral Infections - Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex).

Fungal Infections - Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal culture should be taken when appropriate.

Delayed Healing - Use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation.

Other Potential Corticosteroid Complications - The initial prescription and renewal of the medication order of DEXTENZA should be made by a physician only after examination of the patient with the aid of magnification, such as slit lamp biomicroscopy, and, where appropriate, fluorescein staining. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.

ADVERSE REACTIONS

Ocular Inflammation and Pain Following Ophthalmic Surgery

The most common ocular adverse reactions that occurred in patients treated with DEXTENZA were: anterior chamber inflammation including iritis and iridocyclitis (10%), intraocular pressure increased (6%), visual acuity reduced (2%), cystoid macular edema (1%), corneal edema (1%), eye pain (1%), and conjunctival hyperemia (1%). The most common non-ocular adverse reaction was headache (1%).

Itching Associated with Allergic Conjunctivitis

The most common ocular adverse reactions that occurred in patients treated with DEXTENZA were: intraocular pressure increased (3%), lacrimation increased (1%), eye discharge (1%), and visual acuity reduced (1%). The most common non-ocular adverse reaction was headache (1%).

Please see adjacent Brief Summary of full Prescribing Information.

*93% (187/201) of DEXTENZA patients were satisfied with the insert in the third Phase 3 Study for the treatment of ocular inflammation and pain following ophthalmic surgery.[3]

† 73.6% of physicians in Study 1, 76.4% in Study 2, and 79.6% in Study 3, for the treatment of ocular inflammation and pain following ophthalmic surgery, rated DEXTENZA as easy to insert.[2,5]

References: 1. DEXTENZA [package insert]. Bedford, MA: Ocular Therapeutix, Inc; 2021. **2.** Tyson SL, et al. *J Cataract Refract Surg.* 2019;45(2):204-212 [erratum in: 2019;45(6):895]. **3.** Data on File 00837. Ocular Therapeutix, Inc. **4.** Sawhney AS, et al., Inventors, Incept, LLC, Assignee. Drug Delivery Through Hydrogel Plugs. US patent 8,409,606 B2. April 2, 2013. **5.** Walters T, et al. *J Clin Exp Ophthalmol.* 2016;7(4):1-11.

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multivariable regression analyses were performed to identify significant predictors of MD loss. Main outcome measures included DH size and longitudinal VF progression.

Here are some of the findings:

- The mean follow-up period was 11.1 ±3.6 years.
- The group with large DH showed faster global MD loss relative to the group with small DH (-0.51 ±0.48 dB/y vs. -0.36±0.42 dB/y, p=0.01).
- In the multivariable model, mean DH size, maximum DH size and initial MD were all significantly associated with the overall rate of MD loss (all p<0.05).

Researchers found that optic disc hemorrhage size was associated with the rate of visual field deterioration; eyes with larger disc hemorrhages showed more pronounced visual field progression.

Am J Ophthalmol 2024; Feb 21. [Epub ahead of print].
Jeong Y, Bak E, Jang M, et al.

Biomarkers May Help Predict Non-exudative MNV Conversion to Exudative

Investigators evaluated the incidence and morphological biomarkers to predict the exudative conversion in eyes with type 1 nonexudative macular neovascularization (MNV) using swept-source optical coherence tomography angiography.

MNV was detected using the retinal pigment epithelium-to-RPE-fit slab of SS-OCTA scans. Depending on whether exudation developed within a year, the eyes were divided into two groups: active and silent. Qualitative and quantitative OCTA parameters of the two groups were evaluated to discriminate the biomarkers associated with exudative conversion.

Here are some of the findings:

- Of the 40 eyes, nine developed exudation within one year (incidence rate 22.5 percent).
- The active group exhibited significantly higher "anastomosis and loop" patterns, greater "vessel density," increased "junction density," fewer "number of endpoints" and lower "lacunarity" compared to silent group.
- Anastomosis and loops and higher vessel density were correlated with the active group in multivariate analyses.
- A predictive model combining these biomarkers achieved 95-percent accuracy in predicting exudative conversion.

Investigators found, at 12 months, the risk of exudation was 22.5 percent, and anastomosis and loops and vessel density were useful optical coherence tomography angiography biomarkers for predicting exudative conversion in eyes with type 1 nonexudative MNV. They suggested, for eyes with a high risk of exudative conversion, more frequent follow-up is recommended. ◀

Retina 2024; Feb 12. [Epub ahead of print].
Bae SH, Bae K, Yoon CK, et al.

Pearls for Angle-based Surgery

A veteran glaucoma surgeon shares best practices for MIGS device implantation.

ARSHAM SHEYBANI, MD
ST. LOUIS

The number of minimally invasive glaucoma surgeries performed is increasing every year. Combined with cataract surgery, MIGS offer additional pressure lowering, can reduce patients' medication burden and also decrease the risk for postop pressure spikes. While complications can occur with the addition of a second procedure to cataract surgery, in the hands of an experienced surgeon, this risk is low.

Here, I'll share some pearls to set surgeons up for success with angle-based surgery regardless of technology.

Gonioscopy

Visualizing surgical landmarks is key. Before incorporating MIGS, practice careful gonioscopy in the clinic to get to know the angle anatomy. Once you're comfortable with that, practice gonioscopy in some of your routine OR cases to learn how to find the best view and get used to handling the gonio lens with your non-dominant hand.

Avoid pressing too hard on the eye with the gonio lens as this can create striae. Match the scope tilt with how much you've turned the patient. The scope tilt should offer a direct, perpendicular view of the angle.

Parsing the En-face View

The en face, or forward-facing, view is relative to the observer. In the view shown in Figure 1A, the angle is en face relative to the surgeon, and the structures of the angle—trabecular meshwork, scleral spur and ciliary body band—are clearly differentiated.

As the patient's head rotates toward the surgeon, the perceived height of the angle shortens and the perceived relative distance between the trabecular meshwork and ciliary body band is reduced (*Figure 1B*). Under-rotation is the most common reason why our surgical view is reduced during angle surgery and it's the major mechanism by which clefts occur during goniotomy.

With this view, the surgeon can't determine what layers they're seeing. The ciliary body band looks relatively larger. When we look to treat the band of pigment, we might be in the ciliary body band instead. The trabecular meshwork sometimes looks fused with the ciliary body band, especially when the layers are less distinct with pigment confluent throughout, as we see in some angles.

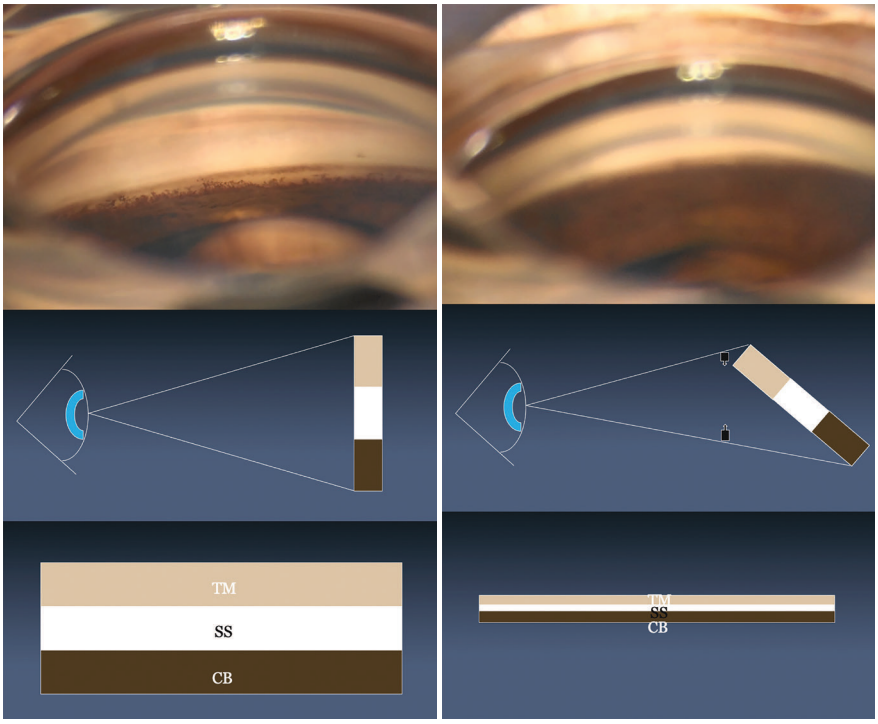


Figure 1. (A) An en face view of the angle with visibly distinct structures. (B) Under-rotation is a common reason for a reduced surgical view. Here, the perceived height of the angle is decreased.

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.

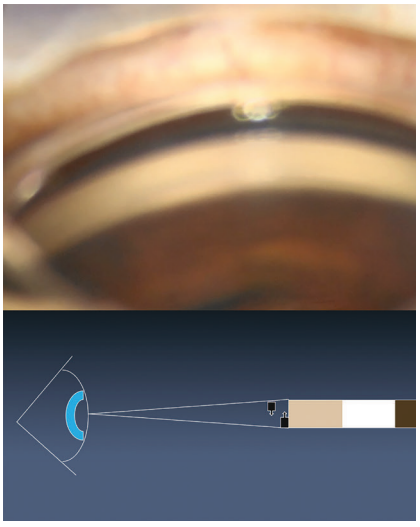


Figure 2. In an extreme example of the eye turned completely toward the surgeon, no distinct angle structures are visible.

To further illustrate with an extreme of this example, if the eye is turned completely toward the surgeon, the trabecular meshwork appears directly in line with the ciliary body band (*Figure 2*). In this view, there are no distinct structures. The view depicted in Figure 1A is what we expect to see on gonioscopy.

Use Trypan Blue

One of the reasons for improper device placement is looking for pigment and not looking for the slight translucency of the canal. Document trabecular meshwork pigmentation during your preoperative evaluation. If the pigmentation is very light, be sure to make a note in the chart to use trypan blue (*Figure 3*). Inject the dye at the beginning of the case, ensuring that it gets into the peripheral angle. Adding intracameral lidocaine can help get the dye into the peripheral trabecular meshwork.

Controlling Heme

If you encounter bleeding while creating your incision, use your second hand or have an assistant wick it away with a Weck-Cel sponge (*Figure 4*). Maintain control of bleeding during and especially post-procedure (more on that below). Don't pull the gonio prism on and off. This can create a

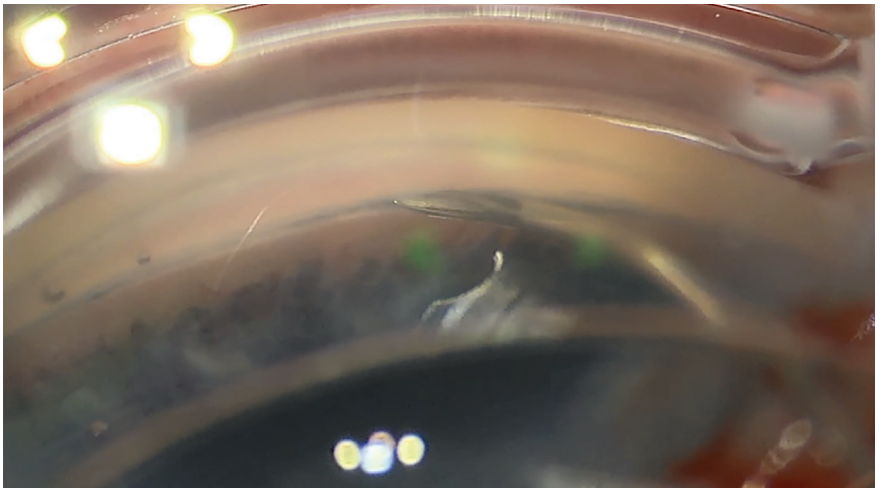


Figure 3. Injecting trypan blue at the beginning of the case will stain the trabecular meshwork, making it easier to visualize the angle structures.

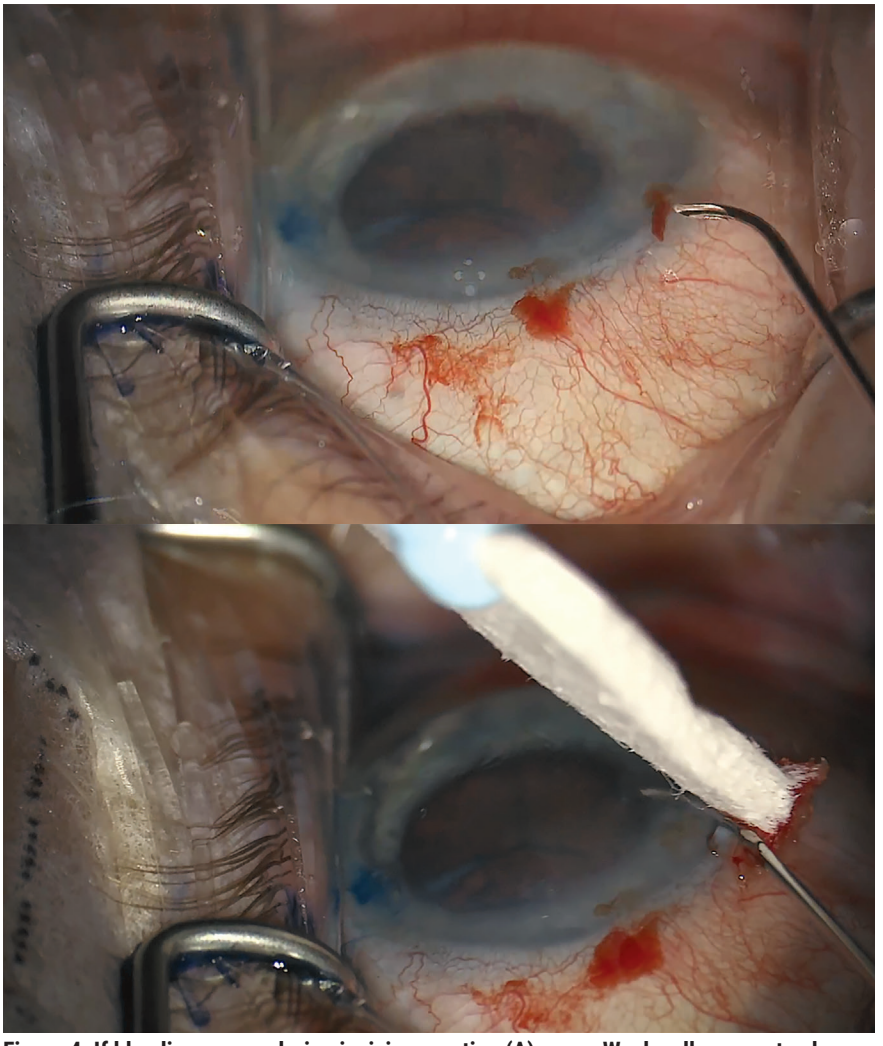
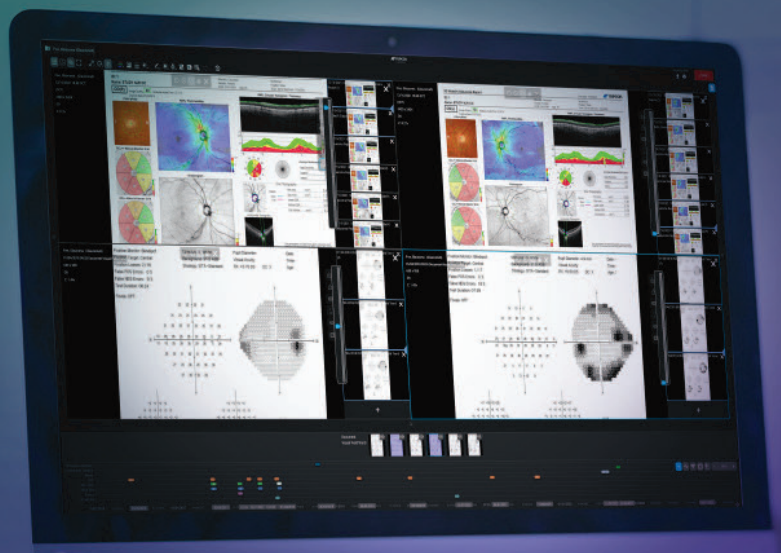


Figure 4. If bleeding occurs during incision creation (A), use a Weck cell sponge to clean up the area (B). At the end of the case, raise the pressure to approximately 25 mmHg and irrigate the blood before letting the patient go. Postoperatively, patients with a significant amount of reflux should stop their glaucoma drops day-of. However, continuing drops is recommended for a patient with severe disease and little reflux.



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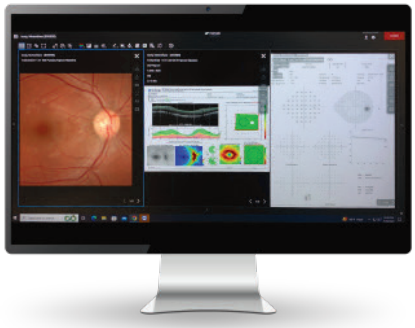

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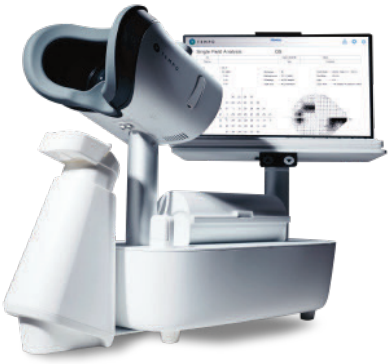

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LAYERS OF THE TRABECULAR MESHWORK

There are multiple tissue planes that devices can be laid into. These include:

- the uveal layer, which is adjacent to the anterior chamber and arranged in bands extending from the iris root and ciliary body band to the peripheral cornea;
- the corneoscleral layer, which consists of sheets of trabeculum that extend from the scleral spur to the lateral walls of the scleral sulcus; and
- the juxtacanalicular meshwork, which is thought to be the main site of outflow resistance. It's adjacent to and forms the inner wall of Schlemm's canal. Aqueous moves between and across the endothelial cells lining the inner wall.

suction effect that draws more blood into it. Making the incision slightly more anterior can avoid additional bleeding.

Placing Devices

Avoid overfilling the eye with OVD, as this can compress Schlemm's canal and make it more difficult to place devices. An exception would be if you're performing a pressurized viscodilating procedure; higher pressures can limit Descemet's detachments. Underfilling the eye may cause the iris to bow forward and obscure your view of the angle.

As you're placing devices, don't push too hard. With stents in particular, the initial portion of device placement involves pushing forward to incise into the trabecular meshwork and holding the tip of the cannula against the back wall of Schlemm's canal. When the first window of the stent is in the canal, particularly with Hydrus or iTrack, you'll want to back the pressure off in order to avoid driving the device more posteriorly.

If the device meets resistance, make space by creating a micro goniotomy. Be sure to place the device about a millimeter just before the goniotomy entry site instead of right at the entry site. Dock the device against the back wall. This allows you to float the device into the angle. Here are a few ways to do this:

1. Use the injector to create a goniotomy by scratching off the trabecular meshwork (*Figure 5*).
2. Use a bent 25- or 27-gauge 5/8ths-inch needle to make a scratch incision (*Figure 6*).
3. Use OVD to open up the channel. Create a small goniotomy and dock a viscoelastic cannula up against it. Push against the back wall and inject a small amount of OVD just to inflate the tissue plane in front of where you want to go.

Postoperative Care

Be sure to follow the postoperative course to determine whether or not the pressure is responding. Look carefully at device placement. If a stent isn't in the right spot, it's not going to work. Especially in some tighter angles, patients could end up with PAS. Larger devices can sometimes cause a little bit of inflammation if they're chronically rubbing against the posterior iris.

There are some angles that you won't be able to get devices in. If you're not satisfied with the device placement, remove the device. Don't leave the device in the wrong tissue plane just to have it in the eye. Setting expectations about this potential outcome before surgery can ease patient concerns.

In the postoperative period, it's also important to manage bleeding. If there was a lot of bleeding during the surgery, then you can consider leaving a little bit of OVD, but we've gone away from using viscoelastic in the eye and moved toward raising the pressure at the end of the case to about 25

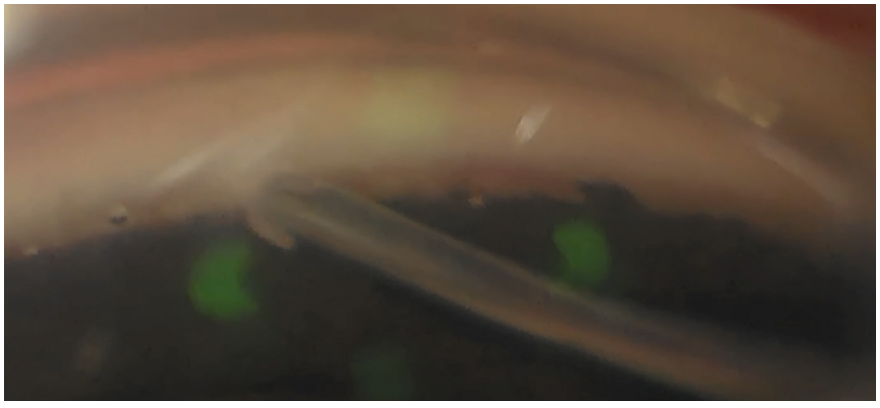

Figure 5. If you encounter resistance upon device insertion, one option is to create a micro goniotomy using the injector tip.

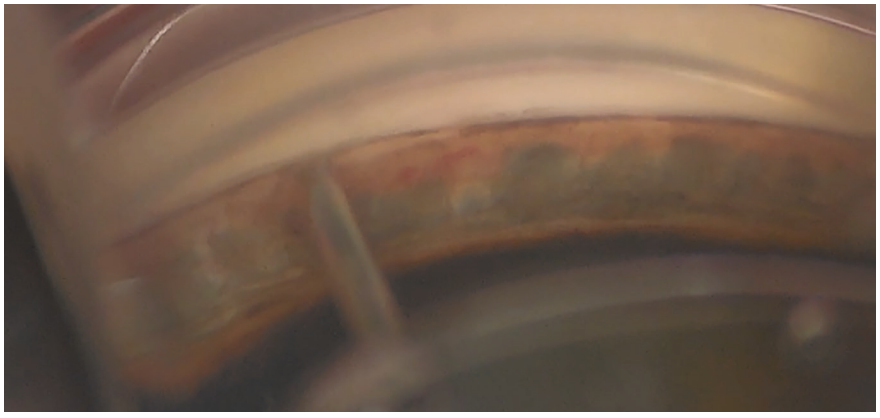

Figure 6. A bent 25- or 27-ga. needle creating a scratch incision to make space for device insertion.

mmHg. Be sure to irrigate the heme before letting the patient go.

Most patients should stop their glaucoma drops on the day of the surgery, especially if they get a significant amount of reflux. If you don't see much reflux in a patient with severe disease, I'd recommend continuing with the drops.

Tackle the TM First

While surgeons will have their own preferences and comfort levels when it comes to combined surgery, there are a number of advantages to performing a trabecular meshwork-based surgery before phacoemulsification. Here are a few reasons to consider:

- If you're confident in your cataract surgery and less used to the angle procedure, start with the angle procedure to get it out of the way.
- Patients undergoing combined surgery are at high risk for pressure spikes after cataract surgery. In the event that you break the capsule while performing cataract surgery first, you probably won't continue with the angle procedure. Performing the angle procedure first gives you at least some backstop of addressing pressure should a cataract surgery complication occur.
- Visualization may be improved during phaco since OVD can deepen the angle. Lens removal isn't necessary to see the angle—if you're in that position, with a tight plateau-like configuration, then you probably shouldn't be placing a device in that patient anyway.
- The I/A during the angle procedure helps to pressurize the system, removes blood reflux as you phaco and allows for less heme at the end of the case.

When performing angle surgery first, be sure to manage the heme. Keep the chamber pressurized to avoid reflux. Blood can sometimes get into the capsular bag, depending on the zonular integrity, and even the posterior segment.

In summary, the best way to practice angle surgery is to do it. Familiarize yourself with angle anatomy. Document the trabecular meshwork pigmentation, using trypan blue to improve visualization if needed. Maintain careful control of heme perioperatively and consider performing the angle-based procedure before phaco. Avoid overfilling the eye with OVD, except in cases of pressurized viscodilation. If the device meets resistance during insertion, make space with a micro goniotomy. Finally, don't hesitate to remove the device if it's in the wrong tissue plane. ◀

ABOUT THE AUTHOR

Dr. Sheybani is an associate professor of ophthalmology and visual science at the Washington University in St. Louis School of Medicine. He's a consultant for AbbVie, Alcon, Nova Eye and Glaukos, and an ad hoc consultant for Santen and New World Medical.

(Continued from p. 27)

Expanding on this last point, the researchers, writing in *JAMA Ophthalmology*,[1] wanted to test this prowess in the ophthalmic field. To do this, they relay that the image-processing capabilities are, right now, less robust in niche subspecialties. Despite this shortcoming, the results here do support the potential of ChatGPT to relatively interpret findings from many ophthalmic imaging modalities, researchers say.

Similarly to the subpar analysis of pediatric ophthalmology images, ChatGPT performed worst in the subspecialty of neuro-ophthalmology. The authors explain this may be due to imaging modalities generally used for neuro-ophth vs. the retina, which was the best-performed category. As the retinal category largely consisted of macular OCT and fundus images, "it is plausible that the current release of the chatbot may be better equipped in interpreting more widely used ophthalmic imaging modalities" compared with neuro-ophthalmology's higher proportion of RNFL and GCC OCT images, they wrote.

This may be the first study using ChatGPT to interpret ophthalmic images, but the chatbot has already been used in the ophthalmic field for other purposes. In a previous study, pitting it against 125 text-based multiple-choice questions used by trainees to prepare for ophthalmology board certification, the previous version of ChatGPT answered 46 percent of these questions correctly. Two months later, this measure rose to 84-percent accuracy. Reflective of this improvement, the authors posit: "Given that this is a novel addition to the chatbot's platform, we anticipate its performance on image-based questions may increase considerably with time, as was previously observed in our analyses of text-based questions."

While the performance of ChatGPT in this investigation achieved moderate accuracy, the large learning model is still inferior to previously published AI systems designed for screening or diagnosing retinal pathologies from ophthalmic imaging like OCT scans and fundus images. However, incorporating more robust AI algorithms into the chatbot may further improve their multimodal capabilities.

The authors warn that with this great technology becoming increasingly widespread, "it is imperative to stress their appropriate integration within medical contexts." However, they look to a future where "as the chatbot's accuracy increases with time, it may develop the potential to inform clinical decision-making in [eye-care settings] via real-time analysis of ophthalmic cases." ◀

1. Mihalache A, Huang RS, Popovic MM, et al. Accuracy of an artificial intelligence chatbot's interpretation of clinical ophthalmic images. JAMA Ophthalmol. February 29, 2024. [Epub ahead of print].

(Continued from p. 40)

the best option is also on the table, surgeon say. "There can be a temptation to just do a treatment, such as a YAG laser capsulotomy when the capsule is actually quite clear, because a lens exchange is a much more involved procedure. However, there are times when it may be necessary," says Dr. Chang.

If you've done everything you can—and ruled out other issues—and the patient just isn't happy, for whatever reason, with the lens, Dr. Meghpara suggests discussing a lens exchange. "Sometimes you just have to bite the bullet and acknowledge that this lens is not perfect," he says. "While, for instance, multifocals work well for the majority of patients, in some patients they're just not well-tolerated."

This holds true for monofocal lenses as well, he notes. "Perhaps your patient is experiencing dysphotopsia such as shadows, streaks and starbursts and you've done everything you can to address the problem. This is another situation that could be attributed to the lens and, while uncommon, this can happen with an IOL placement."

In these cases, Dr. Meghpara would offer a lens exchange as long as their symptoms and dissatisfaction can clearly be attributed to the lens. "On the other hand, if you can't explain their symptoms and their unhappiness by the lens, we won't simply do a lens change and hope that it'll improve a patient's vision because there are risks associated with that procedure."

Expectations & Education

Beyond taking the appropriate clinical action, success also depends on how you approach your patient and respond to their concerns. "Don't dismiss their complaints," urges Dr. Davidson. "Try not to get defensive or frustrated. I always do my best to reassure patients and validate their concerns, letting them know that I am there to help and will do everything I can to address the problem."

Fostering understanding and cooperation with your patients depends—in large part—on education and expectation management. Ophthalmologists must communicate openly with their patients during the entire cataract surgery process from the first preoperative appointment throughout the postoperative stage.

"Setting expectations in advance is critical," says Dr. Meghpara, who encourages his patients to have someone with them during the evaluation and also sends them home with a written record of the key discussion points. "Help your patients understand what's realistic and what isn't. I also avoid absolutes such as 'you'll never have to wear glasses again.' "

"It's important to remember that, in addition to the technical and clinical aspects of cataract surgery, there's a personality and expectation component that must be managed as well," Dr. Chang concludes. "We have to be prepared to problem solve and manage any challenges that arise to achieve the best possible visual outcomes for our patients." ◀

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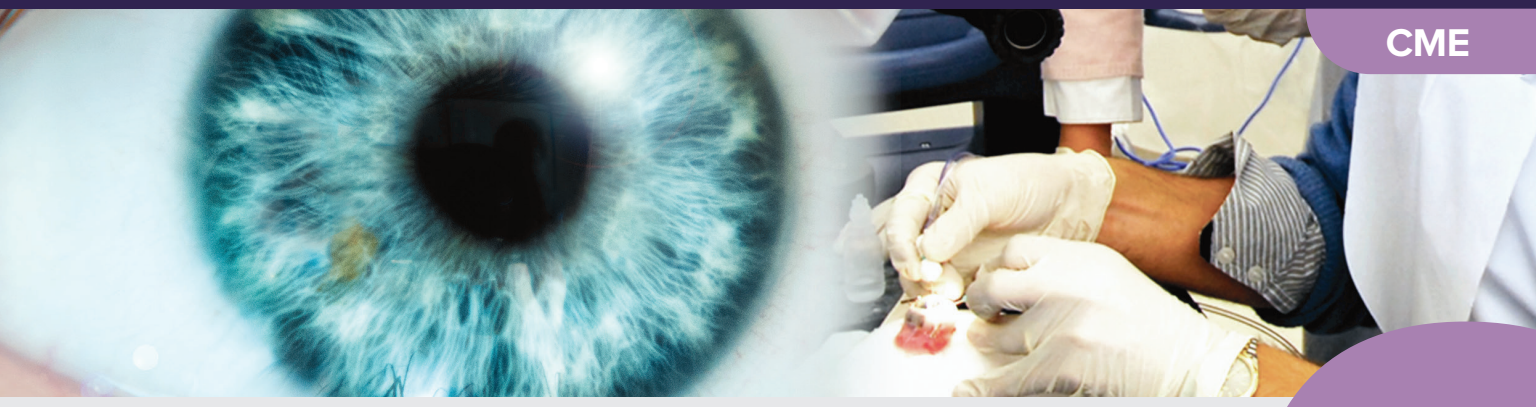

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EDITED BY COLLIN ROZANSKI, MD
WILLS EYE RESIDENT CASE REPORT

A 71-year-old female presents with a red eye and vision loss over several months.

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PHILADELPHIA

Presentation

A 71-year-old female presented to her local ophthalmologist with six months of painless gradual worsening vision in the right eye with associated redness. On examination, she was found to have no light perception and iris neovascularization in the right eye. On B-scan ultrasonography, a retinal detachment with possible intraocular blood or mass was discovered. The patient was then referred for evaluation by the Wills Eye Hospital Ocular Oncology Service.

History

The ocular history was only notable for a prior posterior vitreous detachment in the right eye. Medical history revealed multiple vascular risk factors, including a stroke two years prior that left her wheelchair-bound, type 2 diabetes mellitus of many years, hypertension and obesity. There was no family history of cancer. Social history was unremarkable, notably with no history of tobacco use. Current medications included aspirin, atenolol, prednisone and famotidine.

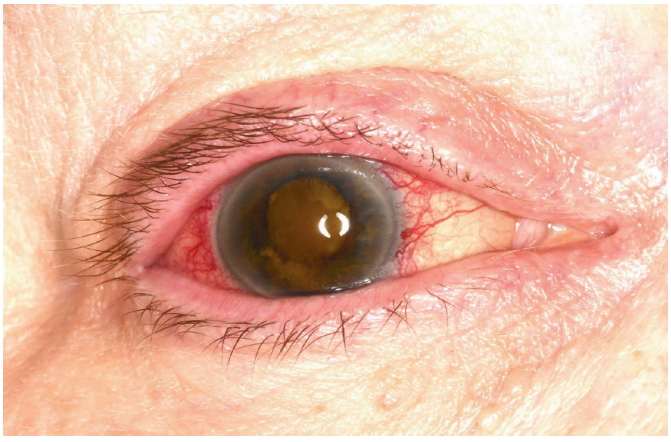

Figure 1. External photograph of the right eye showing eyelid congestion and erythema, conjunctival/episcleral vascular injection, and dense cataract. Iris neovascularization with posterior synechiae was present, limiting dilation.

Examination

On ocular examination, best-corrected visual acuity was no light perception in the right eye and 20/40 in the left eye. The right pupil was non-reactive and the left pupil was round and reactive without afferent pupillary defect. Intraocular pressure was 9 mmHg in the right and 15 mmHg in the left eye. Confrontation visual fields weren't possible in the right eye and normal in the left eye. Extraocular movements were full in both eyes.

In the right eye, there were several additional findings including mild upper and lower eyelid congestion and erythema, marked conjunctival/episcleral vascular injection especially prominent at the limbus, neovascularization of the iris (NVI) with iris atrophy, peripheral anterior synechiae, posterior synechiae and a dense nuclear sclerotic cataract *(Figure 1)*. Fundus examination and optical coherence tomography weren't possible due to the dense cataract.

In the left eye, the anterior segment examination revealed moderate nuclear sclerotic cataract. Fundus examination and optical coherence tomography revealed a flat retina with minimal epiretinal membrane, macular edema and dot-blot hemorrhages.

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

Work-up, Diagnosis and Treatment

On B-scan ultrasonography of the right eye, there was an elevated, echodense mass measuring 15 mm in thickness and 20 mm in diameter with a few lucencies, suspicious for tissue alteration, necrosis or cavitation. The mass demonstrated spontaneous vascular pulsations, suggestive of solid tumor rather than hemorrhage. There was adjacent retinal detachment *(Figure 2)*. Magnetic resonance imaging revealed an intraocular mass that was hyperintense on T1-weighted images and hypointense on T2-weighted images *(Figure 3)*. Importantly, gadolinium contrast showed enhancement within the mass, suggestive of solid tumor rather than hemorrhage or effusion. In the setting of a blind eye with intraocular mass concerning for choroidal melanoma, enucleation was recommended.

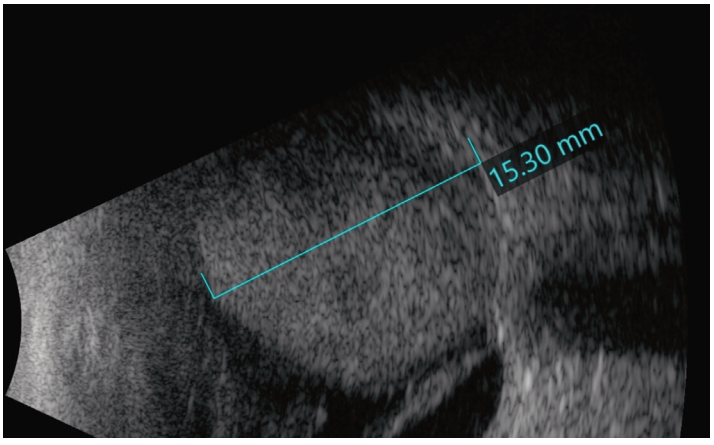

Figure 2. B-scan ultrasonography of the right eye showing an elevated choroidal mass with central cavitation and with retinal detachment inferiorly.

Following enucleation, pathology of the eye *(Figure 4)* grossly revealed a large intensely pigmented tumor arising from the ciliary body and choroid, as well as a 5 x 3 mm area of extraocular extension posteriorly. There were related sequelae from the tumor including extensive posterior synechiae with nearly the entire posterior surface of the iris adherent to the anterior surface to the lens, retinal detachment and dense cataract. Microscopic examination revealed tumor cells consistent with ciliochoroidal melanoma and tumor necrosis.

The patient recovered well from the enucleation and got fitted for a prosthesis. She was referred to a medical oncologist for systemic workup for metastatic disease. At this early point, there were no systemic metastases. Routine follow-up care was recommended.

Discussion

This case of uveal melanoma in a patient presenting with NVI is unique for two reasons: first, in adults, intraocular tumors are a rare cause of NVI or neovascular glaucoma (NVI leading to secondary elevation of IOP). Second, NVI and NVG are seen relatively rarely in uveal melanoma.

The most common causes of NVI and neovascular glaucoma in adults are diabetic retinopathy, central retinal vein occlusion and ocular ischemic syndrome. In total, these top three causes account for 80 percent of all cases of NVI/NVG.[1] A host of other causes make up the remaining 20 percent, including central retinal artery occlusion, uveitis, vasculitis, longstanding retinal detachment and neoplasms which include uveal melanoma, uveal metastasis and retinoblastoma.[1] It's important to note, however, that in children, the differential includes diverse ocular, genetic and systemic diseases, including intraocular tumors; thus, a full ophthalmological examination is needed to establish the underlying diagnosis.[2]

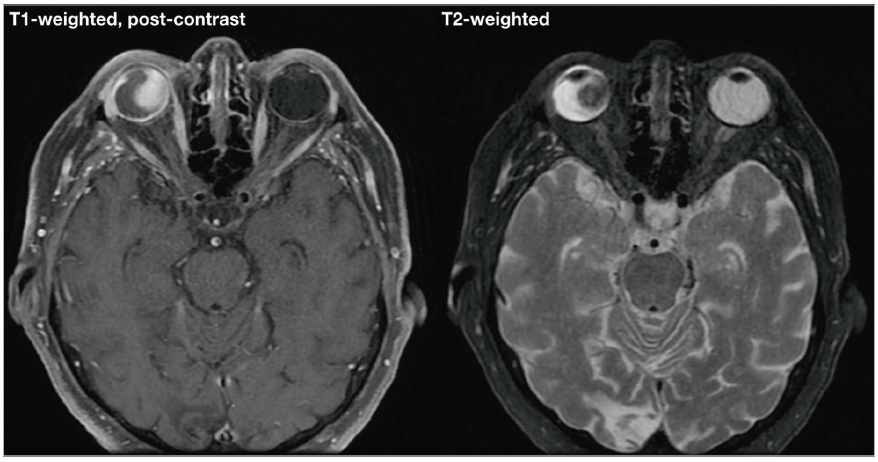

Figure 3. Magnetic resonance imaging showing hyperintense enhancing mass on T1-weighted, fat-suppressed image and hypointense mass on T2-weighted image within the right eye.

Uveal melanoma is rarely associated with secondary glaucoma. In a comprehensive review from the Wills Eye Hospital Ocular Oncology Service, only 3 percent of eyes with an intraocular tumor demonstrated secondary increase in IOP.[3] The frequency and mechanism of IOP elevation varied based on the type of melanoma. Seven percent of iris melanomas demonstrated secondary IOP elevation, most commonly due to direct invasion of the

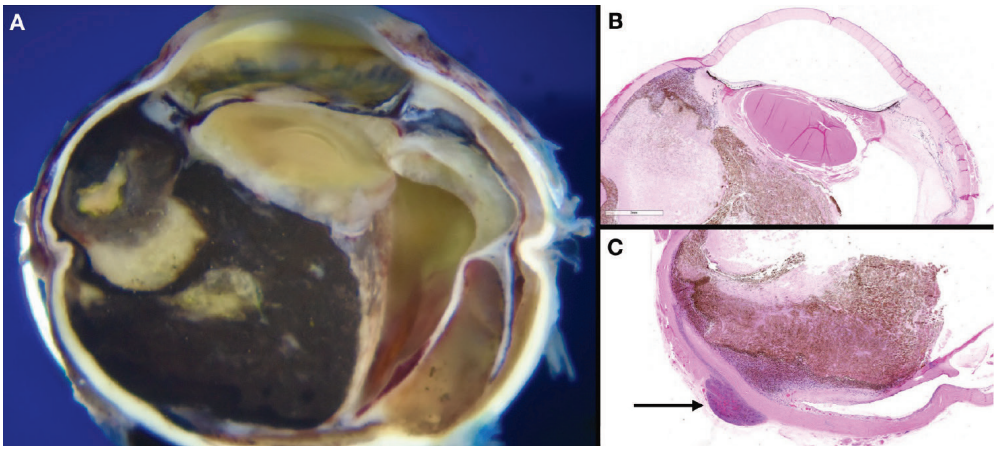

Figure 4. Pathology photos of sections of enucleated right globe. Gross photograph (A); hematoxylin and eosin stained slides (B) and (C). The arrow indicates area of posterior extraocular extension.

angle; 17 percent of ciliary body melanomas demonstrated secondary IOP elevation, most commonly due to pigment dispersion or direct invasion of the angle; and only 2 percent of choroidal melanomas demonstrated secondary IOP elevation, most commonly due to NVI.[3]

It's also valuable to discuss several clinical features of this case that are relevant for prognosis, namely tumor size, extraocular extension size, metastasis and genetic features.

Tumor size is measured by thickness and basal diameter. Small tumors (<3 mm thick and <11 mm basal diameter) have a 16 percent five-year mortality following enucleation; medium tumors, 35 percent mortality; and large tumors (>8mm thick or >15mm basal diameter), 53 percent mortality.[4,5] Our patient's tumor would be classified as large based on both thickness and basal diameter.

Extraocular extension is classified as microscopic with a 37 percent five-year mortality, small (1 to 4 mm) with 24 percent, and large (>5 mm) with 78 percent.[4] Our patient's tumor had a small area of extraocular extension.

Patients with choroidal melanoma demonstrate a high rate of metastasis: 32 percent by five years and 56 percent by 25 years, most commonly to the liver, lung and bone.[6] Metastasis is associated with a high mortality despite treatment, with a median survival of approximately 10 months.[7] As such, imaging surveillance for metastasis is recommended, with either MRI, computed tomography or hepatic ultrasonography at three to 12 month intervals depending on tumor features and cancer center-specific protocols.[8] Given the poor prognosis in metastatic disease, there's great interest in novel therapeutics for these patients. Several new targeted drugs are currently being investigated, such as tebentafusp, a bispecific protein that directly binds T cells to melanoma cells in order to activate the immune response,[9] and darovasertib, a protein kinase C inhibitor that prevents melanoma cells from proceeding with the cell cycle.[10] Metastatic uveal melanoma is the final frontier of treatment and continues to be an active area of research.

Genetic features have become an extremely important prognostic factor. The Cancer Genome Atlas is an international collaboration that's created classification systems for many cancers based on molecular changes in cancer cells.[11] For uveal melanoma, a TCGA group is assigned based on findings in chromosome 3 and 8, with more changes indicating higher risk.[12] This patient ultimately declined genetic testing. However, it should be noted that genetic testing is widely used in ocular oncology as a routine part of counseling patients with uveal melanoma.

In conclusion, in an adult patient presenting with iris neovascularization, uveal melanoma is a rare but serious consideration that should remain on the differential diagnosis. Factors such as tumor size, extraocular extension, and genetic features help to predict prognosis and drive the treatment plan with the goal of reducing the risk of melanoma-related metastasis. ◀

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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

GA unravels so much

Save retinal tissue by slowing progression[1-3]

INDICATION

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

IMPORTANT SAFETY INFORMATION

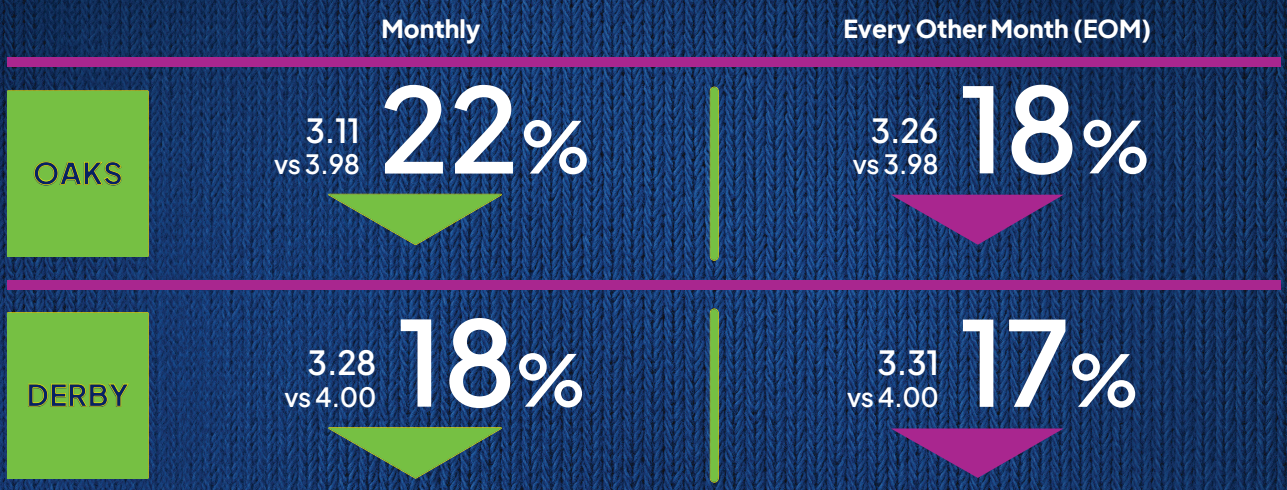
CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

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

SYFOVRE achieved continuous reductions in mean lesion growth rate* (mm^2) vs sham pooled from baseline to Month 24[1]



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

*Slope for baseline to Month 24 is an average of slope of baseline to Month 6, Month 6 to Month 12, Month 12 to Month 18, and Month 18 to Month 24.[1]
Based on a mixed effects model for repeated measures assuming a piecewise linear trend in time with knots at Month 6, Month 12, and Month 18.[1]
GA=geographic atrophy; SE=standard error.

Explore the long-term data

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

- **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.

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

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

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

Apellis

FOR REFRACTORY GLAUCOMA

BRIDGE THE GAP

WITH MINIMALLY INVASIVE FILTERING SURGERY

Not an actual patient.

XEN® Gel Stent is a proven pathway to IOP control for refractory glaucoma patients.[1]

- From a wide range of baseline pressures,* XEN® Gel Stent achieved a mean IOP of 15.9 (± 5.2) mm Hg through 12 months (n = 52)[1,2]
- 76% of XEN® Gel Stent patients achieved a ≥ 20% IOP reduction in the ITT group (N = 65)[1]
- 81% of XEN® Gel Stent patients achieved a ≥ 25% IOP reduction among those completing the 12-month visit (n = 52)[2]
- Pivotal safety data included 0% intraoperative complications (0/65) and 0% persistent hypotony (0/65); transient hypotony† occurred in 24.6% of patients (16/65)[1]

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]

CONSIDER XEN® FOR THE NEXT STOP ON YOUR PATIENT'S TREATMENT JOURNEY.

INDICATIONS

The XEN® Glaucoma Treatment System (XEN® 45 Gel Stent preloaded into a XEN® Injector) is indicated for the management of refractory glaucomas, including cases where previous surgical treatment has failed, cases of primary open-angle glaucoma, and pseudoexfoliative or pigmentary glaucoma with open angles that are unresponsive to maximum tolerated medical therapy.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

XEN® Gel Stent is contraindicated in angle-closure glaucoma where angle has not been surgically opened, previous glaucoma shunt/valve or conjunctival scarring/pathologies in the target quadrant, active inflammation, active iris neovascularization, anterior chamber intraocular lens, intraocular silicone oil, and vitreous in the anterior chamber.

WARNINGS

XEN® Gel Stent complications may include choroidal effusion, hyphema, hypotony, implant migration, implant exposure, wound leak, need for secondary surgical intervention, and intraocular surgery complications. Safety and effectiveness in neovascular, congenital, and infantile glaucoma has not been established. Avoid digital pressure following implantation of the XEN® Gel Stent to avoid the potential for implant damage.

PRECAUTIONS

Examine the XEN® Gel Stent and XEN® Injector in the operating room prior to use. Monitor intraocular pressure (IOP) postoperatively and if not adequately maintained, manage appropriately. Stop the procedure immediately if increased resistance is observed during implantation and use a new XEN® system. Safety and effectiveness of more than a single implanted XEN® Gel Stent has not been studied.

ADVERSE EVENTS

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%).

Caution: Federal law restricts this device to sale by or on the order of a licensed physician. For the full Directions for Use, please visit www.allergan.com/xen/usa.htm or call 1-800-678-1605. Please call 1-800-433-8871 to report an adverse event.

Please see full Directions for Use at https://www.rxabbvie.com/pdf/xen_dfu.pdf

References: 1. XEN® Directions for Use. 2. Data on file, AbbVie, Inc. ABVRRTI75098.

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XEN® GEL STENT

A Powerful, Proven Procedure