Wills Eye Resident Series:A patient presents with decreased vision after an injury, *p. 62*

REVIEW® of OPHTHALMOLOGY

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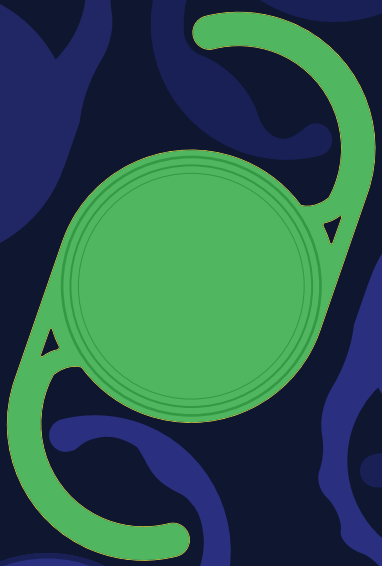
Clinical advice you can trust



Mixing and Matching Intraocular Lenses

Experts describe how they mix different IOL models to get the best results. **P. 33**

ALSO INSIDE:

Tyrvaya® is not another drop
It's an **ocular surface-sparing** nasal spray.[2]

Activates real, basal tears
Tyrvaya® is believed to work by activating the trigeminal parasympathetic pathway resulting in **basal tear production**.[2]*

Real tears, real fast
In 2 clinical trials with **mild, moderate, and severe** dry eye disease patients, Tyrvaya increased tear production from baseline by **≥10 mm in Schirmer's Test Score (STS) in nearly 50% of patients at week 4**, with increased tears seen as early as the first dose and over 12 weeks.[2-8]†

SEE WHAT TYRVAYA CAN DO

*The exact mechanism of action is unknown.
†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.

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

tyrvaya®
(varenicline solution)
nasal spray 0.03 mg

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

INDICATIONS AND USAGE

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

ADVERSE REACTIONS

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

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

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

USE IN SPECIFIC POPULATIONS

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

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

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

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

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

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

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

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

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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VOLUME XXXI • NO. 1

JANUARY 2024

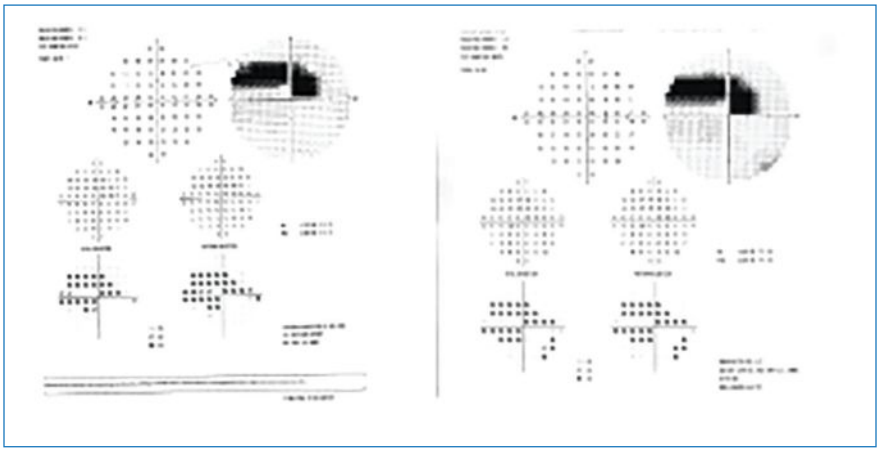
AAO Assessment Finds 10-2 VF Not Useful in Routine Testing

Study shows 10-2 VF testing doesn't detect any additional defect not already seen on 24-2 testing, but it provides sufficient additional information for patients with a repeatable defect within the central 12 locations of the 24-2 VF test.

In a new Ophthalmic Technology Assessment by the American Academy of Ophthalmology, researchers evaluated the current published literature on the utility of the 10-2 visual field (VF) testing strategy for the evaluation and management of early glaucoma, defined here as mean deviation (MD) better than -6 decibels (dB). They concluded that 10-2 VF testing may not be the most useful routine test for patients with early glaucoma, but would provide sufficient additional information for patients with a repeatable defect on the pupillary distance (PD) plot among the central 12 points on the 24-2 or 24-2C VF test. Their results were recently published in *Ophthalmology*.

After review, 26 articles in the PubMed database were selected; the panel methodologist rated them for strength of evidence. Thirteen articles were rated level I and eight articles were rated level II, while five level III articles were excluded. Data from the 21 included articles were abstracted and reviewed.

Results from the study found that the central 12 locations on the 24-2 VF test grid lie within the central 10 degrees covered by the 10-2 VF test. In early glaucoma, defects detected within the central 10 degrees generally agree between the two tests. Defects within the central 10 degrees of the 24-2 VF test can predict defects on the 10-2 VF test, although the 24-2 may miss defects detected on the 10-2 VF test.



A study shows 10-2 VF testing doesn't detect any additional defect not already seen on 24-2 testing, but it provides sufficient additional information for patients with a repeatable defect within the central 12 locations of a 24-2 VF test.

"In addition, results from the 10-2 VF test show better association with findings from OCT scans of the macular ganglion cell complex," the authors noted in their report. "Modifications of the 24-2 test that include extra test locations within the central 10 degrees improve detection of central defects found on 10-2 VF testing."

The authors explained that central VF defects may be underappreciated in the evaluation of early glaucoma. "Although less common in cases in which MD is better than -6 dB, central defects may have a profound impact on a person's visual function and quality of life. Thus, detection of central VF defects is essential in the diagnosis and management of glaucoma even at the earliest stages," they explained.

With the extra central test locations, the Zeiss 24-2C or the Octopus G1 test strategies can improve detection of central defects over the standard 24-2 VF, the authors added. Although the 10-2 VF is considered the gold standard for detecting central VF defects, it's more involved for both the patient and clinician, as it entails additional time, cost and effort, and it may not always detect any additional defect not already seen on 24-2 testing.

The authors say the evidence doesn't support routine testing using 10-2 VF for patients with early glaucoma. "Recent studies provide some evidence

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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. Piers P, Manzanera S, Prieto P, Gorceix N, Artal P. Use of adaptive optics to determine the optimal ocular spherical aberration. *J Cataract Refract Surg.* 2007;33(10):1721-1726.
4. DOF2021CT4002 - RUSH: TECNIS Eyhance™ IOL Monofocal Competitors MTF - US.

INDICATIONS and IMPORTANT SAFETY INFORMATION for TECNIS Eyhance™ and TECNIS Eyhance™ Toric II IOLs with TECNIS Simplicity® Delivery System

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INDICATIONS FOR USE: The TECNIS Simplicity® Delivery System is used to fold and assist in inserting the TECNIS Eyhance™ IOL for the visual correction of aphakia in adult patients in whom a cataractous lens has been removed by extracapsular cataract extraction. The lens is intended to be placed in the capsular bag. The TECNIS Simplicity® Delivery System is used to fold and assist in inserting the TECNIS Eyhance™ Toric II IOLs for the visual correction of aphakia and pre-existing corneal astigmatism of one diopter or greater in adult patients with or without presbyopia in whom a cataractous lens has been removed by phacoemulsification and who desire reduction in residual refractive cylinder. The lens is intended to be placed in the capsular bag.

WARNINGS: Physicians considering lens implantation should weigh the potential risk/benefit ratio for any conditions described in the Directions for Use that could increase complications or impact patient outcomes. The lens should be placed entirely in the capsular bag. Do not place the lens in the ciliary sulcus. Rotation of the TECNIS Eyhance™ Toric II IOL from its intended axis can reduce its astigmatic correction. Misalignment greater than 30° may increase postoperative refractive cylinder. If necessary, lens repositioning should occur as early as possible, prior to lens encapsulation. Do not attempt to disassemble, modify or alter the delivery system or any of its components, as this can significantly affect the function and/or structural integrity of the design. Do not implant the lens if the rod tip does not advance the lens or if it is jammed in the delivery system. The lens and delivery system should be discarded if the lens has been folded within the cartridge for more than 10 minutes.

PRECAUTIONS: The safety and effectiveness of the TECNIS Eyhance™ IOL has not been substantiated in clinical trials and the effects of the optical design on quality of vision, contrast sensitivity, and subjective visual disturbances (glare, halo, etc.) have not been evaluated clinically. This is a single use device, do not resterilize the lens or the delivery system. Do not store the device in direct sunlight or at a temperature under 5°C (41°F) or over 35°C (95°F). Do not autoclave the delivery system. Do not advance the lens unless ready for lens implantation. The contents are sterile unless the package is opened or damaged. The recommended temperature for implanting the lens is at least 17°C (63°F). The use of balanced salt solution or viscoelastics is required when using the delivery system. Do not use if the delivery system has been dropped or if any part was inadvertently struck while outside the shipping box.

ADVERSE EVENTS: The most frequently reported cumulative adverse event that occurred during the SENSAR® 1-Piece IOL clinical trial was cystoid macular edema which occurred at a rate of 3.3%.

ATTENTION: Reference the Directions for Use for a complete listing of Indications and Important Safety Information.

on additional VF testing in some cases, however," they add. "Early 10-2 VF testing would provide sufficient additional information for any patient with a repeatable defect on the PD plot among the central 12 points on the 24-2 or 24-2C VF test or with a depressed average and/or minimum mGCIPL thickness on SD-OCT. A defect on SAP 10-2 VF warrants confirmation and potentially a lifelong commitment to serial 10-2 VF testing."

1. WuDunn D, Takusagawa HL, Rosdahl JA, et al. Central VF testing in early glaucoma. Ophthalmology. December 8, 2023. [Epub ahead of print.]

Daily Smoking Linked to Visual Impairment in NTG

Though the relationship between smoking and glaucoma is controversial, current evidence does suggest that tobacco smoke plays a role in the development of ischemia and oxidative alterations in ocular tissues. A recent study was conducted in Serbia to determine whether smoking patterns might be related to vision-related disability among the different subtypes of glaucoma. It found that a higher number of cigarettes smoked daily was associated with poorer visual impairment only among people with normal-tension glaucoma, but not the other subtypes.

The cross-sectional study included 283 patients with primary open-angle glaucoma, primary angle closure glaucoma, normal-tension glaucoma and pseudo-exfoliative. Information about the duration and quantity of smoking was self-reported. To quantify vision-related impairment, each patient completed a validated Glaucoma Quality of Life-15 questionnaire.

After adjusting for nine confounding variables, including age, gender, glaucoma severity, IOP level and lifestyle, the data revealed that the number of cigarettes smoked per day was negatively correlated with vision-related quality-of-life among people with normal-tension glaucoma subtypes. Smoking duration (in years), on the other hand, did not show the same association in normal-tension glaucoma patients.

"It is believed that normal-tension glaucoma is a distinctive subtype of glaucoma that is characterized by a somewhat different pathogenesis compared to other glaucoma subtypes," the researchers wrote in their paper on the study, published in *Ophthalmic Epidemiology*. This unique pathogenesis may involve ocular blood flow disruption and vascular dysregulation, which also describes the suspected effect of tobacco on ocular tissue, they pointed out.

Oxidative stress may be another nicotine-dependent mechanism at the sub-cellular level that could contribute to worsening visual function. "It has been identified that tobacco smoking can induce cell inflammation and apoptosis in the eye tissue," the researchers noted in their paper. "This finding is in accordance with the notion that, in glaucoma, retinal ganglions and cells of the trabeculum die by apoptosis."

Regarding the lack of an association found between smoking duration and worse visual functioning in normal-tension glaucoma patients, the researchers note that some literature describes a protective effect of nicotine on the optic nerve and suggests it may improve the structure's blood supply. "This could potentially explain why long and moderate cigarette smoking wasn't found to be a risk factor for the onset of glaucoma [and] could also be the underlying reason as to why there are so many controversies when the association between tobacco and glaucoma is being assessed," the study authors wrote.

Limitations of this study include the self-reporting of smoking habits and visual impairment, which introduces inherent bias, as well as the fact that the majority of participants were Caucasian, despite the higher prevalence of certain glaucoma subtypes in people of Asian and African descent.

In conclusion, the authors wrote, "Our findings highlight the need to examine smoking habits among people with glaucoma, especially among people with normal-tension glaucoma, during their health checks and address the issue of smoking as a potential harmful factor that may further damage their vision-related functioning."

Sencanic I, Dotlic J, Jaksic V, Grgurevic A, Gazibara T. Association of smoking patterns with vision-related disability according to glaucoma subtypes. Ophthalmic Epidemiology. December 12, 2023. [Epub ahead of print].

Consumption of Vitamin B1 and Advanced AMD

Investigators studied the association between vitamin B1 consumption and the prevalence of late age-related macular degeneration in a representative U.S. sample.[1]

Data from the National Health and Nutrition Examination Survey (NHANES) between 2005 and 2008 were used for this cross-sectional analysis. The logistic regression model was used to evaluate the association between vitamin B1 consumption levels and late AMD.

The study included 5,107 people ages 40 and older. Vitamin B1 intake levels were inversely associated with the prevalence of late AMD, with OR being 0.40 (CI, 0.26 to 0.62) for crude model 1; 0.53 (CI, 0.29 to 0.94) for adjusted model 2; and 0.55 (CI, 0.31 to 0.99) for the fully adjusted model 3.

Investigators found that vitamin B1 intake levels were inversely associated with the prevalence of late AMD in the United States. They suggested that further randomized clinical trials among multiple centers is warranted to investigate the longitudinal and causal relationship between vitamin B1 intake and late AMD.

1. Zheng Q, Shen T, Xu M, et al. Association between dietary consumption of vitamin B1 and advanced age-related macular degeneration: A cross-sectional observational study in NHANES 2005-2008. Ophthalmic Res 2023; Nov 3. [Epub ahead of print].

AS-OCT Helps Define Late Ectasia After PK Procedures

The subtype of ectatic disease following penetrating keratoplasty (PK) has been defined poorly in the literature, with the terminology not being consistent. In contrast to Scheimpflug tomography, measurements with anterior segment optical coherence tomography AS-OCT are also possible in corneas with opacity. A research team based in Germany has used this imaging modality to describe morphological parameters of ectatic corneas after PK.[1] They noted an acute graft-host interface angle, steep keratometry value, deep AC and a stromal thinning at the interface as significant signs of ectasia. A ratio calculated by the relationship between the thinnest point at the interface and the central corneal thickness was significantly lower in ectatic eyes.

The team included 50 eyes of 32 patients with a history of PK at an average of 25 years earlier were included, 35 ectatic and 15 not. Mean age at time of examination was 63, mean interval between PK and time of AS-OCT examination was 25 years. PK had been performed at an average age of 38. The control group consisted of 30 healthy age-matched eyes (mean age: 62). They assessed steep and flat keratometry readings obtained with AS-OCT (CASIA-2, Tomey) and Scheimpflug tomography (Pentacam, Oculus). OCT findings were correlated with clinical grading of ectasia.

The interval between PK and examination was significantly longer in eyes with ectasia compared with non-ectatic eyes in the study. There was a highly significant difference in lowest corneal thickness at the interface, graft-host interface angle and anterior chamber depth (in pseudophakic eyes) between the groups. The ratio calculated by the quotient of lowest corneal thickness at the interface divided by central corneal thickness (CCT) was significantly lower in ectatic than non-ectatic eyes. In eyes with a ratio of ≤0.7, the odds ratio for the occurrence of a clinical detectable ectasia was 2.4. Steep keratometry values were significantly higher in ectatic eyes.

The researchers thought it was interesting that there was a significant difference of several morphometric and keratometric parameters between the healthy control eyes and the post-PK eyes classified clinically as non-ectatic. "This could be explained either by the steep and thinned corneal recipient rim in keratoconus eyes or by early manifestation of ectasia, which is clinically not yet visible," they wrote in their paper.

"The value of the morphological characterization of ectatic corneas using AS-OCT is limited insofar as the decision whether to perform surgical or other intervention is based on reduced visual function rather than altered corneal morphology," the team

LETTER TO THE EDITOR

To the Editor:
I'd like to comment on the December 2023 article: "The Ins and Outs of Customized LASIK." It's my clinical impression that topography-modified refraction isn't widely used. Phorcides is used by more than 500 surgeons worldwide to make Contoura planning more efficient and far more accurate. The prospective study, published in *JCRS* (https://pubmed.ncbi.nlm.nih.gov/35171146/), shows results far better than those quoted in the article. Also, prospective studies are considered more powerful and meaningful than retrospective.

Phorcides improved results of Contoura in both the retrospective and prospective studies over the FDA study, which is remarkable because the FDA study only used 'perfect' corneas, but the studies [with Phorcides] used real-world corneas that have topographic irregularities.

Mark Lobanoff, MD
Minneapolis
(Disclosure: Dr. Lobanoff is a consultant for Alcon and the CEO and owner of Phorcides)

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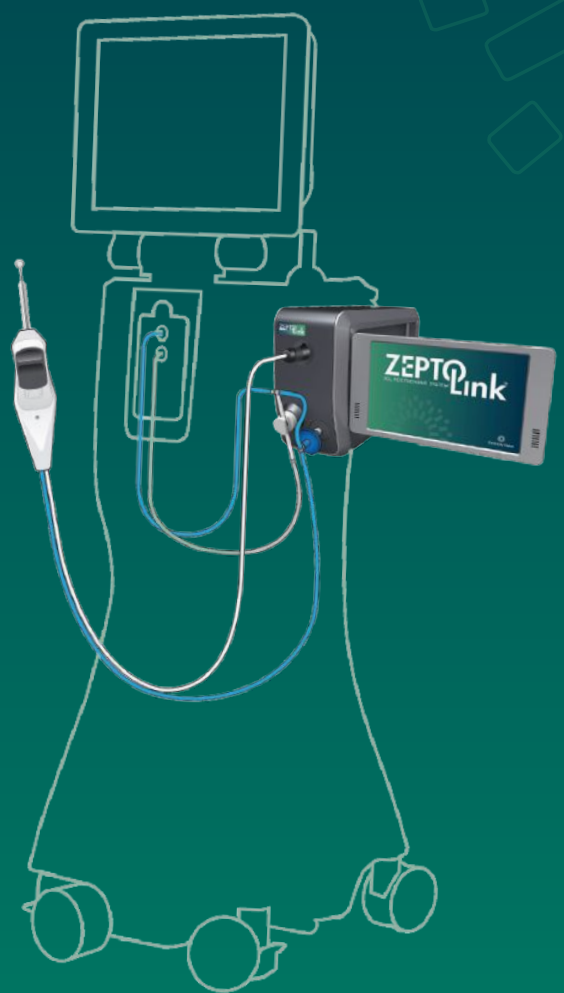

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DEPARTMENTS

January 2024

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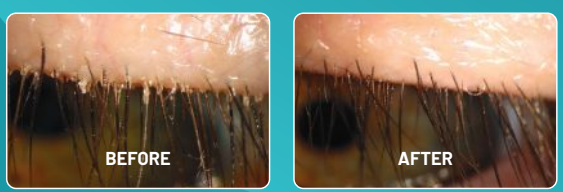

44% and 55% of patients taking XDEMVY in SATURN-1 (N=209) and SATURN-2 (N=193), respectively, achieved a significant improvement in their eyelids (reduction of collarettes to no more than 2 collarettes per upper lid) at Day 43 vs 7% (N=204) and 12% (N=200) of patients taking vehicle ($P<0.01$ in each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

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

INDICATIONS AND USAGE

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

IMPORTANT SAFETY INFORMATION:

WARNINGS AND PRECAUTIONS

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

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

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

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

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

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

tarsus

pointed out. "Since objective and subjective measurements of refraction might prove to be difficult in ectatic eyes, AS-OCT measurements could serve as surrogate markers for progressive ectasia over time but should not be used for surgical decision-making."

1. Weller JM, Hübner L, Kruse FE, Tourtas T. Characterization of ectasia after penetrating keratoplasty in keratoconus eyes using anterior segment optical coherence tomography. Br J Ophthalmol. March 20, 2023. [Epub ahead of print].

Vision Screening Needed in Parkinson's Disease

For individuals living with Parkinson's disease, maintaining good visual function is key for continued ability to work. However, this condition can affect vision, and the findings of a recent survey study showed that few people are aware of this. The paper, published in the *American Journal of Occupational Therapy*, reported that vision dysfunction affects occupational performance and that greater education about vision difficulties in Parkinson's disease is needed.

The cross-sectional analysis included 92 persons with Parkinson's disease who self-reported visual difficulties, diagnosed eye conditions and general awareness of disease-related visual dysfunction in an electronic survey.

The researchers found that almost half of respondents were unaware that Parkinson's disease could affect vision. They also found that awareness wasn't associated with disease duration, and that individuals who reported awareness also tended to report vision difficulties. They reported mild impairment for functional activities requiring vision. The frequency of ophthalmologic symptoms was low. These were mostly related to ocular surface disease. However, the researchers reported that a higher frequency of ophthalmologic symptoms was positively associated with a higher degree of disability in activities of daily living.

"If the effect that Parkinson's disease can have on visual function is not understood by persons with Parkinson's disease or is overlooked by their health-care provider, the underlying cause of difficulties engaging in daily occupations may be missed or mistaken," the researchers pointed out in their paper. "Assessing and evaluating visual function in persons with Parkinson's disease may aid in elucidating changes in occupational performance and help guide targeted treatment approaches as they become available."

1. Tester NJ, Liu C, Shin Y, et al. Visual dysfunction and occupational performance in persons with Parkinson's disease. Am J Occupational Therapy 2023;77:7706206060. [Epub ahead of print].

(Continued on p. 16)

REVIEW of OPHTHALMOLOGY

Clinical advice you can trust

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REVIEW of OPHTHALMOLOGY

WALTER C. BETHKE, EDITOR IN CHIEF

EDITOR'S PAGE

How to Beat the High Cost of Practicing

Each year, barring very bad economic times, the average worker usually gets a cost-of-living increase to offset inflation. In fact, this year, the Federal Register published that a cost-of-living increase of about 3.2 percent would be instituted by the Social Security Administration, based on the past year's Consumer Price Index.[1]

Ironically, it was also announced in the Federal Register that the government is slashing Medicare reimbursement rates by 5.4 percent. It's odd how the powers-that-be acknowledge people need an increase to offset the rising cost of living, while, at the same time, inform ophthalmologists and other physicians they deserve to take a cut. Ambulatory surgical centers, however, got a 2.8-percent increase to their reimbursement rates, as long as they met certain quality criteria in the past year.

This last part is kind of a head-scratcher because, yes, ASCs have overhead, but don't ophthalmologists have costs to worry about, too? According to a poll by the Medical Group Management Association, 96 percent of medical groups experienced either an increase in their operating costs or saw their costs stay the same in the past year.[2] The average increase in costs cited by the poll's respondents was 12.5 percent, owed mostly to increases in wages and salaries, higher supply costs and information technology expenses.[2] In the face of this, a cut of just more than 5 percent is a bitter pill to swallow, especially when cataract surgery is such an integral part of most ophthalmologists' practices. Where's their cost-of-living increase?

Against this backdrop of rising costs due to inflation and cuts to reimbursement, this month's cover story on mixing and matching intraocular lenses *(pg. 33)* takes on added significance. This is because most of the lenses discussed by surgeons in the article are in the premium category, so implanting them would help offset any of the losses imposed by the impending cuts to Medicare reimbursement.

In the past, surgeons have consistently demonstrated a hesitancy to jump into the world of premium IOL implantation, and for good reason—it involves a good deal of expense in terms of education, staff training and new equipment (including purchasing the lenses). However, as the new year dawns, and considering the current Medicare cut and the potential for future cuts to come, it might be time for surgeons to start mixing and matching a Medicare practice with a fee-for-service one.

Whichever path you choose this year, the staff of *Review* wishes you all a heathy, successful 2024.

— Walter Bethke
Editor in Chief

1. The Federal Register. https://www.federalregister.gov/documents/2023/10/23/2023-23317/cost-of-living-increase-and-other-determinations-for-2024#:~:text=The%20CPI%20for%20the%20calendar,title%20II%20of%20the%20Act. Accessed December 21, 2023.
2. Harrop C. Higher costs for medical groups persist even as inflation growth slows. https://www.mgma.com/mgma-stat/higher-costs-persist-for-medical-groups-even-as-inflations-growth-slows. Accessed December 21, 2023.

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Andy Corley is the Chair of the Board of RxSight, Inc. and owns equity interest in the company.

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(Continued from p. 12)

The Benefits of MIGS Plus Cataract Surgery

As many surgeons have suspected, combining a MIGS procedure with cataract surgery may produce meaningful results over time for open-angle glaucoma patients, according to a recent report by the AAO's Ophthalmic Technology Assessment Committee Glaucoma Panel, which reviewed the current literature on combined trabecular MIGS procedure/cataract compared with cataract surgery alone. While both approaches show good track records for lowering pressure, the combined approach may offer patients a small edge.

The researchers' PubMed literature search returned 279 articles, of which 20 were graded for quality and 10 of those studies (all level I randomized controlled trials) were included in the final assessment. The researchers noted that all 10 of these studies were "subject to potential industry-sponsorship bias."

They reported that based on medication washout studies with two-year data in patients with hypertensive, mild to moderate OAG, adding a trabecular procedure to cataract surgery resulted in an additional 1.6 to 2.3 mmHg IOP reduction—i.e., 4 to 9 percent IOP reduction, resulting in an average reduction of about 0.4 medications; vs. cataract surgery alone, which on its own reduces IOP by approximately 5.4 to 7.6 mmHg or by about 21 to 28 percent, possibly eliminating 0.8 to 1 glaucoma medications.

"The three most studied trabecular procedures [iStent/iStent Inject, Hydrus Microstent and excisional goniotomy via Kahook Dual Blade] appear to produce similar results among hypertensive mild to moderate OAG subjects with modest IOP reduction or medication reduction over cataract surgery alone at two years," the researchers wrote in their paper. "There is no clear benefit of adding one trabecular procedure to cataract surgery over another based on these available data."

Future research should focus on standardizing outcome definitions, avoiding sponsorship bias and studying efficacy in normotensive OAG, since all studies were in patients with pretreatment IOP of 21 mmHg or less, the researchers pointed out in their paper.

"Although the primary goal for MIGS surgeons is often to reduce the medication burden, the mild mean IOP reduction of approximately 2 mmHg by a trabecular procedure is estimated to result in a mean reduction in number of medications of 0.4 at two years." Therefore, they wrote that it's good to tell patients that adding a trabecular procedure can further decrease their medication burden. ◀

1. Richter GM, Takusagawa HL, Sit AJ, et al. Trabecular procedures combined with cataract surgery for open-angle glaucoma: Ophthalmic Technology Assessment. Ophthalmology 2023;1-13.

The Winter of our Discontent

Musings on life, medicine and the practice of ophthalmology.

MARK H. BLECHER
CHIEF MEDICAL EDITOR

You must think I love Shakespeare since so many of my columns invoke either his themes or his catchy lines. And you would be right. He was amazing, and despite the many centuries and changes in Western civilization that have passed, his relevance and poignancy remain. Sadly though, most of his themes, and many of my columns, are dark and despairing. It's now January, the days are actually darkest, the weather the most bleak in many parts of the country. And whether you're focusing on world events, politics or the state of ophthalmology, it's tough to find an optimistic corner for your mind to dwell.

I touched on the seemingly endless bad news from Medicare regarding cataract reimbursement, MIGS policy and MIPS cataract cost regulations which have a tendency to spill over into commercial insurances in my online column end of December. Find it on *Review*'s website if you missed it. For this column, I have a need to turn to world events, however grim. In particular the very obvious machinations of Vladimir Putin. So much has been written. I find it hard to believe anyone in the West could support him, yet many do. His ham-handed and obvious lies about his invasion of Ukraine, his assertions that NATO was going to attack Russia, interference with public opinion in the West through the many hackers and propaganda organizations infiltrating social media, and now stirring up hot spots around the world through his proxies are among some of his recent actions.

Additionally, Russia's ally Iran, is encouraging its proxies in the Middle East, both Hamas and Yemen, as well as groups in Iraq. The timing is clearly to distract both media attention and resources from the situation in the Ukraine. And now out of seemingly nowhere, another ally, Venezuela, has annexed a large part of its neighbor, Guyana. I'm sure this is just a coincidence. I suppose I should take my hat off to the master KGB agent for stirring so many pots at the same time. These many regional wars and the disinformation campaigns around the world are brilliant work. Admittedly, the United States and its allies are no angels, and the seeds for these disputes were sown decades ago. I'm finding it very depressing as someone who lived through the Cold War to be reliving a daily fear of nuclear Armageddon with the Russians. Talk about history repeating itself. It all very clearly illustrates that history runs in cycles: Good and Bad. Reactionary and Revolutionary, Fascist and Progressive. I find it hard to feel that our 'arc of history' is bending in any way for the better—just revisiting the same old bad news.

So what can we do about it? I think what we can and need to do, and what we've done a terrible job of so far, is to remember our history. Those who forget it are condemned to repeat it, as they say, and I'm afraid we're condemned—by our own hand. We not only don't teach enough history—including the very unsavory parts—we have elements in our society that are aggressively fighting to prohibit teaching it: Remove the history of slavery, deny the Holocaust, whitewash Naziism. I could go on, but it's not pretty. So, we find ourselves with individuals and groups enamored of some of these themes either by ignorance or evil. And it's not wrong to call something evil. While we struggle to preserve free speech, we must agree that some thoughts, speech and actions are evil, and need to be not only prohibited but shamed and prosecuted. We can't sacrifice our civility and morals to the unfettered anarchy of freedom. There are and should be limits. We have to find them, agree to them and enforce them. Or we will allow evil to not only go unpunished, but unrecognized. ◀

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

MARY PAT JOHNSON, COMT, CPC, COE, CPMA

MEDICARE Q&A

Coding and Payment Updates for 2024

All you need to know about the most recent changes to physician reimbursement, facility reimbursement and more.

The start of the new year is a perfect time to review updates in place for 2024 and perhaps revisit your compliance efforts to help ensure continued accuracy in your billing procedures. Here, we'll highlight important changes for coding, reimbursement and regulations that impact ophthalmic practices.

Q What are the changes to physician reimbursement?

A The 2024 Medicare Physician Fee Schedule (MPFS) was published in the Federal Register on November 1, 2023. The MPFS conversion factor for 2024 is $32.7442, down 3.4 percent from 2023. This is the result of many factors, including a neutral MACRA (0 percent) update to physician payments for 2024, a positive (+1.25 percent) update from the Consolidated Appropriations Act and a negative (-2.18 percent) budget neutrality adjustment. The 2 percent sequestration payment adjustment applied to all Medicare Fee-for-Service (FFS) claims is also in effect. The result is a 5.4-percent cut to Medicare rates in 2024.

Changes in RVUs affect certain services more than others. We see increases in fees for a few codes and decreases in fees for others—the codes aren't impacted equally.

A few of the more notable changes appear in the table above.

RVU CHANGES FOR 2024

CPT	Short Descriptor	2023	2024
92235	Fluorescein angiography	$139	$159
92270	Electro-oculography	$110	$115
92065	Optical coherence biometry	$41	$39
92229	Image retina, autonomous analysis	$46	$40
92284	Dark adaptation exam	$47	$37
65778	Amniotic membrane	$1,346	$1,069
65780	Ocular surface reconstruction	$668	$577
67320	Transposition, add-on	$203	$168
67331	Revise eye muscle, add-on	$193	$156

Q What's new in facility reimbursement?

A Some aspects of reimbursement for facilities have been updated. Here's a breakdown:

• ***Payment rates.*** For ASCs that met their quality reporting requirements there's a 2.8-percent increase to the conversion factor; now $53.397.[2] Those that failed to meet quality requirements in the most recent year will be paid based on a CF of $52.358.

Payment rates for hospital outpatient departments (HOPDs) also went up 2.8 percent. The table on page 18 lists the 2023 and 2024 Medicare ASC and HOPD allowed amounts for a few common ophthalmic procedures.

• ***ASC quality measures.*** For 2024, Quality measures ASC-1 through ASC-4 remain required. Providers will continue submitting through the HQR System for all patients, not just those on Medicare.[3] Quality measure ASC-11 (Cataracts: improvement in function) remains voluntary in 2024.

• ***Reimbursement for Injectables in an ASC.*** There's no change to ASC reimbursement for three frequently used ophthalmic drugs: Omidria (J1097); Dextenza (J1096); and Dexycu (J1095).

Omidria and Dextenza continue to be reimbursed separately in an ASC in 2024, under Medicare regulations for non-opioid pain management drugs and supplies. These won't be paid separately in an HOPD. Dexycu doesn't qualify as a non-opioid pain management drug; no separate reimbursement is made for it.

• ***New ASC eligible CPT code.*** The new ophthalmic surgery code (CPT 65716-Suprachoroidal space injection of medication) was added to the list of codes eligible for an ASC facility payment. The 2024 ASC allowed amount is $63.20.

• ***Patient surveys.*** The Outpatient and Ambulatory Surgery Consumer Assessment initiative was developed as part of a 'patient experience of care' survey, and will be required beginning calendar year 2025. For 2024, ASCs may voluntarily submit data for the survey. Facilities will contract with a CMS-approved vendor to conduct the survey. See the OAS CAHPS website for a vendor list and additional information.[4]

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.

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References: 1. Market Scope Q4 - 2022 US Cataract Quarterly Update **2.** Hill, Distribution Data (2021). **3.** Watanabe. Effect of Experimentally Induced Astigmatism on Functional, Conventional., and Low-Contrast Visual Acuity (2013).

Q Are there notable changes to CPT coding?

A The dawning of 2024 brought 230 additions to the CPT book. Forty-nine codes were deleted and 70 were revised. Code 65716, introduced above, is the only new category I ophthalmic CPT code. None of the revised or deleted codes were ophthalmic specific, although changes to E/M codes for physician time spent and the consolidation of more than 50 CPT codes related to COVID may have limited impact on ophthalmic practices.

Four category III codes that were set to expire but were renewed January 1, 2024, include:

- 0330T–Tear film imaging, unilateral or bilateral, with interpretation and report
- 0506T–Macular pigment optical density measurement of flicker photometry, unilateral or bilateral, with interpretation and report
- 0507T–Near infrared dual imaging (i.e., simultaneous reflective and transilluminated light) of meibomian glands, unilateral or bilateral, with interpretation and report
- 0509T–Electroretinography (ERG) with interpretation and report, pattern (PERG)

One new category III code was introduced, effective January 1, 2024:

- 0810T–Subretinal injection of a pharmacologic agent, including vitrectomy and one or more retinotomies

One category III code was deleted, effective December 31, 2023:

- 0456T–Suprachoroidal injection of a pharmacologic agent (does not include supply of medication).

Q What's changed in HCPCS Coding?

A The new HCPCS add-on code, G2211, is defined as: "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 of a complex condition."

This is a CMS-generated add-on code. So far, CMS hasn't issued instructions for its use. However, the CMS website includes a listing of pertinent "practitioner primary care specialties," and it doesn't include ophthalmology. Currently, it doesn't appear that the new code will be helpful to ophthalmology in recovering any of the MPFS decrease.[5]

There are two other new HCPCS codes for covering the two new treatments for geographic atrophy:

- J2781 for Syfovre (pegcetacoplan injection)
- J3490 (unlisted drug) for Izervay (avacincaptad pegol intravitreal solution).

Q What's new in ICD-10 coding for 2024?

A Changes to diagnosis codes for 2024 are already in effect. ICD-10 changes and updates apply on October 1 each year. There were 842 new, revised or deleted codes.

ASC AND HOSPITAL ALLOWED AMOUNTS

CPT	Short Descriptor	ASC 2023	ASC 2024	HOPD 2023	HOPD 2024
66984	CEIOL	$1,101	$1,184	$2,159	$2,223
15823	Blepharoplasty	$899	$946	$1,726	$1,739
66821	YAG capsulotomy	$276	$302	$531	$544
67036	PP vitrectomy	$1,969	2,045	$3,996	$3,878

Those that affect ophthalmology are noted here. In many cases the code series were simply expanded to add more detail and laterality.

- H36–Retinal disorders in diseases classified elsewhere
- H36.8–Sickle-cell retinopathy
- H50.62–Inferior Oblique muscle entrapment
- H50.63–Inferior Rectus muscle entrapment
- H50.64–Lateral Rectus muscle entrapment
- H50.65–Medical rectus muscle entrapment
- H50.66–Superior oblique muscle entrapment
- H50.67–Superior rectus muscle entrapment
- H50.68–Unspecified extraocular muscle entrapment
- H52.51–Specificity added to eye and category
- H52.51–Internal ophthalmoplegia
- H57.8A–Foreign body sensation eye (ocular)

Q What coding requirements exist for anesthesia administration?

A Since COVID-19, the shortage of anesthesia providers has impacted care at ophthalmic ASCs. Schedules had been disrupted with cases being postponed or canceled when no anesthesia provider was available. Costs have risen. Some ophthalmic surgeons and ASCs are looking for alternatives. If considering conscious sedation, know the requirements for moderate conscious sedation as detailed in the CPT handbook, including:

- qualified independent trained observer;
- continuous monitoring;
- sufficient work to support CPT billed;
- intraservice time of at least 10 minutes;
- adequate documentation;
- not MAC (Code 0014x);
- it meets state statutes; and
- the surgeon is approved for conscious sedation.

Q What's new in coverage for glaucoma surgeries?

A Several Medicare Administrative Contractors (MACs) published revised policies for minimally-invasive glaucoma surgery in October, effective 12/24/23. One carrier, NGS, subsequently pushed the effective date to March 22, 2024. Others may follow suit. These proposed policies cover most areas in the country. Currently only First Coast Service Options, covering Florida and Puerto Rico, and Novitas Solutions—both jurisdiction JH in Texas and surrounding states and jurisdiction JL in and around Pennsylvania—are excluded.

The details of these policies are beyond the scope of this article; they affect almost all glaucoma procedures and, in many cases, greatly restrict coverage. Careful review of the policies is needed to understand the reimbursement implications.

Q Are there any changes to telehealth reimbursement in 2024?

A The COVID-19 Public Health Emergency has ended and changes to telemedicine will take effect in 2024.[6] For 2024, providers are no longer instructed to bill telehealth claims with the place of service they would have billed for an in-person visit. Instead, report claims with:

- POS 02–teleheath provided with an originating site other than the patient's home; or
- POS 10–telehealth provided while the patient was in their home

Claims billed with POS 02 will be paid at the Physician Fee Schedule facility rate while those reported with POS 10 will be paid at the higher non-facility PFS rate. Modifier 95 is no longer needed on telemedicine claims.

Q Will any changes affect Medicare beneficiaries?

A The Medicare Part B basic premium will increase to $174.70 for most beneficiaries. The Part B deductible increases to $240, a $16 increase.

Part C Medicare (Medicare Advantage) continues to grow. Fifty-one percent of all eligible beneficiaries were enrolled in an MA plan in 2023.[7] The Congressional Budget Office estimates that enrollment will rise to about 62 percent of eligible beneficiaries by 2033.[8] Penetration of Medicare Advantage plans varies widely by state.

In conclusion, coverage, coding and billing rules change each year. Staying educated on the current codes and instructions is an important aspect of your compliance efforts. ◀

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8. May Congressional Budget Office Medicare Baseline for 2023. https://www.cbo.gov/system/files/2023-05/51302-2023-05-medicare.pdf.

SMILE Complications: What Not to Do

The most common problems that surgeons experience when starting small-incision lenticule extraction procedures.

LIZ HUNTER
SENIOR EDITOR

Once surgeons become skilled at a particular type of refractive surgery, they may think they can easily move to another form of refractive surgery without complications, according to Ashvin Agarwal, MD, who is a cataract and refractive surgeon and the chief clinical officer of Dr. Agarwal's Eye Hospital in Chennai, India. "When starting out with small-incision lenticule extraction, it's easy to be bullish," he says. "It's like having a new toy in your hands and you want to explore the boundaries of it. The manufacturer has recommended parameters, and surgeons start testing how much further they can push those limits."

The SMILE Technique

SMILE is being embraced by more refractive surgeons year after year for a number of reasons, including its lack of flap creation which significantly lowers the risk of flap dislocation and reduces issues that could occur during the healing process. The procedure, approved by the FDA in 2016, requires a specific femtosecond laser (Zeiss VisuMax) to create a disc-shaped lenticule inside the cornea. The lenticule is then removed through a 2- to 3-mm corneal incision.

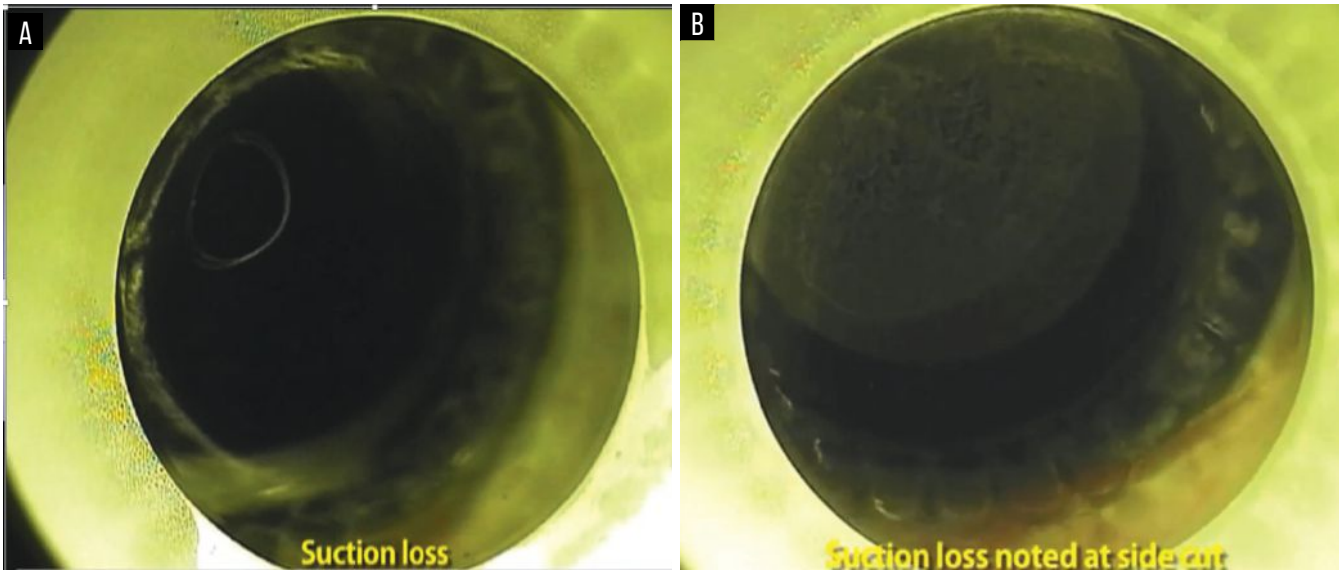
There's a learning curve to SMILE, as with anything, so some initial bumps are to be expected as you get to know the procedure, explains Dr. Agarwal. "When I began my SMILE journey, I was faced with several issues. These are commonly experienced by those within their first six months of SMILE, but don't fret: You'll learn quickly and soon enough you won't have these complications," he says.

"The key words to remember are: Abort mission. If something goes wrong and you can't recover, just stop," asserts Dr. Agarwal.

We spoke with him about some of the most common SMILE complications and what not to do if they happen to you.

Problem: Suction Loss

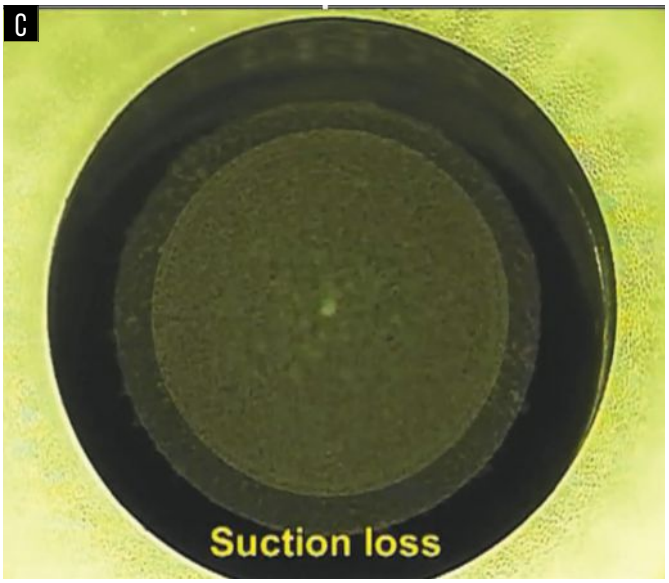
Suction loss can happen at different stages, Dr. Agarwal says. "I person-



If suction loss occurs during the posterior lenticule cut after 30 percent (Figure A) or at the side cut (Figure B), it's best to stop the SMILE procedure and wait a few months before performing LASIK or PRK, suggests Ashvin Agarwal, MD.

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.



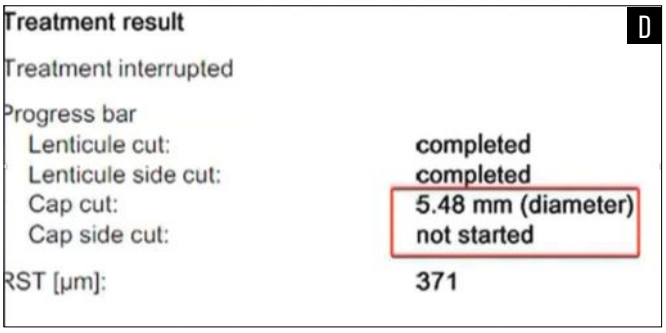


Figure C shows suction loss during the anterior cut. Figure D shows where the treatment was interrupted. At this point, the surgeon could feasibly remove the lenticule through the side cut, but it wouldn't be worth it, surgeons say.

ally wouldn't recommend continuing the procedure if it occurs. However, I was fortunate to continue these cases successfully with great results for the patients," he says.

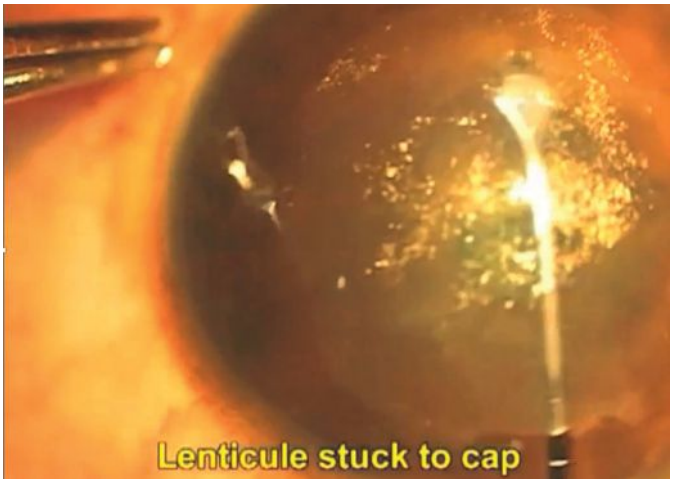
"Let's say your suction loss happens when the posterior lenticule is being cut, you're safe if it's between 10 and 20 percent. Anything after 30 percent, if you have suction loss, just abort. Come back after two or three months," says Dr. Agarwal. "I'd recommend doing a PRK or LASIK procedure in that scenario.

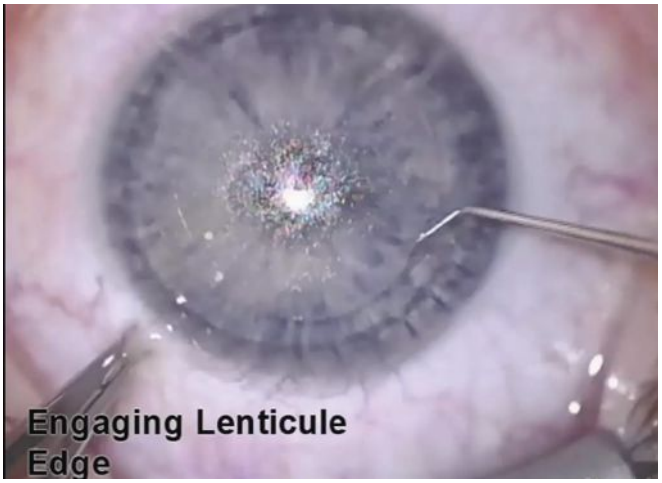
"Next, what if you have suction loss between the posterior lenticule and the side-cuts? Once the laser crosses the posterior lenticule side-cut, you're fine, but until then, there's about 23 seconds with the VisuMax 500 and six seconds with the VisuMax 800 SMILE Pro," he continues. "If suction loss occurs anywhere in between, you should abort the mission.

"In my case, I went ahead and did a repeat docking and a repeat transfer of spots, which led to issues such as a small skirt of tissue, which you have to actually peel off and use for your ablation in case you're doing a flap," he says. "You could consider a CIRCLE enhancement, which converts the SMILE cap into a larger-diameter LASIK flap with the creation of lamellar rings and junction cuts to connect to the primary cap interface. If you were to lose suction between the 20 percent and the side-cuts, if you re-dock and make the side-cuts separately, they will be dislocated at some point. That can lead to issues of transitional zones so you have to be careful about that area."

Another issue is suction loss during the anterior lenticule cut, meaning the side-cuts are complete and the laser is starting on the anterior lenticulae. "If you try to re-dock at this point, no matter how well you center and position it, it'll be off," says Dr. Agarwal. "You can manage, but it's going to be in a piecemeal format and you'll be peeling out tissue from the side. It's just not worth it."

He continues, "Now, on the other hand, if just the anterior lenticule crosses the side-cut, you're still in the scope zone. The lenticule is fine and





Glen Carp, MD, and Dan Reinstein, MD

If the lenticule becomes stuck to the cap, it's important to know the cap recovery technique popularized by Dan Reinstein, MD, and Glen Carp, MD, which involves using a modified Sinskey hook to catch the edge of the stuck lenticule.

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INDICATIONS AND USAGE

IYUZEH™ is a prostaglandin analogue indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Known hypersensitivity to latanoprost or any other ingredients in this product.

WARNINGS AND PRECAUTIONS

Pigmentation: Topical latanoprost ophthalmic products, including IYUZEH™ have been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periorbital tissue (eyelid), and eyelashes. Pigmentation is expected to increase as long as latanoprost is administered.

The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes.

After discontinuation of latanoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. The long-term effects of increased pigmentation are not known.

Iris color change may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. While treatment with IYUZEH™ can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

Eyelash Changes: Latanoprost ophthalmic products, including IYUZEH™ may gradually change eyelashes and vellus hair in the treated eye; these changes include increased length, thickness, pigmentation, the number of lashes or hairs, and misdirected growth of eyelashes. Eyelash changes are usually reversible upon discontinuation of treatment.

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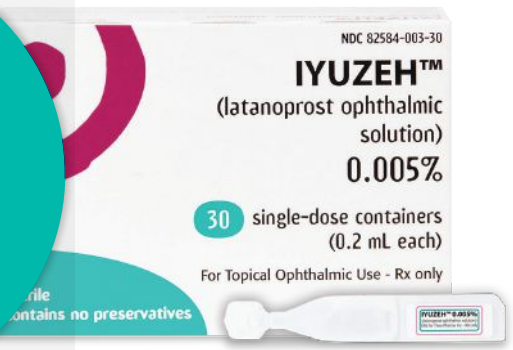
Reference: 1. IYUZEH™ (latanoprost ophthalmic solution) 0.005%. Prescribing information. Thea Pharma Inc; 2022.

iyuzeh™
(latanoprost ophthalmic solution) 0.005%

IYUZEH™ HAD SIMILAR MEAN IOP REDUCTION WHEN COMPARED WITH XALATAN®

IN PHASE III TRIALS, REDUCED IOP WITH PROVEN EFFICACY

IYUZEH LOWERED IOP
by 3-8 mmHg (n=165)
vs
4-8 mmHg (n=169)
for XALATAN[1]



We owe it to our patients with elevated intraocular pressure, with open-angle glaucoma or ocular hypertension to provide a new evidence-based best practice. It is an extremely exciting time to prescribe IYUZEH for my patients.

Monique M. Barbour
MD, MHA, FAAO

Dr. Barbour is a paid consultant of Thea Pharma Inc.

Intraocular Inflammation: IYUZEH™ should be used with caution in patients with a history of intraocular inflammation (iritis/uveitis) and should generally not be used in patients with active intraocular inflammation because inflammation may be exacerbated.

Macular Edema: Macular edema, including cystoid macular edema, has been reported during treatment with latanoprost ophthalmic products, including IYUZEH™. IYUZEH™ should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Herpetic Keratitis: Reactivation of herpes simplex keratitis has been reported during treatment with latanoprost. IYUZEH™ should be used with caution in patients with a history of herpetic keratitis. IYUZEH™ should be avoided in cases of active herpes simplex keratitis because inflammation may be exacerbated.

Contact Lens Use: Contact lenses should be removed prior to the administration of IYUZEH™ and may be reinserted 15 minutes after administration.

ADVERSE REACTIONS

The following adverse reactions have been reported with the use of topical latanoprost products: iris pigmentation changes, eyelid skin darkening, eyelash changes (increased length, thickness, pigmentation, and number of lashes), intraocular inflammation (iritis/uveitis), and macular edema, including cystoid macular edema.

DRUG INTERACTIONS

The combined use of two or more prostaglandins, or prostaglandin analogs including IYUZEH™ is not recommended. It has been shown that administration of these prostaglandin drug products more than once daily may decrease the IOP lowering effect or cause paradoxical elevations in IOP.

Please see full Prescribing Information at www.iyuzeh.com and Brief Summary on the next page.

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iyuzeh™

(latanoprost ophthalmic solution) 0.005%

HIGHLIGHTS OF PRESCRIBING INFORMATION

This brief summary does not include all the information needed to use IYUZEH safely and effectively. See full prescribing information for IYUZEH.

Initial U.S. Approval: 2022

----------INDICATIONS AND USAGE----------

IYUZEH is a prostaglandin F2α analogue indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

----------CONTRAINDICATIONS----------

Known hypersensitivity to latanoprost or any other ingredients in this product.

----------WARNINGS AND PRECAUTIONS----------

Pigmentation: Topical latanoprost ophthalmic products, including IYUZEH have been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periorbital tissue (eyelid), and eyelashes. Pigmentation is expected to increase as long as latanoprost is administered.

The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. After discontinuation of latanoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. The long-term effects of increased pigmentation are not known.

Iris color change may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. While treatment with IYUZEH can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

Eyelash Changes: Latanoprost ophthalmic products, including IYUZEH may gradually change eyelashes and vellus hair in the treated eye; these changes include increased length, thickness, pigmentation, the number of lashes or hairs, and misdirected growth of eyelashes. Eyelash changes are usually reversible upon discontinuation of treatment.

Intraocular Inflammation: IYUZEH should be used with caution in patients with a history of intraocular inflammation (iritis/uveitis) and should generally not be used in patients with active intraocular inflammation because inflammation may be exacerbated.

Macular Edema: Macular edema, including cystoid macular edema, has been reported during treatment with latanoprost ophthalmic products, including IYUZEH. IYUZEH should be used with caution in aphakic patients, pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Herpetic Keratitis: Reactivation of herpes simplex keratitis has been reported during treatment with latanoprost. IYUZEH should be used with caution in patients with a history of herpetic keratitis and should be avoided in cases of active herpes simplex keratitis because inflammation may be exacerbated.

Contact Lens Use: Contact lenses should be removed prior to the administration of IYUZEH and may be reinserted 15 minutes after administration.

----------ADVERSE REACTIONS----------

The following adverse reactions have been reported with the use of topical latanoprost products and are discussed in greater detail in the prescribing information:

- Iris pigmentation changes
- Eyelid skin darkening
- Eyelash changes (increased length, thickness, pigmentation, and number of lashes)
- Intraocular inflammation (iritis/uveitis)
- Macular edema, including cystoid macular edema

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 the two clinical trials conducted with IYUZEH (latanoprost ophthalmic solution) 0.005% comparing it to XALATAN the preserved 0.005% latanoprost reference product, the most frequently reported ocular adverse reactions were conjunctival hyperemia and eye irritation (Table 1).

Table 1. Adverse Reactions

	Adverse Reactions [n (%)]	
Symptom/Finding	**IYUZEH (n=378)**	**XALATAN (n=358)**
Conjunctival hyperemia	129 (34)	133 (37)
Eye irritation	72 (19)	112 (31)
Eye pruritus	57 (15)	58 (16)
Abnormal sensation in eyes	51 (14)	52 (15)
Foreign body sensation in eyes	44 (12)	36 (10)
Vision blurred	28 (7)	30 (8)
Lacrimation increased	19 (5)	14 (4)
Photophobia	13 (3)	17 (5)

----------POSTMARKETING EXPERIENCE----------

The following adverse reactions have been identified during post-approval use of topical latanoprost products. 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. The reactions, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to ophthalmic latanoprost products, or a combination of these factors, include:

- Nervous System Disorders: Dizziness; headache; toxic epidermal necrolysis
- Eye Disorders: Eyelash and vellus hair changes of the eyelid (increased length, thickness, pigmentation, and number of eyelashes); keratitis; corneal edema and erosions; intraocular inflammation (iritis/uveitis); macular edema, including cystoid macular edema; trichiasis; periorbital and lid changes resulting in deepening of the eyelid sulcus; iris cyst; eyelid skin darkening; localized skin reaction on the eyelids; conjunctivitis; pseudopemphigoid of the ocular conjunctiva.
- Respiratory, Thoracic and Mediastinal Disorders: Asthma and exacerbation of asthma; dyspnea
- Skin and Subcutaneous Tissue Disorders: Pruritis
- Infections and Infestations: Herpes keratitis
- Cardiac Disorders: Angina; palpitations; angina unstable
- General Disorders and Administration Site Conditions: Chest pain

----------DRUG INTERACTIONS----------

The combined use of two or more prostaglandins, or prostaglandin analogs including IYUZEH is not recommended, and administration of these prostaglandin drug products more than once daily may decrease the IOP lowering effect or cause paradoxical IOP elevations.

----------USE IN SPECIFIC POPULATIONS----------

Pregnancy: There are no adequate and well-controlled studies of IYUZEH administration in pregnant women to inform drug-associated risks.

Lactation: It is not known whether this drug or its metabolites are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when IYUZEH is administered to a nursing woman. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for IYUZEH and any potential adverse effects on the breastfed child from IYUZEH.

Pediatric Use: The safety and effectiveness of IYUZEH have not been established in pediatric patients.

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

----------OVERDOSAGE----------

Intravenous infusion of up to 3 mcg/kg of latanoprost in healthy volunteers produced mean plasma concentrations 200 times higher than during clinical treatment with latanoprost ophthalmic solution and no adverse reactions were observed. IV dosages of 5.5 to 10 mcg/kg caused abdominal pain, dizziness, fatigue, hot flushes, nausea, and sweating.

----------HANDLING THE CONTAINER----------

IYUZEH is a sterile solution that does not contain a preservative supplied in a single-dose container. The solution from one individual container is to be used immediately after opening for administration to one or both eyes. Since sterility cannot be maintained after the individual container is opened, the remaining contents should be discarded immediately after administration. Open a new single-dose container every time you use IYUZEH.

Manufactured for: Thea Pharma Inc. Waltham, MA.

U.S. Patent N°. 8,637,054.
Revised: 04/2023

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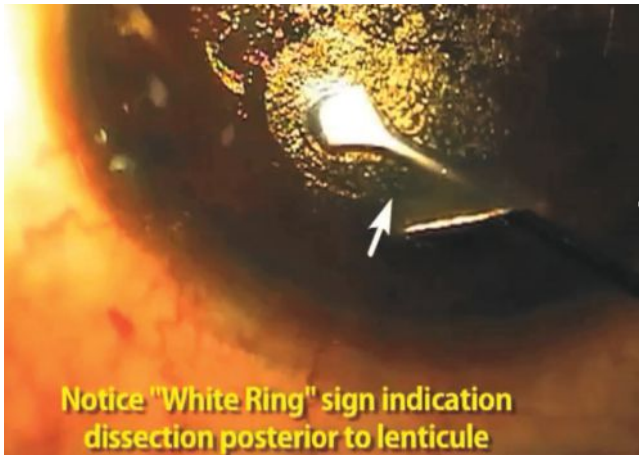
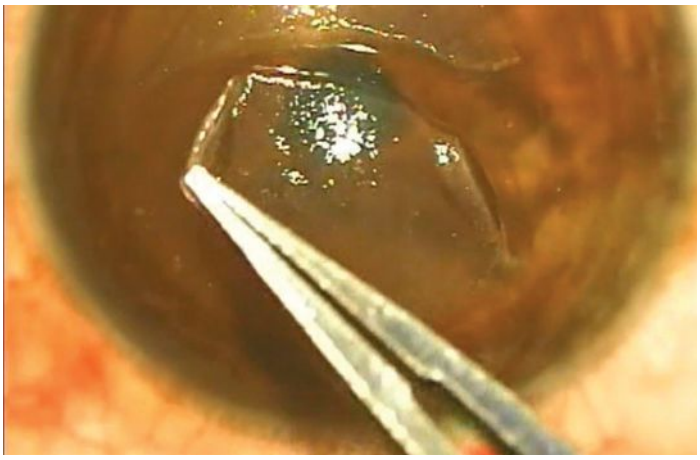
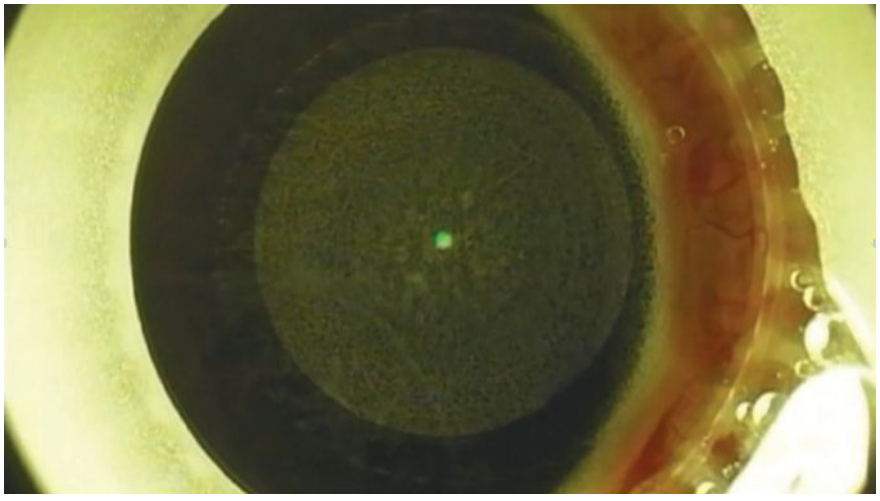


The white ring sign is a way to confirm that the surgeon is in the correct plane of dissection.



Once the lenticule is removed, the surgeon must piece it together on top of the eye to ensure all pieces were retrieved.



Although rare, if you notice conjunctiva bunching while the cut is being made, it's best to abort and do a PRK three months later, recommend surgeons.

the vision will be perfectly fine, but the problem is you'll only have access to the lenticule through the external cut, which you need to make in the 2 to 4 mm zone."

Problem: Lenticule Stuck to Cap

This is very common. "In this scenario it's important to know the rescue mechanism," Dr. Agarwal says. "The cap recovery technique, popularized by Glen Carp, MD, and Dan Reinstein, MD,[1] is an alternative to the traditional technique of dissecting in the plane. It describes dissecting the lenticule first with a modified Sinskey tip inserted through the superior end of the incision and rotated anteriorly to catch the edge of the stuck lenticule. Once you take a Sinskey tip and go into the cap to split the lenticule from it, then you hold and can dissect from there as you normally would. It's a small technique but very important to understand in order to rescue yourself."

In their study, Dr. Carp and Dr. Reinstein were able to show equivalent visual results of their technique compared to the traditional SMILE dissection, which first opens the primary small incision to separate the cap interface, followed by the lenticule interface.[1]

Problem: White Ring Sign

"This isn't so much a problem in particular, but it can help prevent problems," Dr. Agarwal says. "This was first described by Soosan Jacob, MD, and denotes the plane of dissection after the laser. An error in the plane can cause disaster. When dissecting in the posterior lenticule, the white ring sign is caused by the reflection of the microscope lights off of the dissection rod, making the edge of the lenticule clearly visible. When you're doing an anterior dissection, you shouldn't see a white ring sign. It's a very interesting way to know that you're in the correct plane."

Problem: Torn Lenticule

After retrieving the lenticule, you must ensure that you've removed it completely all the way around. "Don't remove the lenticule and throw it aside because the minute you do that, there's no way to know if something was left behind," says Dr. Agarwal. "Always lay the lenticule on top of the eye and make sure it's complete before discarding."

Problem: Bunching of Conjunctiva

This is rare, says Dr. Agarwal. "If it doesn't cross any part of the laser you were lucky and you can proceed," he says. "But if it does cross the laser, just stop and don't worry about it. Let it go and three months later do a PRK and you'll be fine."◀

1. Carp GI, Reinstein DZ, Stuart A, Vida RS, Archer TJ, Finkel JN. Cap recovery technique and double-edge sign during small-incision lenticule extraction. J Cataract Refract Surg 2021;1:7:9:1191-1195.

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Medication Adherence in The Digital Age

It's hard to form healthy habits, but there are many new ways to improve patients' health and adherence to their medication.

ANDREW BEERS
ASSOCIATE EDITOR

There's no doubt that many individuals struggle to adhere to their treatment regimens. It can be overwhelming for patients when they begin to take new medications and experience undesirable side effects. Research has shown that patient nonadherence towards medication for chronic diseases has reached approximately 50 percent.[1] In order to drive patients to adhere to their medications, physicians need to use all the resources and tools at their disposal to better educate, facilitate and motivate their patients.

There's more than one reason why patients struggle to take their medication. In a study to understand the interventions needed to improve glaucoma medication adherence, Paula Anne Newman-Casey, MD, MS, an associate professor of ophthalmology and visual sciences at the University of Michigan, and her colleagues laid out the framework on how counseling and education can improve medication adherence. "We did a systematic literature review to discover what barriers glaucoma patients struggle with in terms of taking their medications, and we came up with eleven different reasons that seemed to be repeated with some frequency," she says. "The different barriers patients identified in our study were not knowing the severity of glaucoma, not trusting in the benefits of the medication, side effects and forgetfulness, among others," lists Dr. Newman-Casey.

"People mentioned issues with how difficult the medication's schedule is sometimes, especially with midday doses," Dr. Newman-Casey continues. "Some people have difficulty physically instilling the eye drop. They miss a lot, run out of medication early or a lot of it gets on the skin of their eye and it can irritate the skin and cause periocular skin maceration and breakdown. Also, people talked about not trusting their doctor, not trusting their doctor's recommendations, or not trusting the health-care system and having trouble with accessing the health-care system or insufficient time and feedback from their doctor.

"Obviously, medications are expensive, and a lot of the burden is on people over the age of 65 who are often on a limited and fixed income," Dr. Newman-Casey continues. "So, their income isn't going up as the price of drugs and copays go up. Another reason, which is a big one, is life stress. I think that's magnified by your socioeconomic status because the less money you have, the more stressful and difficult life becomes."

In her study, Dr. Newman-Casey surveyed glaucoma patients to understand which barriers patients struggled with the most, and her results led her to realize medication nonadherence couldn't be easily fixed. "We surveyed around 180 people in two different practices, a private practice setting and an academic practice setting," she says. "About 30 percent of people endorsed every single problem. I think motivation towards adherence can be complicated and you really have to discuss patients' problems with them. Try to meet them halfway because there's not really a magic bullet."

Glaucoma medication nonadherence isn't the only issue for ophthalmologists, but Dr. Newman-Casey's study brings up a valid point in the realm of glaucoma treatments: eye drops are difficult for some people to instill. "It requires more dexterity because it's a movement that's outside the norm of what you're used to doing (i.e. taking your pills with your coffee)," she says. "Sometimes people use a mirror to assist with their eye drops. Sometimes people like to instill them lying down. These are tactics that can be perceived as more of a nuisance than taking pills."

For every barrier a patient must overcome, there are often ways clinicians can help guide them. "The first step that clinicians can take is normalizing the fact that taking chronic medications, in particular eye drops, isn't easy," says Dr. Newman-Casey. She explained how monitoring patients' adherence can help a physician better assess and manage the patients who are struggling with their treatment plans. For example, in another study conducted by Dr. Newman-Casey, patients were asked, "Over the past month, what percentage of your drops do you think you took correctly?"[2] She says, "If patients responded that they took 85 percent or less of their medications, then they were at a high risk for poor medication adherence. Simply asking patients this screening question can help identify which patients need additional support for optimal glaucoma self-management."

Another way to assist patients is by providing them with support staff. Dr. Newman-Casey is currently conducting a randomized controlled clinical

This article has no commercial sponsorship.

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

trial of the Support, Educate, Empower (SEE) program, a personalized glaucoma coaching program. The SEE program uses a care team model where health educators, trained as glaucoma coaches, work to provide additional support to patients who report poor glaucoma medication adherence. "The glaucoma coach is someone who's been trained in motivational interviewing, which is a style of coaching that attempts to promote a person's autonomy rather than telling them what to do," she says. "The whole part of the motivational interviewing-based health coaching is trying to get people to identify their own problems and solutions. Additionally, the coach helps guide patients through their glaucoma diagnosis. They also have access to a software program that individualizes a glaucoma education program to help explain a patient's test results and the doctor's recommendations."

During a pilot study for the SEE program, a total of 48 participants with glaucoma were enrolled. Each participant received medication alerts, in-person coaching with personalized education sessions and between-visit phone calls with their coach. Researchers measured baseline adherence using an electronic medication monitoring system for three months. They reported that the baseline adherence started at 59.9 percent and improved to 81.3 percent by the end of the seven-month trial.[3]

Throughout the SEE trial period, glaucoma coaches met with participants for three counseling sessions, each lasting a different length of time. The first counseling session on average lasted 68.2 minutes, the second session on average lasted 27.9 minutes and the third session on average lasted 31.7 minutes. According to the study, the researchers hope their robust findings will shape clinical practice guidelines by promoting evidence-based models that will improve overall medication adherence and ultimately, visual outcomes.[3] "We saw a huge increase in adherence just with electronic dosing reminders," says Dr. Newman-Casey. "Then, a boost in adherence on top of that after the coaching session started, and that adherence was maintained throughout the study period when coaching was ongoing."

Dr. Newman-Casey explained how an alarm system is very helpful but may not be the only necessary tool for all patients. "Over time, people get sick of alarms and reminders unless they've already made taking their medication into a habit," she says. "It doesn't always elicit the same behavioral response overtime." She referenced the Medication Adherence in Glaucoma to Improve Care (MAGIC) study by Kelly Muir, MD, which was a randomized, controlled trial to test the efficacy of a comprehensive education-based intervention to improve medication adherence in glaucoma patients.[4] "That's a seminal trial in medication adherence interventions," she explains. "[Dr. Muir] and her colleagues compared an educational intervention arm combined with dosing reminders to a control arm. Overtime, there was a 20-percentage point difference in adherence between the two arms, which is a remarkable effect. However, adherence in both arms went down over time even though the intervention arm continued to receive dosing reminders."

Rather than enforcing an alert system in their trial, the SEE program combines various components and enables patients to choose what might work best for them in terms of a dosing reminder. "Participants can elect to not have reminders, or they can elect to have multiple reminders," says Dr. Newman-Casey. "We didn't want to make that decision for people."

Smart Devices

For patients who struggle with adherence and would prefer an alert system, there are many devices and applications that have been developed for these needs.

• ***Aidia (AdhereTech).*** Smart pill bottles offer a simple solution to medication adherence for patients taking oral prescriptions. The Aidia system, from AdhereTech, is a smart pill bottle given to patients by their health-care provider. According to AdhereTech, the device is shipped to the patient's pharmacy with their pre-set dosing schedule. An hour before a dose is scheduled, the device will light up blue at the base of the bottle.

Aidia can be set to alert caregivers about upcoming doses. They can receive text and/or phone reminders.

When it's time for the patient to take their medication, the device will remind the patient with a gentle chime as well as a text or phone call alert. Once the patient opens the pill bottle, the alert will stop, and the device will reset its alarms for the next scheduled dose.

AdhereTech states that if a patient needs to edit their dosing schedule, then they must contact their pharmacy or an Aidia Specialist to assist them with their changes. The Aidia system may not come prefilled with a patient's medication. Therefore, they must take their prescription and load it into the pill bottle themselves. Additionally, the device holds a charge for 10 months, but it can be recharged if needed. Patients shouldn't get the device wet, allow it to overheat or clean it with chemical-based cleaners due to the sensitive electronic controls inside the device, so they need to keep the smart pill bottle in a safe and secure location.

Furthermore, AdhereTech offers the Aidia Smart Cap, a separate device compatible with standard pill bottles. Similar to the Aidia system, the Smart Cap is used to alert patients about their upcoming dose. According to AdhereTech, the Smart Cap is equipped with a blue button that provides information about previously scheduled doses, upcoming doses and battery life. The cap's battery life lasts about two to three months, but it can be recharged easily. Both the Aidia system and Smart Cap are HIPAA-compliant products.

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• ***ID-Cap System (etectRx).*** Imagine a pill that could be monitored after ingestion. EtectRx's novel solution to medication nonadherence provides just that. According to etectRx, the ID-Capsule is a digital pill consisting of a pharmaceutical-grade capsule shell with an embedded ingestible sensor. When a capsule is consumed, the ID-Tag sends a low frequency signal to a portable device that must be on the patient when taking their medication. This device sends a message via Bluetooth to the ID-Cap Patient App. This app allows patients to view their medication history and set reminders and alerts for their next dose.

This unique system helps clinicians monitor their patients. According to etectRx, the patient's information stored in the Patient App gets uploaded to their clinician's dashboard provided by etectRx. The dashboard allows physicians to monitor adherence and follow their patient's schedule.

For patients worried about digesting the capsule, etectRx notes that the ID-Cap's sensor is ultra-thin and flexible, allowing for it to pass naturally through the patient's gastrointestinal tract. Additionally, the capsule is FDA-approved for addressing patient adherence to oral medications.

• ***e-Novelia (Nemera).*** Glaucoma patients struggling to adhere to their eye drop medications may benefit from this device. E-Novelia is a smart ophthalmic add-on that facilitates the use of preservative-free multidose eye droppers. Nemera offers the Novelia eye droppers to work effectively with the e-Novelia.

According to Nemera, patients can insert the eye dropper into the smart device, which will then provide the patient with a host of information to assist with adherence. The e-Novelia is equipped with a tile sensor and LED indications for positioning the device, a drug indicator to monitor the level of medication left in the eye dropper, and an electronic IFU, or information for use, to assist patients with using the device. Treatment history and compliance can all be monitored through a patient's dashboard online. The e-Novelia will alert the patient when they need to instill another dose.

The device is bulkier than the average eye dropper, but Nemera mentions that it was designed with an ergonomic eye cup to assist patients with the instillation process. The device is re-usable and rechargeable, so patients can continue using the device after every prescription refill.

• ***Medisafe.*** There's a whole host of medication adherence applications on the iTunes and Google Play stores. One in particular is Medisafe, the HIPAA-compliant medicine reminder app. According to Medisafe, users can create an account to manage their health or another patient's health. The dashboard features will be slightly different depending on the user's choice.

Once logged into the app, users can set their medications or the medications of another patient. Medisafe states that it's compatible with the Apple Health App, so if a patient is an Apple user, then they can upload their prescriptions from the Health app to Medisafe. Otherwise, Medisafe users will have to add their medications manually. The app offers the ability to set treatment duration, set refill reminders, add instructions and more.

Medisafe's toolbar features user-friendly buttons to navigate through Home, Updates, Medications and More dashboards. The Home dashboard organizes the patient's dosage schedule and allows the user to interact with their different medications. They can choose to skip, take or reschedule a dose and even edit or delete selected medications. The Updates dashboard provides the user with notifications about upcoming doses and changes to the Medisafe app. Next, the Medications dashboard allows the user to edit their medicines and access information about their medications, conditions and dosage reminders. Lastly, the More dashboard provides the option for patients to manage and organize their appointments, doctors and diagnosis reports. Medisafe offers a Health Tracker where the user can identify and measure their disease or illnesses by documenting symptoms as they progress. This is similar to the Diary feature which allows the user to document their medications and other notes. This application does include an extensive catalogue of ophthalmic medications.

• ***EyeDropAlarm.*** Also offered on iTunes and Google Play stores, Eye DropAlarm is a free, ophthalmic-patient-centered medication reminder app. The app offers an extensive database of eye drops that can be selected or searched manually.

EyeDropAlarm will alert the patient based on the treatment plan that they manually add to the app. According to EyeDropAlarm, eye specifications, start date, treatment length, frequency of dosage, taper drops and multiple alarms can be set for alerts. Patients can also change the alarm sound, snooze duration and gap between drops that are scheduled for the same time.

For patients who are struggling with instilling their eye drops, EyeDropAlarm provides a guide on how to properly put in drops. Once the patient instills the drops, then they can open the app and check off which medications they took. Patients should remember to turn on notifications on their phone's control panel whenever using a medication reminder app.

Between the number of smart devices and in-house counseling options, there's no doubt that patient nonadherence can be effectively addressed. "I think, intrinsically, clinicians are motivated to do everything they can to preserve vision," says Dr. Newman-Casey. "People who aren't taking their medications are going to lose vision. That lies at the heart of the problem." ◀

1. Kleinsinger F. The unmet challenge of medication nonadherence. Perm J 2018;22:18:033.
2. Cho J, Niziol LM, Lee PP, et al. Comparison of medication adherence assessment tools to identify glaucoma medication nonadherence. Ophthalmol Glaucoma 2022;5:2:137:145.
3. Newman-Casey PA, Niziol LM, Lee PP, et al. The impact of the Support, Educate, Empower Personalized Glaucoma Coaching pilot study on glaucoma medication adherence. Ophthalmol Glaucoma 2020;3:4:228:237.
4. Rosdahl JA, Hein AM, Bosworth HB, et al. Randomized controlled trial of an education-based intervention to improve medication adherence: Design considerations in the medication adherence in glaucoma to improve care study. Clin Trials 2021;18:3:343:350.

DISCLOSURES

Dr. Newman-Casey has no financial interests to disclose.

A MATCH MADE IN HEAVEN

Similarity doesn't always mean compatibility. Experts explain how mixing different IOL models can get the best results.

CHRISTINE YUE LEONARD
SENIOR ASSOCIATE EDITOR

Techniques for mixing and matching intraocular lenses have been around for several years now. Experts say these lens pairings have continued to evolve as IOL technology gets more advanced. "In an ideal world," says Kendall E. Donaldson, MD, of Bascom Palmer Eye Institute in Plantation, Florida, "we wouldn't have to mix and match because the patient would achieve optimal quality and range of vision in the first eye and would want the second eye to be the same. However, the reality is that increased range can be accompanied by a loss in clarity and may be associated with dysphotopsias such as glare and halos. Due to this type of compromise, mixing and matching may help provide a functional range while maintaining adequate quality of vision."

Here, cataract surgeons share their go-to lens combinations and pearls for ensuring patient satisfaction with a mix-and-match approach.

The Best of Both Worlds

Using a different lens in each eye is possible thanks to the brain's ability to neuroadapt, explains Marjan Farid, MD, of the Gavin Herbert Eye Institute, University of California, Irvine. "The brain is an amazing computer and can take the images from each eye and combine them into one," she says. "We've been taking advantage of this ability with monovision for years. Similarly, we can also mix and match different lens technologies to optimize range and quality of vision for patients."

"Nighttime visual disturbances such as glare and halos are frequently associated with diffractive presbyopia-correcting IOLs, so mixing and matching lenses can decrease some of those visual side effects," says Dagny Zhu, MD, of Hyperspeed LASIK (NVISION) in Rowland Heights, California. "Another reason surgeons might mix and match lenses is if the two eyes are different in terms of which lens they're candidates for. If one eye has pathology—a significant epiretinal membrane, for example—you can typically put only a monofocal in that eye. But if the other eye is healthy, the patient could still gain some spectacle independence with a presbyopia-correcting lens in the contralateral eye. So, a different lens could be used in each eye, based on pathology and what the patient qualifies for."

Experts say that when mixing and matching IOLs, it's best to choose two lens models from the same platform to ensure some degree of IOL uniformity, such as the material platform, the correction for spherical aberration or whether there's any lens tint.

"The thought is that the optics of lenses from the same platform won't be too different, and the patient will be better able to tolerate the differences between the optical designs," Dr. Zhu explains. She says that for some patients she likes "to mix and match within the Clareon family (Alcon) using the

This article has no commercial sponsorship.

Dr. Farid is a consultant for Johnson & Johnson Vision, Bausch + Lomb and Alcon. **Dr. Zhu** is a consultant for Johnson & Johnson Vision, Bausch + Lomb, LensTec and Alcon. She also receives research grants from Alcon. **Dr. Shultz** is a consultant for Johnson & Johnson Vision and a consultant and investigator for Bausch + Lomb. He has an investigative contract with RxSight. **Dr. Dewey** is a consultant for Johnson & Johnson Vision. **Dr. Donaldson** is a consultant for Johnson & Johnson Vision, Bausch + Lomb, Alcon and Zeiss.

Vivity and the PanOptix lenses" and for others, she mixes and matches "the Symfony OptiBlue and Synergy, which are part of the Tecnis InteliLight platform (Johnson & Johnson Vision)."

Dr. Farid says she's seen some patients in which lenses from two different companies or two different platforms were implanted. "Because of neuroadaptation, this sometimes works out very well," she says. "However, keeping the platforms the same usually results in a better combination profile. When I mix and match lenses, I try to keep the platforms consistent between the two eyes."

Alcon

The PanOptix trifocal (left) and Vivity EDOF (right) can be combined in a mix-and-match strategy to reduce dysphotopsias.

If a mix-and-match combination results in a high amount of anisometropia, patients are likely to become preoccupied with comparing one eye to the other. Mixing diffractive and refractive optics or different lens tints isn't advisable. "If a yellow chromophore is used in the first eye, this should also be used in the second eye," Dr. Donaldson adds.

Strategies for Different Goals

Mix-and-match combinations can include monofocals, multifocals, EDOFs and other lens technologies. Here are some ways surgeons create complementary strategies to improve patients' quality and range of vision:

• ***EDOFs and multifocals.*** Dr. Zhu says, "a common strategy I use to reduce dysphotopsias is to mix and match the Vivity and PanOptix. I place the Vivity, which is an EDOF lens, in the dominant eye, and I place the PanOptix, which is a trifocal, in the non-dominant eye. In that manner, I've found I've been able to decrease some of the nighttime halos and glare for the patient, compared to bilateral trifocal implantation, while still providing a good level of spectacle independence.

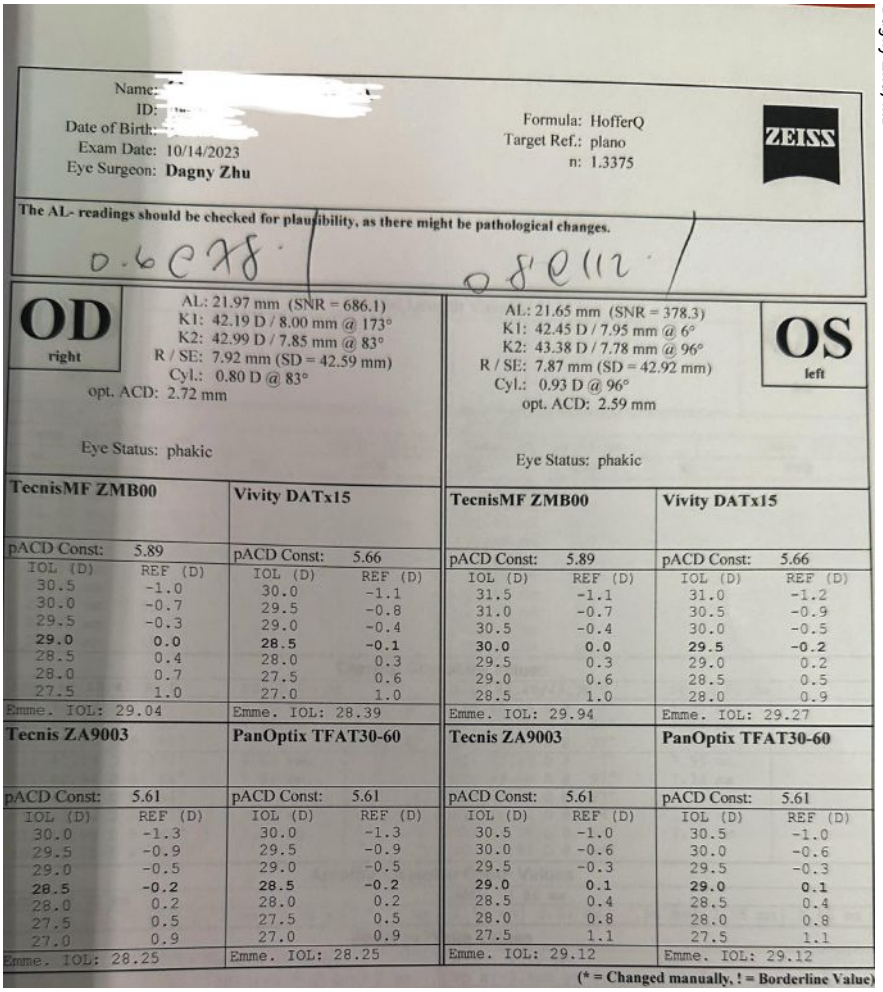
"Based on my mix-and-match data, which I presented at ASCRS this past year, close to 90 percent of my patients are still able to achieve complete spectacle independence with the Vivity-PanOptix approach," she continues. "I've also found in my own data that there are far fewer complaints about significant visual disturbances with this mix-and-match combination vs. bilateral PanOptix. My younger, active patients are better able to drive at night with a mix-and-match approach."

Mitchell C. Shultz, MD, of Shultz Chang Vision in Los Angeles, says, "I tend to use EDOF technologies in combination with trifocal technologies, making the decision [to mix and match] based on the first eye. My preference is minimizing night-vision aberrations. So, if I can achieve an excellent range of vision with an EDOF lens, then I'm likely to use it in the other eye, but if the patient isn't satisfied with the near vision of the dominant eye with an EDOF lens, then as long as everything looks okay to support using a trifocal lens in the other eye, I'll certainly do that to maximize range."

One of Dr. Farid's favorite presbyopia-correcting mix-and-match combinations is the Symfony EDOF in the dominant eye and the Synergy [a hybrid multifocal-EDOF] in the non-dominant eye. "The Symfony EDOF provides good distance and intermediate vision with a great contrast sensitivity profile," she says. "If the patient needs more reading vision, I use the Synergy, which is also on the Tecnis platform. You do lose a little more contrast with this particular lens because it's a multifocal optic, but it helps to maximize near vision. Patients have been very happy with this combination of lenses because they get distance, intermediate and near vision with the two eyes combined.

Steven H. Dewey, MD, of Colorado Springs Eye Clinic, also favors the Synergy-Symfony combination to maximize range of vision. "One of my go-to combinations is a Synergy in the non-dominant eye targeted for the least amount of hyperopia that I can target and then a Symfony in the dominant eye targeted for plano. Probably about 70 to 75 percent of my patients with a Synergy in their non-dominant eye are pleased with their range of vision. They get good distance, intermediate and reading vision."

Dr. Dewey says that he uses this mix-and-match combination in some patients who, after receiv-



Name:
ID:
Date of Birth:
Exam Date: 10/14/2023
Eye Surgeon: **Dagny Zhu**

Formula: HofferQ
Target Ref.: plano
n: 1.3375

ZEISS

The AL- readings should be checked for plausibility, as there might be pathological changes.

0.6 C X8 ° / 0.8 C 112 °

OD right

AL: 21.97 mm (SNR = 686.1)
K1: 42.19 D / 8.00 mm @ 173°
K2: 42.99 D / 7.85 mm @ 83°
R / SE: 7.92 mm (SD = 42.59 mm)
Cyl.: 0.80 D @ 83°
opt. ACD: 2.72 mm

Eye Status: phakic

OS left

AL: 21.65 mm (SNR = 378.3)
K1: 42.45 D / 7.95 mm @ 6°
K2: 43.38 D / 7.78 mm @ 96°
R / SE: 7.87 mm (SD = 42.92 mm)
Cyl.: 0.93 D @ 96°
opt. ACD: 2.59 mm

Eye Status: phakic

TecnisMF ZMB00		Vivity DATx15	
pACD Const:	5.89	pACD Const:	5.66
IOL (D)	REF (D)	IOL (D)	REF (D)
30.5	-1.0	30.0	-1.1
30.0	-0.7	29.5	-0.8
29.5	-0.3	29.0	-0.4
29.0	**0.0**	**28.5**	**-0.1**
28.5	0.4	28.0	0.3
28.0	0.7	27.5	0.6
27.5	1.0	27.0	1.0
Emme. IOL: 29.04		Emme. IOL: 28.39	

TecnisMF ZMB00		Vivity DATx15	
pACD Const:	5.89	pACD Const:	5.66
IOL (D)	REF (D)	IOL (D)	REF (D)
31.5	-1.1	31.0	-1.2
31.0	-0.7	30.5	-0.9
30.5	-0.4	30.0	-0.5
30.0	**0.0**	**29.5**	**-0.2**
29.5	0.3	29.0	0.2
29.0	0.6	28.5	0.5
28.5	1.0	28.0	0.9
Emme. IOL: 29.94		Emme. IOL: 29.27	

Tecnis ZA9003		PanOptix TFAT30-60	
pACD Const:	5.61	pACD Const:	5.61
IOL (D)	REF (D)	IOL (D)	REF (D)
30.0	-1.3	30.0	-1.3
29.5	-0.9	29.5	-0.9
29.0	-0.5	29.0	-0.5
28.5	**-0.2**	**28.5**	**-0.2**
28.0	0.2	28.0	0.2
27.5	0.5	27.5	0.5
27.0	0.9	27.0	0.9
Emme. IOL: 28.25		Emme. IOL: 28.25	

Tecnis ZA9003		PanOptix TFAT30-60	
pACD Const:	5.61	pACD Const:	5.61
IOL (D)	REF (D)	IOL (D)	REF (D)
30.5	-1.0	30.5	-1.0
30.0	-0.6	30.0	-0.6
29.5	-0.3	29.5	-0.3
29.0	**0.1**	**29.0**	**0.1**
28.5	0.4	28.5	0.4
28.0	0.8	28.0	0.8
27.5	1.1	27.5	1.1
Emme. IOL: 29.12		Emme. IOL: 29.12	

(* = Changed manually, ! = Borderline Value)

This hyperopic patient initially tested left-eye dominant, but the biometry and refractive error suggested the opposite (i.e., right-eye dominant, based on longer/closer-to-normal axial length). A loose-lens trial confirmed that the patient indeed preferred the add over her left eye, and so an EDOF was placed in her right eye, and a trifocal was placed in her left eye. The patient was very happy with her final visual outcome.

Dagny Zhu, MD

ing a Synergy lens in the first eye, notice that their distance vision isn't necessarily as sharp as they were hoping for. "In those cases, we put the Symfony in the dominant eye to enhance distance clarity," he says. "I had a patient a few months back who had a Synergy in her first eye. Based on our conversations, she was sure she was going to get the Synergy in her second eye as well. During the check-in between the two surgeries to confirm the plan for the second procedure, I found that between the time I had first met her and time I was doing her second surgery, she'd taken up birding. She was now a birdwatcher. And she had noticed that she wasn't seeing the birds at the same distance that other people were seeing them. These were little birds at 50 to 60 yards away, not large birds at 10 feet. So, we put the Symfony in her second eye, and she was thrilled."

• ***Monofocal combinations.*** "I sometimes use a monofocal lens in the distance eye of a patient, and if they do well with that and still want more range in the second eye, I'll implant an EDOF, multifocal or trifocal in the non-dominant eye," Dr. Farid says. "This approach requires more patient education because the patient won't have the same degree of dysphotopsias in the monofocal eye as they will in the multifocal eye. As long as they understand that the night vision and degree of glare in the two eyes will be different, then I'm okay using this combination as well."

An epiretinal membrane or some kind of macular pathology in one eye but not the other eye can also be grounds for a mix-and-match strategy with a monofocal. "It's important to think about quality of vision first whenever an eye has a compromised visual pathway," says Dr. Shultz. He adds that it's also important to explain to patients that "sometimes we'll stick with a monofocal or monofocal toric, or even an EDOF. I think with Vivity, it's sometimes safe to place it in an eye that may have a mild epiretinal membrane, but the other eye is okay. We can use technology that achieves the patient's visual demands in that respect, so we may choose to use a PanOptix lens in the second eye to give them that range they're looking for."

• ***Small-aperture combinations.*** The Apthera (Bausch + Lomb) lends itself well to mix-and-match approaches since it's typically placed in only one eye. Dr. Shultz says the Apthera is a good option for "patients who want to have extended range of vision but can't necessarily afford having technology in both eyes. One of the nice things with the Apthera lens is being able to provide depth of field without compromising distance significantly, certainly during the daytime." He says patients who have the Apthera lens in one eye "still wind up with excellent distance vision and an enhanced range of vision" in that eye.

"Sometimes patients have corneal pathology, whether it's a scar from previous pterygium excision or something else, or irregular astigmatism, and though this may be slightly off-label for the technology, using the Apthera lens to help reduce the

Johnson & Johnson Vision

A Symfony IOL in the dominant eye can provide good distance and intermediate vision in mix-and-match approaches, surgeons say.

visual aberrations associated with those problems is another reason for mixing and matching," he says.

When Dr. Shultz uses the Apthera, he says he usually implants a monofocal spherical, monofocal toric or distance plus lens in the other eye. "I've used Eyhance (Johnson & Johnson Vision) lenses in the other eye," he says. "Now we have access to the Aspire (Bausch + Lomb) monofocal as well for maximizing range of vision. Those two lenses offer a kind of slight distance plus, and then we can get a little bit more out of the Apthera or stick with a straight monofocal, depending on what the issues are."

Dr. Shultz says he's also had success using an Apthera and a Light-Adjustable Lens mix-and-match combination in certain patients with mild or forme fruste keratoconus. "I use the Light-Adjustable Lens to maximize the vision in the eye [with milder disease] and in the eye that may have more advanced keratoconus or more than a diopter and a half of manifest cylinder refraction, I'll use the Apthera with the Light-Adjustable Lens to maximize the astigmatic treatment and also reduce the aberrations from the keratoconus."

Dr. Donaldson says the Apthera/Light-Adjustable Lens combination is also good for patients with aberrated eyes, such as post-LASIK or post-RK. "A Light-Adjustable Lens in the dominant eye (targeted for distance) and an Apthera lens in the non-dominant eye (targeted at -0.75)," is another useful combination, she says.

Dr. Shultz agrees that post-RK patients are sometimes good candidates for a mix-and-match approach with the Apthera. "If they've had more than an eight-cut RK, they tend to have lots of peripheral aberrations that don't do well with any IOL technology, so this is another area we've started using the Apthera, at least in one eye," he explains. "Sometimes we'll use it in both eyes, depending on the outcome of the first eye and how satisfied the patient is with both the quality of vision and the potential issues with their night vision."

Pearls for Success

Here are some points to keep in mind when mixing and matching IOLs:

• ***Check for previous experience with monovision.*** If a patient has previously had monovision in contact lenses, they're likely a good candidate for a mix-and-match approach because they've already demonstrated neuroadaptability.

Dr. Dewey says, "One of my favorite combinations for these patients is an Eyhance in the dominant eye for distance and a Symfony in the non-dominant eye targeted anywhere from -0.75 D to -1.25 D, depending on the height of the individual and their previous myopic refraction. I employ this specific option for patients who've been monovision contact lens wearers. If they drove at night with a nearsighted contact lens in their non-dominant eye, they were dealing with glare and halos. With this mix-and-match approach, they'll still have glare and halos in the non-dominant eye, but they're pre-adapted to it. It gives them something they didn't have before, because a lot of these monovision patients were wearing glasses for intermediate distance, so when you give them the enhanced depth with the Symfony, they're ecstatic."

This form of augmented monovision also solves a bigger issue—that of anisometropia. "Most of these patients are in the 24/40 range at distance, so they achieve the -2.50 effect at near, with only 1.25 D of anisometropia. It's very well tolerated," Dr. Dewey says.

> **"We have to explain upfront what the potential risk factors are in their case if they're not a great candidate for the same technologies as their friends or family."**
>
> ***— Mitchell C. Shultz, MD***

• ***Perform a careful evaluation and get consistent measurements.*** Myriad factors can impact a lens plan, so conducting a careful evaluation of the visual pathway and the ocular surface is always necessary. "We have to be realistic about what patients and their eyes can tolerate," Dr. Shultz says, noting that dilating the patient and evaluating for dry eye is key. "Fluorescein staining without any anesthetic is critical for looking at the ocular surface before surgery to evaluate candidacy for

certain technology and how we're going to optimize vision."

"I like to have consistent keratometry, topography and astigmatism measurements on two different machines," Dr. Farid says. "Regardless of the type of lens I put in, I want to make sure I nail the refractive outcome in each eye. I like to use the newer generation formulas such as the Barrett Universal formula to ensure I'm hitting my targets."

For multifocal lenses, such as PanOptix, Dr. Donaldson says she generally targets first plus. "For monofocal plus lenses such as the Eyhance or Rayner EMV, I target first plus in the dominant eye and second minus in the non-dominant eye to extend the range of vision," she explains. "I find these targets to be similar for the Light-Adjustable Lens as a starting point, but then tend to dial up the near closer to a -1 D in the non-dominant eye to achieve optimal range without loss of distance."

• ***Set realistic expectations.*** As with any premium lens technology, experts say it's important that patients understand the limitations of their own vision compared with that of their friends, as well as the limitations of the technology. "We have to explain upfront what the potential risk factors are in their case if they're not a great candidate for the same technologies as their friends or family," Dr. Shultz notes.

"From the outset, patients should be advised that cataract surgery is a process involving two eyes," Dr. Donaldson says. "We tell them that the two eyes work together to fill in gaps and to give us a more complete range of vision. Starting with the non-dominant eye helps assess the dysphotopsia profile for an individual patient—the non-dominant eye tends to be a bit more forgiving of side effects. Also, always remember to be honest with the patient and discuss potential compromises and limitations before surgery in order to set reasonable expectations."

Johnson & Johnson Vision

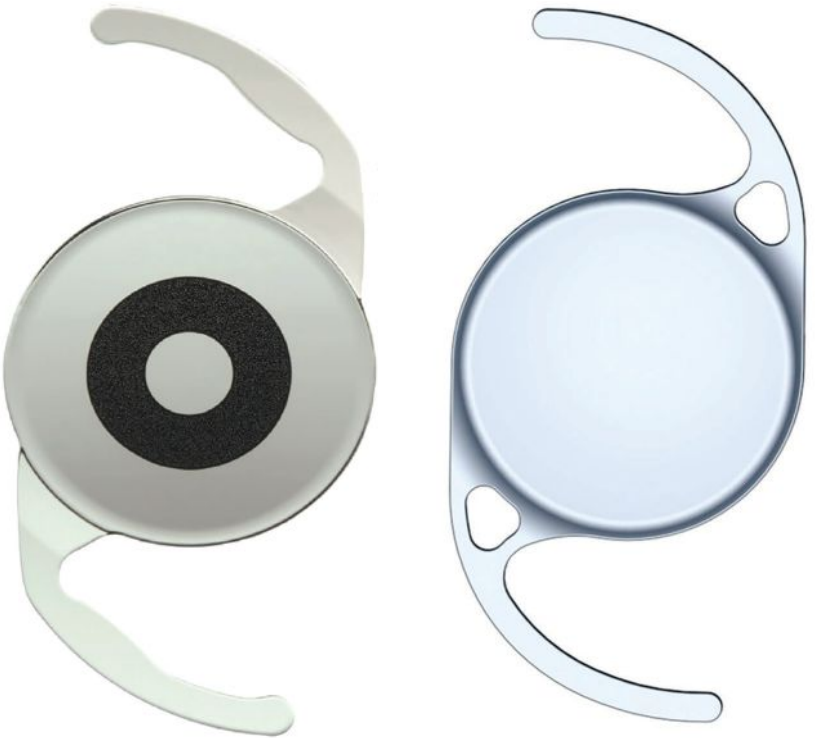
The Synergy IOL (above) is often paired with the Symfony to provide reading vision.

"I make sure that every patient understands the potential refractive issues we may be encountering, such as how conditions such as keratoconus or previous refractive surgery are going to affect the outcome," Dr. Dewey says. "If you explain to patients the limitations on the choices they're making, they better understand why things aren't as sharp and crisp as they'd like. Patients going through the premium lens channel have higher expectations, so for them this is a given. Patients not going through the premium channel deserve to know what the likely outcome of their surgery is going to be every bit as much [as premium-channel patients].

"It amazes me that even when you've got all the bases covered as well as you possibly can, patients are still going to find ways to end up needing task glasses," he continues. "One cautionary tale is to emphasize to that -4 myope who wants amazing clarity throughout all ranges that their near vision with our current technologies is going to stop at about 12 inches close to their nose, as opposed to eight. So, for some patients who are really accustomed to being able to take their contacts out or glasses off and just hold things right under their nose and see them, you just have to point out that this will put them back to where their bifocals had them. If they want to hold things closer, they'll need some supplemental magnification."

• ***Determine true eye dominance.*** "It's really important to determine the proper dominant and non-dominant eye in the patient," Dr. Zhu says. "We typically check eye dominance by having the patient hold up their hands to create a circle, and then with both eyes open, they'll place a distance target within that circle, then close each eye. Whichever eye maintains that distance target within the circle is typically the dominant eye, or distance eye, and you'd place the monofocal or EDOF in that eye. The other eye would be the non-dominant eye or near eye, and you'd place the full-range vision (e.g. trifocal or multifocal) lens in that eye.

"However, in my experience, about 20 to 25 percent of patients don't follow that rule, meaning that even though the test might show the left eye as dominant, the patient actually prefers that eye as their 'near' or 'reading' eye—meaning that they prefer the multifocal in their left eye, which is the opposite of what you might think," she continues. "So, I don't rely solely on that test for some patients. I often have my in-house optometrist double check the 'true dominance' by placing a loose lens over each eye. Basically, I correct both eyes with the patient's manifest refraction and then I place a +2 loose lens first over the left eye and then over the right eye. In both situations, I tell



Bausch + Lomb

Surgeons say the small-aperture Apthera (left) can be mixed with monofocals such as Aspire (right) and enhanced monofocals such as Eyhance and the Light-Adjustable Lens to improve the range of vision in certain patients.

the patient: 'This loose lens is going to make the distance vision look worse. But over which eye is the distance vision a little bit less blurry, or over which eye is it more clear?' I document whichever eye the patient preferred the add over (i.e., felt less blurry), and that becomes the true non-dominant eye or near eye, in which you'd place the full-range presbyopia correcting lens."

Dr. Zhu says she doesn't use this approach with every patient, as it's not always necessary and can be more time-consuming, but finds it helpful in patients whose eye dominance seems to switch back and forth from one eye to the other; in patients who have a similar refractive error in both eyes; or in patients where the eye dominance appears to be the opposite of expectations. "For example, I'd generally expect the shorter eye to be the non-dominant eye in a hyperope, and I'd expect the longer eye to be the non-dominant eye in a myope," she says. "If that doesn't correlate with the initial eye dominance test where they hold out their hands, then I'll definitely have the OD double check by doing the loose-lens trial. Oftentimes, the loose-lens trial will confirm the opposite dominance of what was initially obtained and align with what I would have expected based on the refractive error or axial length."

• ***First eyes first.*** Waiting and assessing the first-eye outcome before operating on the second eye creates more opportunity for better-informed lens selection, surgeons say. "When possible, I prefer to start with the non-dominant eye, particularly when implanting a multifocal or EDOF lens," Dr. Donaldson says. "This gives us an opportunity to assess any potential dysphotopsias. If the patient notices the dysphotopsias and is significantly bothered by them, I'll combine this with a monofocal or EDOF lens in the dominant eye—for example, a PanOptix in the non-dominant eye and an EDOF lens (such as the Vivity or Synergy) or monofocal plus distance lens in the dominant eye, targeted for distance (such as the Eyhance or the Rayner EMV)."

"My preference is typically, when possible, to operate on the dominant eye first, so that I can really assess whether or not the non-dominant eye is going to get the same technology or if we need to use a secondary technology, depending on the outcome of the first eye," says Dr. Shultz.

Dr. Dewey agrees with the sequential approach, saying he doesn't perform bilateral simultaneous cataract surgery. "My surgeries are usually two weeks apart, or more if the patient prefers," he explains. "As much as I love the enthusiasm about bilateral simultaneous, when the patient is going to be living with the result for the rest of their life, and I can give them a better result by tailoring their second surgical result to meet the needs that we're working to achieve by reviewing their first surgical result, I think two weeks out of a lifetime is probably worthwhile."

Laying out the steps of the mix-and-match process is helpful for patients. Dr. Farid says, "When I'm talking to patients, I let them know what I'm planning to do. I tell patients, 'Let's do the first eye with the lens I think is going to be ideal for this eye.' We start with that. And then I say, 'Before we do the second eye, we're going to have a conversation to see how you're doing with the first eye and to then use your second eye to fill in gaps.' Those are the words I use so that patients realize we're really personalizing their vision. We're taking our time even between the two eyes to find out where we landed with the first eye before we finalize our decision on the second eye. Patients really like that because they're playing an active role in their final lens decision." ◀

MARCO

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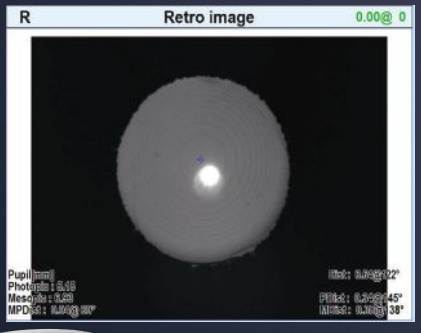

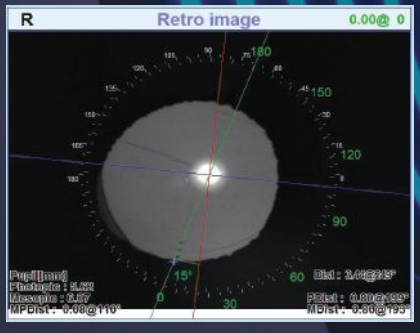

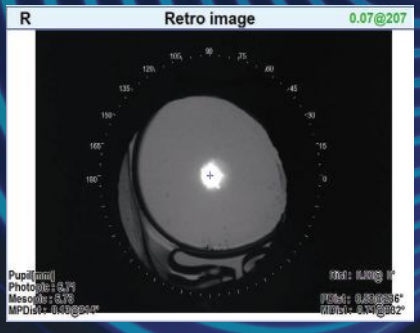

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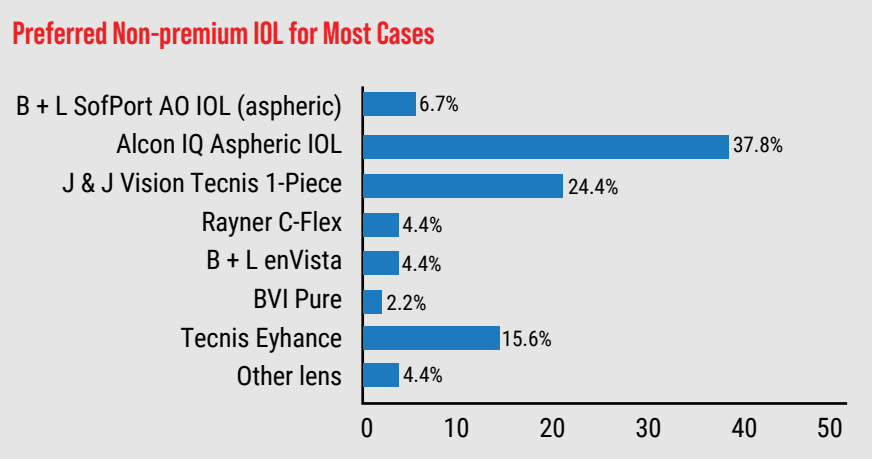
SURVEY: SURGEONS WEIGH IN ON IOLS

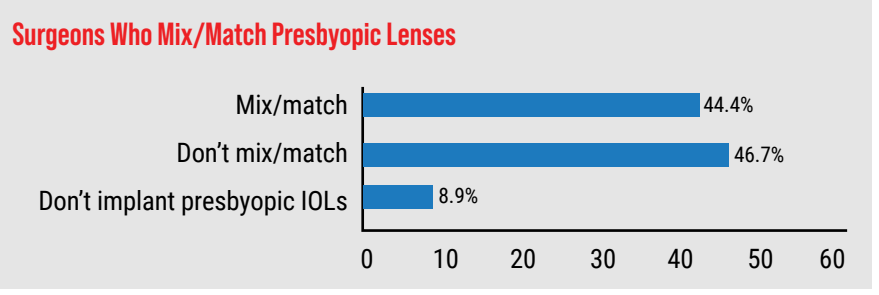
Cataract surgeons share their thoughts on monofocal, toric, premium and phakic intraocular lenses.

WALTER BETHKE
EDITOR IN CHIEF

Surgeons need to master the techniques of cataract surgery, but the tools they use also play a part in the success of a procedure, and one of the most important tools at their disposal is the IOL they choose to implant. On this year's survey of surgeons' IOL preferences, doctors weigh in on such topics as the attributes of the monofocal lenses they use the most, how their favorite premium IOLs are performing and whether mixing and matching IOLs is a viable strategy.

For this year's survey, 26 percent of the 10,150 surgeons on the email list opened the survey, and 49 respondents completed it. To learn about their usage patterns, as well as their views on various IOL technologies, read on.





Monocular Options

Surgeons opined about their go-to lenses for the bulk of their cases, the monofocal IOLs.

The Alcon IQ Aspheric was the most popular, chosen by 38 percent of the physicians.

Richard Wieder, MD, of St. Louis says he prefers the Alcon IQ because it gives him "long-term great results." A surgeon from Ohio says he uses the lens because of the "lens material and predictability." Jonathan Adler, MD, of Bradenton, Florida, likes that the lens has "very few visual obscurations."

The next most popular lens on the survey was the Johnson & Johnson Tecnis 1-piece, selected by 24 percent of the surgeons. A surgeon from Indiana says she likes the lens for its "superb visual

This article has no commercial sponsorship.

acuity, consistent performance, and outstanding patient outcomes without glistenings." Louisville, Kentucky, surgeon Asim Piracha uses the lens because it "is clear, has no glistenings, centers well, has a very good preloaded system, has excellent optics, resists scratching, and has negative asphericity."

The next most popular option was the Tecnis Eyhance (16 percent). "I like the clarity of the lens, the ease of delivery and the fact that it gives some (minimal) EDOF for patients," says a surgeon from Delaware.

The rest of the surgeons' choices for non-premium lenses appear in the graph on pg. 40.

The Premium Arena

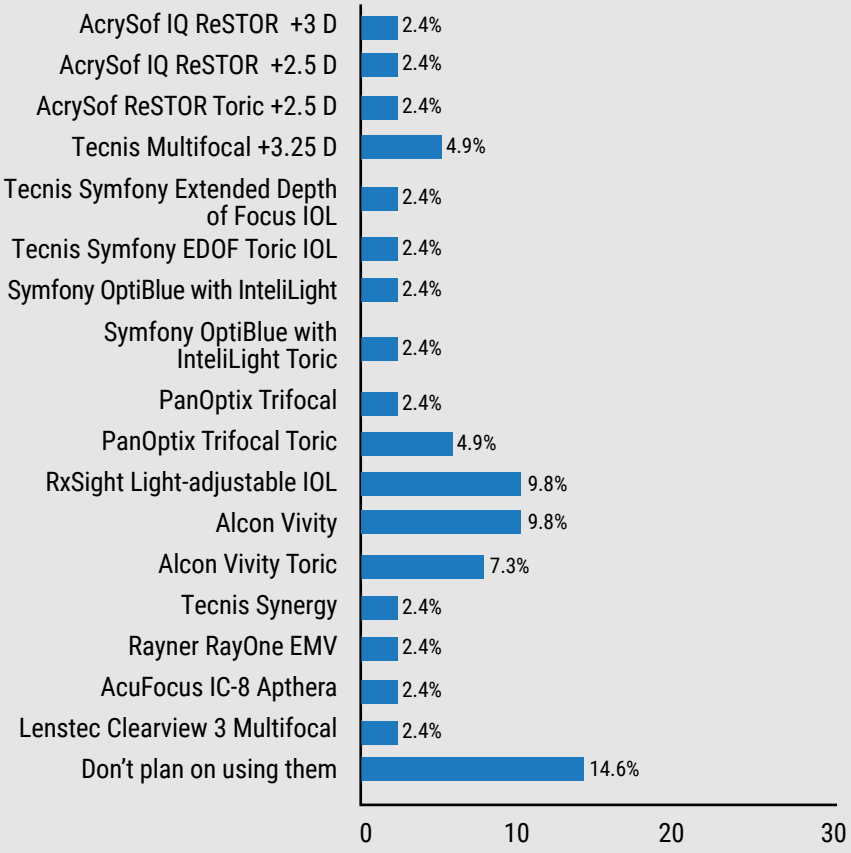
Similar to last year's survey, when it comes to premium lenses, trifocal IOLs were the most popular with the surgeons (some respondents chose more than one option), with the Alcon PanOptix trifocal IOL being used by 35 percent of respondents. However, this is a decrease from last year's 52 percent, possibly indicating surgeons are giving other options a try. The respondents who implant the PanOptix report that they implant an average of six per month, and charge an average of $3,100 per eye. A Philadelphia surgeon says he gets "good visual results for Clareon Panoptix. I'd like a preloaded option." A surgeon from North Carolina says he's satisfied with the lens, but is "still concerned about glistening and I have some concerns about quality of vision and halos."

The next most popular lens on the survey was the Symfony OptiBlue with InteliLight, chosen by 32.5 percent of surgeons. They say they implant an average of five per month, at an average charge of $1,583/eye.

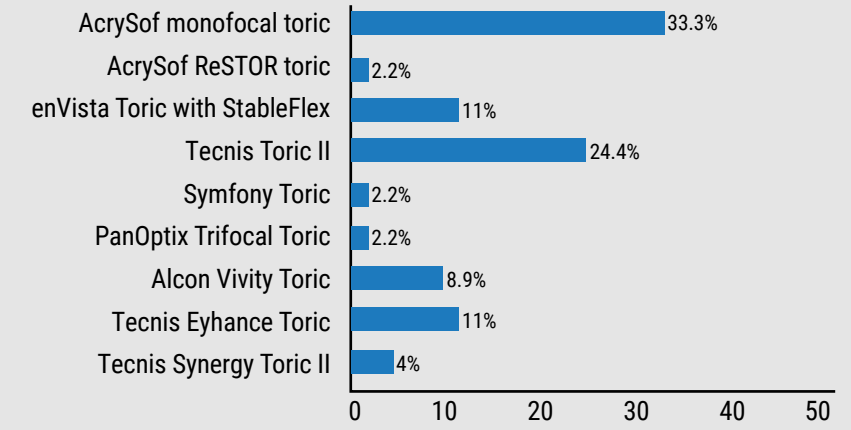
The Alcon Vivity lens was also chosen by 32.5 percent of the respondents, who average four implants per month at a price of $3,141/eye. "It's pretty good right now," says New York City surgeon R. Scott Russell of the Vivity. "Maybe extend the spherical and toric range." Following the Vivity was the PanOptix toric version, chosen by 30 percent of surgeons, who implant an average of 5.36/month at a price of $2,763. Richard Wieder, MD, from St. Louis says he likes the "great patient satisfaction" after implanting a PanOptix toric.

The Tecnis Synergy was chosen by 27.5 percent of surgeons. The average number implanted per month on the survey was 3.33, at a price of $3,220/eye. "The lens gives a great range of vision and great contrast sensitivity," says a Colorado surgeon. I'd love less halos around headlights, but there is no such thing as a free lunch." Next in line

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



Preferred Toric IOL



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was the toric version of the Symfony OptiBlue/InteliLight, at 25 percent (5.6 implanted/month, $3,020/eye).

The high-tech RxSight Light-adjustable Lens was chosen by 25 percent of the surgeons. The average implanted per month was 15, at a price of $3,658/eye. "It gives excellent, predictable results," says a Mississippi surgeon. Edward Jones, MD, of Oklahoma City likes the LAL, saying, "No halos. Predictability. Controlled refractive outcome." A surgeon from New Orleans likes the RxSight, but sees a little room for improvement. "A faster lock adjustment would be nice," he says. The Alcon Vivity toric also came in at 25 percent (6/month; $2,925/eye).

The Rayner RayOne EMV was selected by 15 percent of the surgeons. The average number implanted per month on the survey was 10, at $1,850/eye). One surgeon likes it for several reasons: "cost, better night-vision profile, and improved near vision without compromising night vision," he says.

Forty-four percent of the surgeons say they occasionally mix-and-match IOLs (i.e., use different lenses in each eye). There are many possible combinations. A surgeon from Indiana says he mixes "Symfony OptiBlue and synergy. By mixing and matching, I give my patients the benefit of the overall quality of vision and the quality of distance vision of the Symfony OptiBlue, combined with the excellent near vision that the Synergy provides." A surgeon from California says, "When indicated, I use any combination of Alcon toric: PanOptix and Vivity." G. Peyton Neatrour, MD, from Virginia Beach, isn't sold on mixing and matching though. "Mixing increases patient complaints with limited improvement in range of vision," he says.

Toric Topics

When it comes to treating patients' astigmatism, the lens that got the most votes on the survey (33 percent) was the AcrySof monofocal toric. This was followed by the Tecnis Toric II (24 percent) and the enVista Toric with StableFlex (11 percent). The rest of the toric choices appear in the table on pg. 41.

A surgeon from California says he likes the AcrySof toric because of the "stability and wider landing zone." Krishnarao Rednam, MD, of St. Louis, prefers the Tecnis Toric II because it yields "good visual outcomes." In the enVista Toric with StableFlex camp is Ronald Glassman, MD, of Teaneck, New Jersey, who says he prefers it because it has "no rotation" and gives "long-term stability."

IOL Attributes Surgeons Value
(1= least important, 9=most important)

Attribute	Average score
Asphericity/neutral asphericity	5.9
Bifocal Multifocality	5.53
Blue-light blocking	5.44
Edge design to decrease PCO	5.42
Extended Depth of Focus Design	5.37
Toric Design	5.13
Violet-light blocking	4.95
Trifocality	4.49
Ability to adjust IOL power post-implantation	4.33

The Phakic Option

Twenty-seven percent of the respondents implant phakic IOLs. Their lens of choice is the Staar EVO/EVO+ Visian.

An EVO Visian user from California says, "It's good for moderate/high myopes if they have enough anatomic space for placement. There are no dry-eye issues, and there's no increased higher order aberrations." A surgeon from Philadelphia agrees, saying, "They're an excellent choice for high myopia."

The surgeons who don't implant them have some reservations. John C. Hart Jr., MD, of Farmington Hills, Michigan, says, "I don't implant these IOLs. Phakic IOLs can be a good option but the cost and risk is greater than corneal refractive surgery."

Securing Loose Lenses

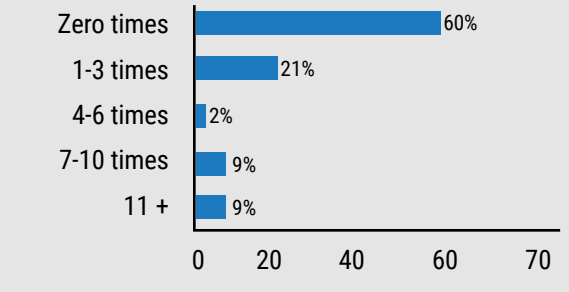
Surgeons also opined about situations where a lens needs to be sutured.

Most of the respondents (60 percent) fortunately don't have to suture an IOL in any given year. However, 21 percent have to suture one to three lenses, and around 9 percent have to suture 11 or more. The rest of the results appear on the graph to the left.

Some of the reasons cited for suturing include:

- capsular injury;
- dislocated IOL, fixated using a scleral flange technique;
- dislocated lens due to zonule insufficiency, repaired with a scleral suture;
- no capsular support, so the lens is sutured to the iris; and
- a patient who was referred to the surgeon for "dead bag" syndrome. ◀

How Often Surgeons Suture an IOL in a Year



THE TOOLBOX FOR NONINFECTIOUS UVEITIS

From steroids and immunomodulators to biologics and more, there's a wide array of therapies to consider for this disease. Experts discuss the best ways to balance the risk-to-benefit profile to bring relief to these patients.

LIZ HUNTER
SENIOR EDITOR

Uveitis is one of the most challenging diseases to treat, both in its infectious and non-infectious forms. Specialists who regularly help manage the condition have to consider the many types of uveitis and the various therapeutic pathways that are available, some of which come with considerable side effects and can take years to work fully.

In this article, experts discuss the more severe cases of uveitis and the treatment plans that work best.

Categorizing the Uveitis

"I think the trickiest thing is that uveitis is heterogeneous," says Christopher R. Henry, MD, a medical and surgical retina specialist practicing in Houston. "Uveitis encompasses hundreds of different ocular conditions which can be autoimmune, infectious or a masquerade. There's a broad spectrum in terms of how serious a disease is, how much of a risk to sight it is, and there's a really broad range of treatment strategies. For instance, a problem such as an isolated, unilateral, acute anterior uveitis can be very easy to treat, but bilateral, severe, chronic panuveitis will likely be a lot harder."

In a way, the challenge can be exciting, according to Sruthi Arepalli, MD, an assistant professor in the Vitreoretinal and Uveitis Service at Emory University. "What attracted me to the field of uveitis is that no two patients will present exactly the same, and that keeps the job fun," she says. "Despite this, there are overarching similarities, which allows us to rely on pattern recognition while teasing out their nuances. These nuances include a different constellation of systemic signs, or maybe their ocular manifestations and complications aren't exactly the same as the person before them. These differences can dictate treatment algorithms. The field of uveitis becomes an art of balancing their manifestations, medication side effects and patients' short- and long-term goals."

Dr. Henry says there are some key factors to examine before proceeding with treatment. "You'll want to assess how serious the disease is," he says. "You're going to look at:

- is it unilateral or bilateral disease;
- the anatomic location: anterior; intermediate; posterior; or panuveitis;
- is it an acute disease or chronic;
- how aggressive the process is;
- the degree of vision loss at baseline; and
- how likely is this to progress quickly?

"For the majority of cases I'll usually order lab testing—unless it's a straightforward, isolated anterior uveitis—to try to figure out the cause. The lab work will really be driven by the clinical appearance of what the disease looks like," Dr. Henry says.

Dr. Arepalli first rules out infection. "My first rule of thumb when I'm seeing a uveitis patient is to rule out an infection or masquerade condition," she says. "While masquerades can take a while to present themselves, infectious causes should be ruled out immediately. Emory is a big referral center for vitreoretinal lymphoma and I often get referrals for uveitis that isn't improving with the standard regimen, so I think about masquerades a lot."

This article has no commercial sponsorship.

Dr. Arepalli is a consultant for AbbVie and Alimera. **Dr. Dahr** has no relevant disclosures. **Dr. Henry** is a consultant for Bausch + Lomb, Clearside Biomedical, EyePoint Pharmaceuticals and has previously consulted for Allergan.

"For severe disease, once you're sure it's noninfectious uveitis, most of those patients will need more than just topical steroids, and that can include oral steroids, local steroid injections, and some patients will need systemic immunosuppression," says Dr. Henry.

Steroids, Immunomodulators or Both?

Starting off with steroids is common, say experts. "I'd say the majority of times you'll treat with both topical and oral steroids initially and then depending on what the lab work-up shows and how a patient responds, and whether the disease is likely to be chronic or vision-threatening, then you may need to transition them over to a longer term steroid-sparing agent," says Dr. Henry.

Dr. Arepalli gathers information while initiating steroids. "I'll typically first start with topical steroids for two reasons: First, I'm building a relationship with this patient, so it gives me an opportunity to see how they tolerate a regimen and see how compliant they're going to be," she says. "It's also an easy thing to stop if something surprises me in their workup and I want to change directions. Lastly, it helps me test how they're going to react to steroids, like if they will develop a pressure response."

More often than not, her patients will need treatment with immunomodulators. "At Emory, I'm often seeing tertiary referral patients, and they've failed topical or oral steroids," Dr. Arepalli says. "With these patients, I often graduate them to immunosuppression or local therapy pretty quickly because I can see evidence of uncontrolled inflammation."

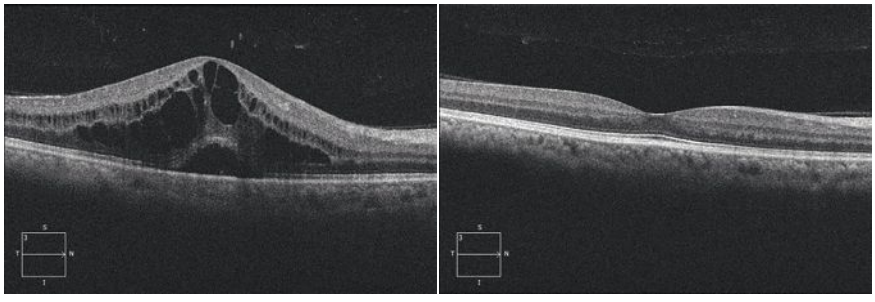
For aggressive disease, it often requires early and aggressive management, Dr. Henry says. "A common mistake that doctors make is to undertreat. You want to squash the inflammation quickly and taper in a structured manner. Where you actually run into more trouble is if you don't quiet it quickly and you let it linger," he says. "I think patients end up doing more poorly that way. If you do keep them on topical steroids for a long period of time, it's critical that you monitor the eye pressure. If a patient is a steroid responder you need to be on top of that and treat that as well."

Moving forward with long-term immunomodulatory therapy (IMT) is a major decision. "What are the thresholds that prompt the treating ophthalmologist to recommend IMT?" asks Sam S. Dahr, MD, MS, the director of the retina division in the Ruiz Department of Ophthalmology and Visual Science at the University of Texas Health Houston McGovern Medical School. "In cases of chronic or recurrent anterior uveitis, prevention of anatomic sequelae such as inflammatory glaucoma, cataract, progressive posterior synechiae, peripheral anterior synechiae, band keratopathy and macular edema may also indicate IMT. Regarding intermediate uveitis, chronic macular edema that repeatedly recurs after local therapy with an intravitreal steroid injection is often an indication for IMT. In cases of posterior uveitis or panuveitis, macular edema, chorioretinal scarring, inflammatory choroidal neovascularization, inflammatory retinal degeneration, visual field loss or severe retinal vasculitis can be indications for immunomodulatory therapy.

"To answer the question of whether or not to initiate IMT, we really use all of our metrics," he continues. "We use our ophthalmic exam. We may use OCT, the fluorescein angiogram, and visual fields. If we have a sense that the disease is progressing or is going to progress because of the nature of the disease, then we have to step up and go in the direction of immunomodulatory therapy."

Due to her uveitis fellowship training, Dr. Arepalli says she has a low threshold for immunosuppressives. "In general, we've seen in the uveitis literature that the 'see-saw' effect, or those situations in which we chase flares with steroids rather than preventing them, results in worse outcomes," she says. "In particular, if a patient has bilateral disease or disease in their good eye that's encroaching on their central vision, I push for immunosuppression. We have really good data from the SITE (Systemic Immunosuppressive Therapy for Eye Disease) study that has shown us that when you get complete control of posterior or panuveitis with immunosuppression, you can significantly decrease the complications from uveitis, particularly things like choroidal neovascular membrane formation. That data also shows us that you don't get that same effect if patients are minimally controlled, meaning that we let them smolder and they're not completely quiet. That forms my treatment paradigm and I lean on immunosuppression earlier, because I know that we get better results.

"Also, I see a good number of pediatric uveitis patients, and in addition to balancing everything we've already discussed, I'm also trying to keep them with good vision and functioning for as long as possible," continues

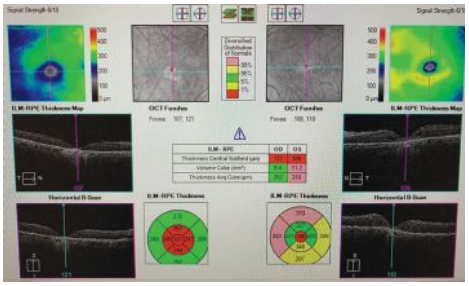


Sam S. Dahr, MD, MS

The image on left demonstrates 4+ uveitic macular edema with a subretinal fluid component. The image on right shows macular edema resolution after treatment with intravitreal steroids and immunomodulatory therapy.

Dr. Arepalli. "Therefore, I may opt for immunosuppression earlier in these patients as well to prevent long-term complications from their uveitis."

SITE was a retrospective cohort study showing that, one year after starting IMT, sustained control of inflammation was attained in 62.2 percent, 66 percent, 73.1 percent, 51.9 percent, and 76.3 percent of patients taking azathioprine, methotrexate, mycophenolate mofetil, cyclosporine and cyclophosphamide, respectively.[1] It also revealed that the rate of inflammatory control dropped when oral prednisone was stopped, regardless of the IMT agent used.



This 58-year-old female presented with a 30-year history of idiopathic intermediate uveitis. Vision is currently 20/200 bilaterally. The patient had a documented history of macular edema in the first 10 to 15 years of her disease course treated with topical steroids only. This case demonstrates that undertreated macular edema may develop foveal thinning and central vision loss.

Antimetabolites, Biologics and More

We asked these experts about the combination of agents they typically turn to first for patients with noninfectious uveitis.

"With immunosuppression, we have a lot of different treatments that we can consider," says Dr. Arepalli. "There are antimetabolites, which tend to be the first-line therapy, and that's made up of methotrexate, azathioprine and mycophenolate. Then you've got your biologics like adalimumab and newer drugs as well. You also have other therapies, including alkylating agents or calcineurin inhibitors and each one of those carries a very specific panel of side effects. It's a matter of matching what the patient wants and can tolerate with what the side effects of those treatments are." (More on side effects later.)

"In the era before anti-TNF inhibitors such as Humira (adalimumab), and Remicade (infliximab), we would often use an anti-metabolite plus a T-cell inhibitor," says Dr. Henry. "But now, we generally start a patient with an antimetabolite such as methotrexate or mycophenolate, and we have good Level I evidence for that pathway from the FAST trial."

FAST (First-line Antimetabolites as Steroid-sparing Treatment) was a trial that screened 265 adults with noninfectious uveitis who were randomized to receive oral methotrexate, 25 mg weekly, or oral mycophenolate mofetil, 3 g daily. In the posterior or panuveitis patients, treatment success occurred in 74.4 percent of patients in the methotrexate group vs. 55.3 percent in the mycophenolate group, whereas 33.3 percent of those with intermediate uveitis had success with methotrexate vs. 63.6 percent with mycophenolate.[2]

"The two first-line agents I use the most often are antimetabolites (such as methotrexate, mycophenolate or azathioprine) and biologic agents," Dr. Henry says. "The anti-TNFs are probably the most common biologic that I use: Humira; Remicade (infliximab); Simponi Aria (golimumab); or Cimzia (certolizumab pegol). For more aggressive diseases, I'll sometimes use rituximab."

Dr. Dahr says approximately 40 to 60 percent of patients will need combination therapy. "Then we typically add the anti-TNF agent to the antimetabolite," he says. "This pathway has become acceptable for both children and adults: first, the antimetabolite and then, as needed, go to combination therapy and add the anti-TNF agent."

Some patients who need combination therapy may not tolerate the antimetabolite, or they may not tolerate the anti-TNF, continues Dr. Dahr. "In those patients, we could consider a T-cell inhibitor such as tacrolimus or cyclosporine as a component of combination therapy. Even though it's a steroid and is injected into the vitreous as a form of local therapy, the Yutiq (fluocinolone 0.18 mg) implant features a long duration of action (two to three years) and can function as a building block in a long-term treatment regimen," he says. "Hence, many different combinations exist. For example, an antimetabolite plus a T-cell inhibitor is a classic combination that can work well and is inexpensive. As another combination, we may use a Yutiq implant in conjunction with an anti-TNF in a patient who doesn't tolerate the antimetabolite but needs more than the anti-TNF alone."

Sam S. Dahr, MD, MS

Dr. Henry says he rarely uses T-cell inhibitors, such as cyclosporine. "There are some uveitis specialists who use that regularly, but in my practice, I use it very sparingly," he says. "I typically will use mainly antimetabolites and biologics and then supplement with local steroids if they need extra control."

"T-cell inhibitors and alkylating agents (cyclophosphamide and chlorambucil) are, in my mind, the heaviest hitters," says Dr. Arepalli. "I've reserved those for patients who have the most severe disease. I really rely on rheumatology for going down that route because they can cause a lot of side effects. I have a handful of patients who are on alkylating agents. One that comes to mind is a patient who has a terrible case of scleritis in the setting of granulomatosis with polyangiitis. We had gone through everything else and ended up on cyclophosphamide because she just couldn't get controlled any other way. So while they're older drugs and they're among the harshest drugs we have, they're still very useful on patients for whom you can't get control with some of our newer medications."

Interleukin-6 inhibitors are a new frontier for treating noninfectious uveitis. "IL-6 antibodies, like tocilizumab, are relatively new," Dr.

Arepalli continues. "I've had really nice success in certain patients, particularly those with posterior uveitis and uveitic macular edema. We also have studies that are looking at the intravitreal administration of IL-6, such as DOVETAIL, a Phase I study, with positive results."

Preliminary results from the Phase I DOVETAIL study showed injection of RG6179 resulted in improvement in both vision and retinal thickness in all dosing cohorts, and was well-tolerated.[3]

In terms of future therapies to watch, Dr. Arepalli believes IL-6 is the most promising right now. "DOVETAIL showed a significant reduction in uveitic macular edema with intraocular administration," she says. "Traditionally, intravitreal treatment for uveitic macular edema requires steroids, so this presents an opportunity to do a local, steroid-sparing treatment."

Dr. Henry mentions that patients are currently in clinical trials for janus kinase (JAK or JAK/Tyk2) inhibitors. "It can be another tool in our toolbox," he says. "There's a lot to learn in uveitis. As we gain more knowledge about different disease entities, we may find that one systemic therapy has advantages over others for certain conditions."

With any of these therapies, it's best to discuss expectations with patients, not only regarding their efficacy, but also what's expected of the patient while undergoing treatment.

"With the classic traditional agents such as the antimetabolites and the T-cell inhibitors, those often take three to six months to start to take effect, and their full effect may take six to 12 months," Dr. Dahr says. "During that initial period we're often using oral corticosteroids or some form of local corticosteroid injection in an 'induction' fashion until the immunomodulatory agent takes effect. With regards to the anti-TNFs, those work a little bit faster. We often start to see some effect within six to eight or six to 12 weeks. I explain to patients that we have short-term goals, medium-term goals and long-term goals. Of course, most patients desire to achieve drug-free remission in the future. Some patients can achieve that goal over a period of time; some patients can't, but it certainly is a goal for which to aspire."

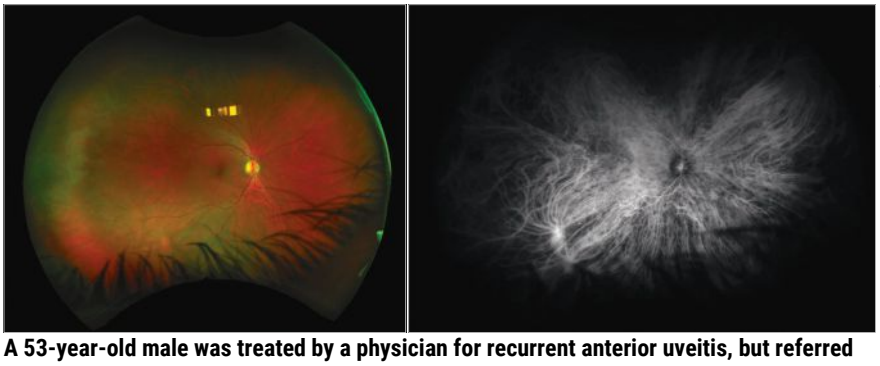
When it comes to taking patients off of treatment, that's an in-depth discussion, says Dr. Arepalli. "A lot of my younger patients are in their family-planning stages of life," she says. "In these patients, we'll talk to them about what is safe during pregnancy. I generally leave this up to rheumatology, but adalimumab has good evidence to be well-tolerated during the majority of pregnancy, and azathioprine is safe as well. I also tell patients that uveitis tends to calm down during pregnancy, so if they want to come off immunosuppression, we can try to treat locally or with oral steroids if necessary."

"Our hope is that the corticosteroid essentially goes to zero, the immunomodulatory agents take effect and the disease remains controlled," adds Dr. Dahr. "Once we achieve that status of the disease control and the patient is off the corticosteroid, we then essentially start a clock. Our goal is a minimum of one year and most specialists really like two years with essentially no need for corticosteroids. If a couple of years pass and the disease stays quiet with no need for corticosteroids, we may then consider a taper of the immunomodulatory agents. That's the approach most uveitis specialists follow.

"I call that period the 'cruise-control' period," he continues. "If the patient's doing well—no corticosteroids, tolerating immunomodulatory therapy well, exam looks good—I will typically follow that patient every four months or so. Of course the patient is encouraged to call and come for an appointment should he or she perceive a flare up. If, upon a slow taper of IMT, the disease reactivates, one usually goes back to IMT (often with some corticosteroid re-induction) and tries again a few years later."

Patients will also need to be monitored over the course of treatment. "Those on antimetabolites are going to need regular lab testing approximately every three months looking at a CBC and their liver and kidney function," says Dr. Henry. "Once in a while, we can see liver enzymes go high with antimetabolites, or we can see the blood counts drop too low, so that's something that needs to be regularly monitored."

Dr. Arepalli says it's helpful to work closely with rheumatology, especially if the patient has multiple medical conditions in addition to their uveitis. "Here at Emory, we have a lot of patients with multiple chronic and complicated systemic conditions, or they're traveling from far away and it makes monitoring them hard to do by myself. In those patients, I really think it's nice to work synergistically with rheumatology," she



Sruthi Arepalli, MD

A 53-year-old male was treated by a physician for recurrent anterior uveitis, but referred for poor control with topical steroids. The patient was treated with local steroids for years. On dilated eye examination, there was a small amount of vitreous cell, and while the fundus examination was fairly bland, an ICG revealed a multitude of choroidal granulomas. A review of systems revealed that the patient had a history of tattoos that would periodically swell, and chest imaging was consistent with sarcoidosis. The patient was started on immunosuppression and has done well since.

says. "When monitoring these medications each one carries its own set of requirements. Most commonly, every drug requires a CBC and CMP. You're often checking for anemia, low white blood cell counts, kidney function and renal function. Other medications might require that you get a urine analysis. There's not one algorithm for every drug, it's more personalized based on the mechanism of the drug."

Tolerance and Side Effects To Expect

Side-effect profiles further complicate treatment of uveitis, and that goes for both steroids and immunomodulators. It's best to have an open discussion with patients about the risks and benefits of pursuing treatment.

"I remind patients that they have a vision-threatening, sometimes debilitating disease and my job as a uveitis specialist is to put them on the medication that's going to quiet their disease with the least amount of side effects," says Dr. Arepalli. "I also remind them that when we coordinate with other subspecialities, it's my job to update the other physicians on the status of the eyes, because these can flare up independently of the rest of the body, and that may mean that they need to change around their medications. I also set the stage when I first meet patients that their medication cocktail is going to fluctuate until we find the best fit for them, and this can take many months to years."

Every single drug comes with side effects, including topical and local steroids. "With oral steroids, we have literature that shows that patients are often treated for too long and too high of a dose before they transition over to immunosuppression," continues Dr. Arepalli. "Our literature also says that 7.5 milligrams or lower of oral steroids is the best tolerated long-term, but that's often too low of a dose to get control of uveitis."

Antimetabolites carry side effects that are typically well-tolerated, but become more serious depending on a patient's lifestyle.

"Around two-thirds of patients tolerate anti-metabolites pretty well," says Dr. Henry. "The most common side effects I see are probably fatigue or nausea on the day of treatment. If they're not able to tolerate oral methotrexate, it's also available in an injectable form. In my experience, biologics are really well-tolerated. Humira, for instance, is a shot that patients give themselves every two weeks and you need to get at least an annual chest X-ray but the lab testing and monitoring aren't as intensive on a biologic. Some patients do experience fatigue, but many patients can't even really tell they're on a biologic. They feel normal. With Remicade, or other infusions given in an infusion center, occasionally we can see infusion or allergic reactions, so you do need to discuss this with patients in advance of this possibility."

Depending on a person's stage of life, there are some considerations to make about these medications and requires frank conversations with patients, says Dr. Arepalli. "This is by no means a complete review of the side effects or considerations for immunosuppression, but when I start the conversation with a patient, I mention a few key things," she says. "When discussing antimetabolites, there are certain ones that you can't prescribe if the patient is in the family-planning stages of life. Also, if you drink a certain amount of alcohol per week, you're not a candidate for methotrexate. It's really important that they're open with me about those things so we can come up with the best plan with rheumatology.

"Occasionally, I'll have a patient who's been doing well on methotrexate, but now they're interested in trying alcohol," continues Dr. Arepalli. "In these cases, we can switch them from one antimetabolite to another, or to a biologic. Alternatively, I might tell them since they've been quiet for a few years we can talk to rheumatology about tapering the medications and seeing how they do."

Even though there's a lot for patients to think about, it's best to remind them of the reliable and safe track record for these drugs. "We tell patients that all of these immunomodulatory medications have been used by hundreds of thousands of patients in the last several decades, and a Google search will find a broad spectrum of reported complications for any of the medicines we use," Dr. Dahr says. "Certainly, those potential complications sound scary. What's important to keep in mind is that the overall incidence of complications is low. There's always a benefit-to-risk calculation that's being made and the treating ophthalmologist and the patient should always discuss the benefit of a medication in terms of treating the uveitis and preserving vision vs. the risk. In most cases, the benefit-to-risk ratio for these severe uveitides favors using the medication, but no pathway is risk free. At the same time, losing vision in an irreversible fashion because of uveitis increases the risk of everyday life."

This is exactly what uveitis specialists are balancing daily. "It's helpful to keep in mind that this is all a balancing act of what we're trying to achieve and the medication side effects," says Dr. Arepalli. "Especially because we want to focus on the short term of controlling their inflammation, but also keeping them an active member of society by preserving vision and allowing every chance to enjoy their life. And if there's concern that you're not striking the right balance, it can be helpful to get a second opinion. Referring early can be really powerful." ◀

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GLAUCOMA: DETECTING OCT ARTIFACTS

OCT devices are powerful tools to ophthalmologists, but clinicians should be aware of the potential artifacts that come with using OCT.

ANDREW BEERS
ASSOCIATE EDITOR

Optical coherence tomography has advanced significantly since it was first developed in 1991, but artifacts still remain. For glaucoma patients, OCT is used to assist with diagnosis, but if clinicians and technicians aren't careful, they may end up with misinformation and an inaccurate interpretation of the results. Here, experts outline the various artifacts that can appear on OCT and how to detect and/or avoid them.

Reasons for not Catching Artifacts

One reason artifacts get overlooked by clinicians is due to lack of time. "The most common reason that an artifact gets overlooked is that everyone has a busy practice and we don't take time to review the raw images that constitute the result," says Sanjay Asrani, MD, a glaucoma specialist at Duke Eye Center in North Carolina. "So, if you were to carve out extra time during the visit, or even afterwards, to review the raw images that make up that report, then identification of artifacts would become much easier."

Another reason artifacts get overlooked is because clinicians have access to intelligent OCT devices, so they rely heavily on the report analysis rather than the raw images. "There's progression analysis software that's readily available," says Lucy Shen, MD, the director of the Glaucoma Fellowship at Massachusetts Eye and Ear. "So, a lot of times people tend to look at that. If you look at that analysis, it doesn't always show you the raw image and you're more likely to miss the artifacts."

Cirrus HD-OCT (Zeiss) is one OCT machine that offers progression analysis capabilities. This function uses a glaucoma progression-algorithm based on both event and trend analyses. It can obtain data samples of the retina nerve fiber layer as well as display RNFL thickness changes from baseline for each pixel in the scanned area.[1]

In order to make the best

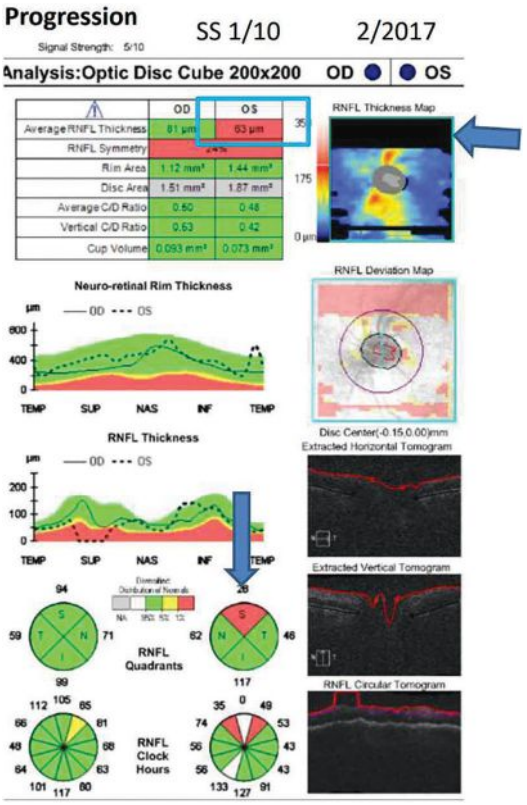

Figure 1. An example of a missing data artifact mimicking glaucoma progression. Average RNFL thickness in the left eye was 63 µm due to missing data in the RNFL Thickness Map indicated by the arrow.

This article has no commercial sponsorship.

Dr. Asrani received an honorarium from Heidelberg Engineering. **Dr. Ramulu** is a consultant for Alcon Vision. **Dr. Shen** has no financial interests to disclose.

assessment of a progression analysis report, Dr. Shen recommends comparing the report with other OCT data. "When I look at OCT reports, I look at the raw images first and then I'll look at the progression analysis, because the raw images usually tell me more about signal strength and also the artifacts are more visible," she says. "If the raw images showed a lot of artifacts, then I wouldn't even bother to use the measurement in the progression analysis. But, if the OCT looks like it doesn't have many artifacts, then I would look at the progression analysis."

There are various measures in an OCT scan that should be assessed by the clinician or technician. "The general rule is to spend some time looking at the details of the scan, not just the summary measures," says Pradeep Ramulu, MD, PhD, the chief of the Glaucoma Division at Wilmer Eye Institute in Maryland. "Of course, some summary measures such as signal strength and scan quality should be assessed as well. One should also be aware of typical floor and ceiling measurements for the instrument you are using. If the whole scan or regions of the scan show values outside of the typical floor and ceiling values, that should make one highly suspicious of artifacts."

Another way to avoid and detect artifacts is by getting a second scan. "In cases where the artifact is due to a poor signal strength, the image isn't very clear because the patient may have severe dry eye," says Dr. Asrani. "Then, it's absolutely a great idea to put in some artificial tears and repeat the scan or call the patient back on a different day when the eye isn't so dry and then repeat the scan. If you do these scans at the end of an eye examination, then the ocular surface is quite dry, and the quality of the OCT scan isn't going to be the best.

"Rarely it can happen that the technician didn't place the OCT centrally on the optic nerve, or the image wasn't centered in the window of acquisition, then the image edges got cut off and

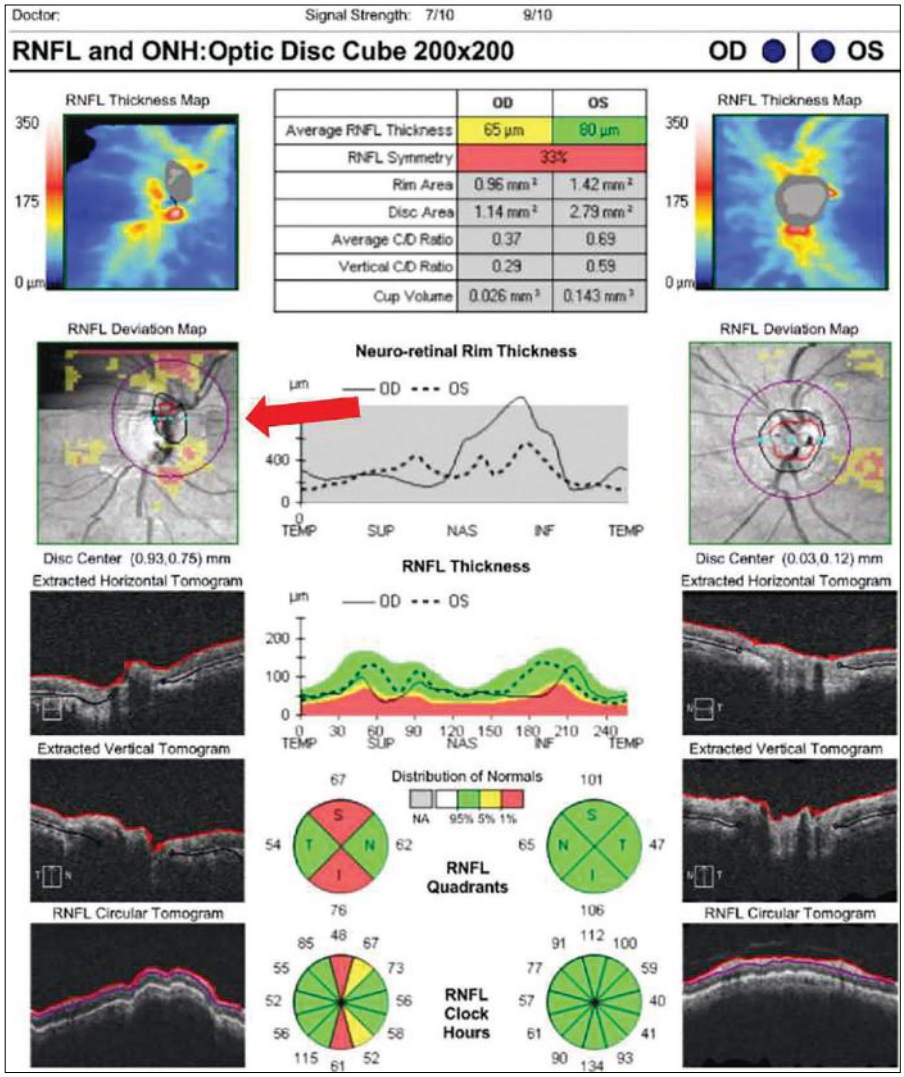

Figure 2. An example of a motion artifact and erroneous measurements. The motion artifact appears as a horizontal line on the Deviation Map indicated by the red arrow.

the OCT result is artifactual," continues Dr. Asrani. "In such cases, again, it's important to repeat the OCT scan, and you can identify the artifacts that have occurred when the thickness of the nerve fiber layer drops down to zero. Since that never happens in reality, any measurement of zero typically is an artifact. So, if you see a measurement of zero, there's been an image cut off in that area typically."

While a second scan can help uncover artifacts and assist with diagnosis, a second opinion from another clinician isn't the best idea. "One thing to keep in mind is that different OCT devices measure differently," says Dr. Shen. "If a provider were to get a second opinion from someone else and that doctor uses a different device, then they may not be helpful. You would have to look into providers in the same practice that can pull up the same series of OCTs to actually be able to provide an opinion. In other words, they're not interchangeable."

Currently, AI technology is being developed to assist clinicians and technicians with detecting artifacts. "Of course, this isn't in clinical practice yet, but this is a research area of mine," says Dr. Shen. "My colleagues and I started with a good OCT image and then manually generated artifacts. Then, we trained AI to be able to generate the correct image and compared that to the original."

In Dr. Shen's study, researchers

inserted artifacts into 27,319 scans: 53.4 percent of scans had an artifact ratio of ≤10 percent, 46.6 percent had an artifact ratio of >10 percent and 18.4 percent had an artifact ratio of >20 percent. According to the results, the artifact correction accuracy in the retina nerve fiber layer thickness map had a mean absolute error of 10 µm among scans with a ≤10 percent artifact ratio, 8 µm among scans with a >10 percent artifact ratio and 11.1 µm among scans with a >20 percent artifact ratio.[2] "Here we're addressing just missing data artifacts," says Dr. Shen. "We didn't look at a lot of the other ones, but there are definitely efforts on the way to see how we can supplement the OCT device and improve the imaging quality."

Artifact Awareness

There are a number of artifacts that can appear during an OCT scan for glaucoma diagnosis. For example, in the study of one device, for whatever reason, the report included at least one artifact 46 percent of the time.[3]

"One source for artifacts for younger clinicians to be aware of is to not make the diagnosis based on the red, green, yellow colors that are printed on the report," says Dr. Asrani. "Those are averages. Those are compared to normative databases, and those aren't indicative of glaucoma, necessarily. However, it could be glaucoma. But, for example, if there's a focal defect, it gets defined as a normal sector average thickness because the rest of the tissues are normal.

"The other example is if the sector's thickness is low, it's because there are shifted retinal peaks of the nerve fiber layer due to myopia, then those sectors may be classified as abnormal, or 'Red,'" continues Dr. Asrani. "So, we don't want to go just by the color indications on the report. We have to look at the entire picture by looking at the scans and segmentation so that we can identify correctly if this is glaucoma or not."

Instead of assessing the red, green, yellow color indicators, there's a simpler solution to diagnosing glaucoma. "It's extremely rare for glaucoma to be symmetrical, except when both eyes are end stage, because asymmetry is the hallmark of glaucoma," says Dr. Asrani. "If the clinician looks at the symmetry plot, or the symmetry graph, then they can adjust the two images side by side and see if there's any symmetry, that's one of the easiest ways of diagnosing glaucoma."

Be aware of missing data in the OCT's deviation map. "Missing data is common because if you don't have the eye correctly centered, you're not going to be able to scan all of the area," says Dr. Shen. "If the missing data is within the scanning circle, usually the technician will scan the patient again, but if the missing data is outside the scanning circle, then often the technician will move on to the next patient to image." (*Figure 1*)

Deviation maps can present artifacts that go undetected when looking at the raw images. Motion artifacts are a common example. "These are subtle and a little bit harder to detect because you don't see it on the raw image," says Dr. Shen. "If you look at the raw image, it looks nice and smooth. If you look at the deviation map and you notice horizontal lines and if they're inside the scanning circle, then they get registered to become a thinning in the nerve fiber layer. Unfortunately, it's hard to see it using progression analysis alone, but the best way to look at motion artifacts is with the deviation map." (*Figure 2*)

Preexisting conditions, underlying pathologies and other diseases can increase the frequency of artifacts and lead to an inaccurate diagnosis. "One should be aware of other potential optic nerve diseases or retinal diseases that can masquerade as glaucoma," says Dr. Ramulu. "Also, there can be abnormal thickening of the retina or nerve fiber layer in settings such as uveitis, diabetic macular edema or vein occlusion. These mistakes are particularly important as they can lead to unnecessary treatment for glaucoma, and failure to treat or address a different eye condition."

Dr. Asrani explains further, "Artifacts may be due to an epiretinal membrane on the surface of the retina that makes it appear that the thickness is normal when in fact the tissues underneath it may have thinned out significantly," he says. "Because it's present on the surface (the segmentation), I'll go over it and fix that up as the top part of the nerve fiber layer.

"Cysts, or schisis cavities, in the nerve fiber layer in myopic patients can cause the nerve fiber layer to look normal in thickness," continues Dr. Asrani (*Figure 3*). "Also, uveitis causes edema of the nerve fiber layer. So, whenever there's a coexisting diagnosis of uveitis, then OCT must be used with extreme

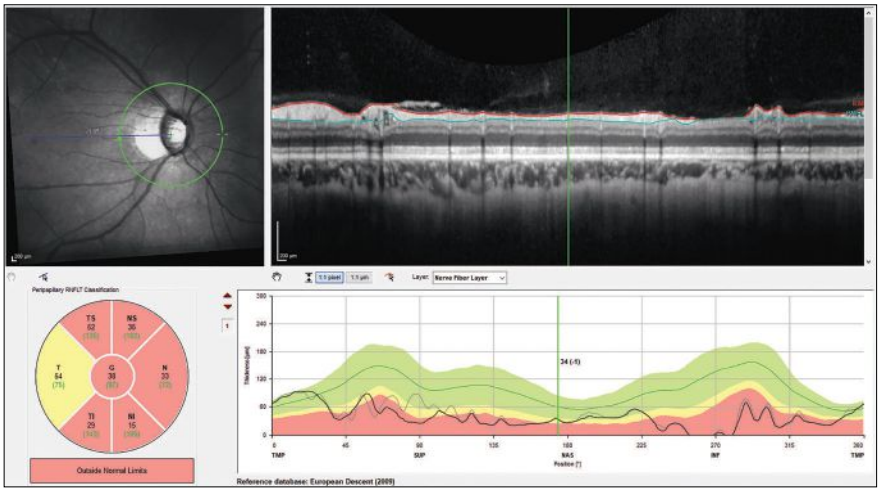

Figure 3. High myopia segmentation artifact in patient with a schisis cavity in the nerve fiber layer. These cavities make the RNFL appear normal in thickness.

caution, because what might appear as a normal nerve fiber layer may be artificially normal since it's not made up of tissue but made up of fluid. Therefore, the results of the OCT have to correlate with the visual field in patients with uveitis.

"The correlation there is that sometimes treatment of uveitis causes the edema to decrease, making it appear as if the glaucoma is getting much worse because the tissue wears out," continues Dr. Asrani. "Additionally, there may be real glaucoma progression in uveitic glaucoma, but because there's active uveitis, the thinning of the tissue may not become apparent because of the swelling in the tissue.

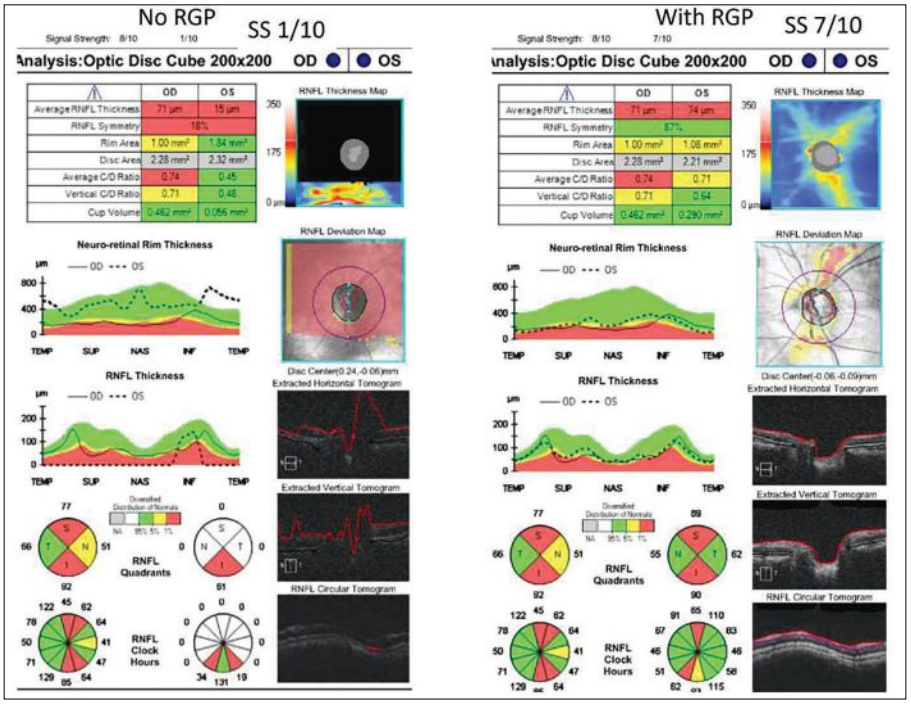

Figure 4. (Left) An OCT report of a patient with keratoconus without a rigid gas permeable lens. (Right) An OCT report of a patient with keratoconus with an RGP lens. Both reports were taken using a Cirrus OCT device. Without the lens, less light can travel through the eye, resulting in missing data in the RNFL Thickness Map with a signal strength of 1/10. With the lens, no missing data was identified, and the signal strength was 7/10.

"One of the most common artifactual conditions is high myopia, because the nerve is tilted, the retina is stretched and there may be a staphyloma," continues Dr. Asrani. "Any of these conditions will cause the OCT to have artifactual results. The other thing is retinal pathologies such as a focal scar in the retina. That can cause nerve fiber layer loss. Also, severe hypertension can cause patients to develop multiple cotton wool spots. When these spots resolve, they result in a nerve fiber layer defect, and it looks like the patient's glaucoma got worse.

"There are diseases that do masquerade as glaucoma, and they look exactly like glaucoma on an OCT when they're actually neurological conditions," adds Dr. Asrani. "So, these masqueraders need to be kept in mind, because you could be missing a life-threatening condition."

Besides preexisting conditions, there are implants that can skew a glaucoma diagnosis. Dr. Shen conducted a study comparing artifacts in patients with a KPro implanted in one eye alongside patients without keratoprosthetics. All patients in the study had similar glaucoma progression. Through their findings, Dr. Shen and her colleagues discovered how KPro impedes the signal strength of the OCT. "Sometimes, in terms of signal strength, we have eyes that allow less light to travel back to the OCT device, such as a KPro implant that might be blocking that," she says. "Since it's a smaller optic, all the light has to shine through that small optic to image the back of the eye."

Conversely, contact lenses can correct artifacts even in patients with high comorbidities and preexisting conditions. "For example, take a patient with keratoconus," explains Dr. Shen. "If they look around and the cornea doesn't focus the light, then light from the OCT can't be focused; the signal strength is only 1 out of 10 [for the Cirrus]. However, these patients often walk around with a rigid gas permeable contact lens. Usually, the thought is that you want to take their contacts out or basically anything that's blocking the eye to get the best image, but for these patients they should be wearing the contact lens for the imaging because it helps focus the light. It has also been helpful with high myopic contact lens users. Sometimes it helps a bit more in terms of how far you're focusing with the OCT image, because these patients' axial lengths are very different than normal." (*Figure 4*)

OCT devices have given clinicians the power to make more accurate glaucoma diagnoses, and they should take advantage of all the information an OCT report provides. "It's vital that we take the time to review the raw images off the OCT scans," says Dr. Asrani. "Otherwise, we're doing a disservice to our patients. This is the only way we can confirm that the artifacts aren't present. Therefore, be sure to give enough attention to the OCT results." ◀

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Navigating Narrow Angles

An expert reviews practice patterns and shares useful AS-OCT landmarks for diagnosis.

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When it comes to treating narrow angles, the recommendations have changed over the last few years. Today, observation is a reasonable option to consider for primary angle-closure suspects (PAC-S) in addition to prophylactic laser peripheral iridotomies, and clear lens extraction is more widely accepted for treating primary angle-closure (PAC) and primary angle-closure glaucoma (PACG).

Timely diagnosis of narrow angles is crucial. Common risk factors for primary angle closure, according to the Academy's *Preferred Practice Pattern*,[1] include Asian descent, hyperopia, older age, female sex, short axial length, thick and anteriorly positioned crystalline lens. Darkroom gonioscopy should always be performed to verify the diagnosis of PAC and monitor response to treatment. Ultrasound biomicroscopy and anterior segment optical coherence tomography are useful for diagnosing angle closure.

Here, I'll review two trials that have shaped our approach to primary angle closure treatment and discuss key anterior segment optical coherence tomography parameters and landmarks to aid diagnosis.

Shaping Practice Patterns

Here's an overview of the studies behind these changes:

The Zhongshan Angle-Closure Prevention (ZAP) Trial[2] was conducted in 889 Chinese primary angle-closure suspect patients in 2019. In each patient, one eye received a peripheral iridotomy under the superior lid and the other eye was observed. Because of concerns for safety, these patients were tightly monitored and treated if any evidence of peripheral anterior synechiae, elevation of intraocular pressure, or other symptoms of angle closure were observed. In clinical practice, one might be a little more permissive than ZAP's primary endpoints, which included IOP >24 mmHg at two visits, one clock hour of PAS in any quadrant, or an episode of acute angle closure. Secondary endpoints included visual acuity, IOP, total angle width on gonioscopy, limbal anterior chamber depth and adverse events with LPI or on follow-up.

This study's population had several interesting, but not unexpected, baseline characteristics. Eighty-three percent of patients started with four quadrants of closure. The average axial length was 22.5 mm. Most patients had mild hyperopia.

Interestingly, no benefit of either LPI or observation was seen at three years. Because ZAP subjects didn't reach primary endpoints in the initial 36 month timeframe, the trial was extended out to 72 months to determine a difference between LPI and observation. This tells us that it's safe to watch primary angle-closure suspects, as long as they have access to care and are able to report problems.

At six years, iridotomy resulted in a 50-percent reduction in relative risk for conversion to primary angle closure with 2 percent (19/889 eyes) of the LPI group and 4 percent (36/889 eyes) of the control group reaching a primary endpoint. Only four cases (0.4 percent) of acute angle closure in three patients were observed in the entire study. One case was bilateral, so that patient was likely predisposed in some way to acute angle closure as both the treated and untreated eye were affected. Six participants (1 percent) of the LPI group experienced a pressure spike of >30 mmHg after the procedure that resolved. Much more steroid was used in this trial than is typically used in U.S. clinical practice—dexamethasone 0.1% hourly x 24 hours, then q.i.d. for one week

Definitions

Irido-trabecular contact of 180 degrees +	IOP	Nerve	Symptoms	Treatment?
Primary Angle-Closure Suspect				Observation vs. LPI
Primary Angle Closure	+	+	+/-	LPI vs. Cataract
Primary Angle-Closure Glaucoma	+	+	+/-	LPI vs. Cataract vs. Filter *AACG: maybe Cataract*

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.

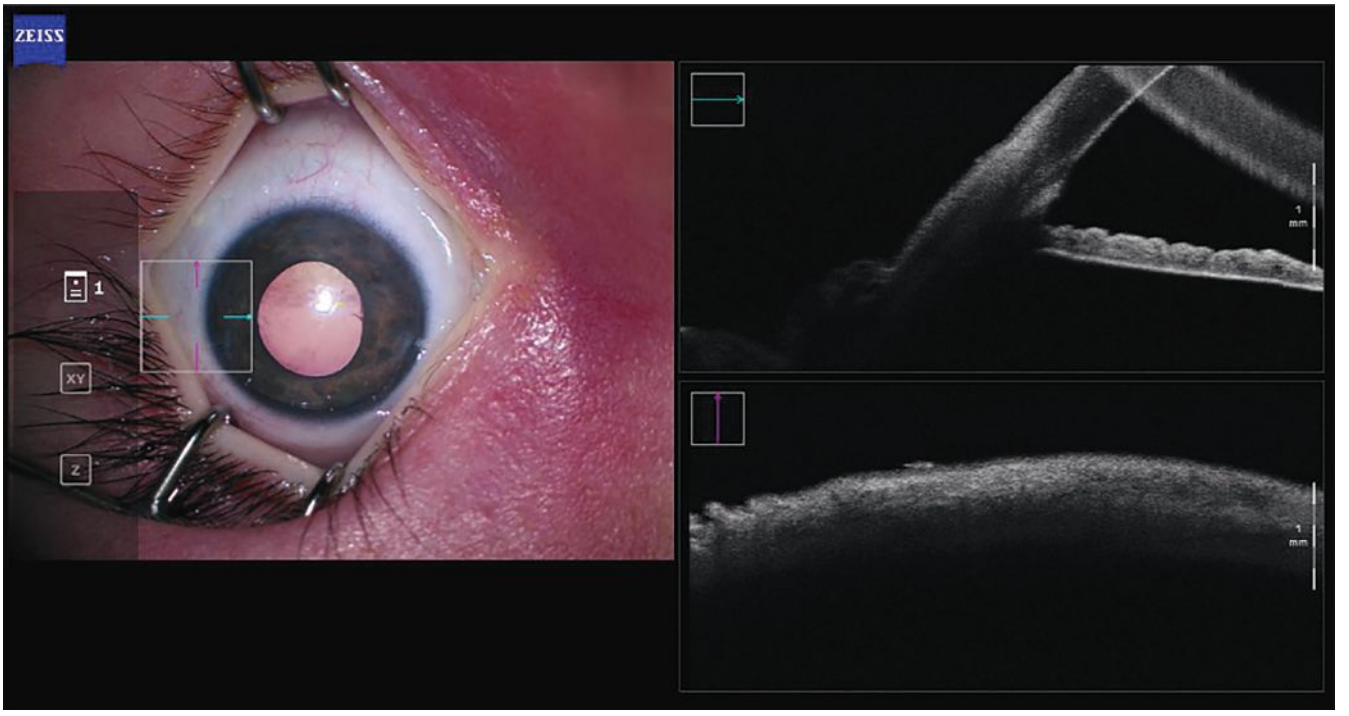

Figure 1A. An intraoperative AS-OCT image of the native angle of a pediatric patient with Sturge-Weber syndrome. Pre-goniotomy, both BELL and the trabecular meshwork are visible.

postop.

The findings from ZAP demonstrated that LPI decreased the relative risk of angle closure by half, but because the absolute risk of progression to primary angle closure was exceedingly small (4 percent), the authors concluded that, in a Chinese population, it isn't justifiable to perform LPI in all primary angle-closure suspects. This trial demonstrated that narrow angles don't change as quickly or as drastically as we once thought. Observation should now be considered an alternative to LPI for primary angle-closure suspects who have access to care. Nevertheless, LPI has prophylactic advantages in reducing the risk for and/or preventing acute angle closure crisis.

The EAGLE Trial[3] was conducted at 30 eye hospitals in five countries. Participants were 15 years and older, didn't have visually significant cataracts, and were newly diagnosed with primary angle closure (IOP >30 mmHg) or frank primary angle-closure glaucoma (IOP >21 mmHg and demonstrable visual field or optic nerve changes). Both clear lens extraction (n=208) and LPI (n=211) groups were similar, with 30 percent Chinese ethnicity; approximately 40 percent primary angle closure and 60 percent primary angle-closure glaucoma; a mean baseline IOP of 30 mmHg and a mean axial length of 22.5 mm.

Unlike ZAP, this trial didn't differentiate between appositional and synechial closure, so there wasn't a good baseline reference of who actually had PAS vs. appositional closure that could be opened up with compression or intervention. But because the EAGLE group had higher baseline pressures and the population skewed more toward primary angle-closure glaucoma, we might assume there was greater PAS burden at baseline in this population.

This study is notable for its inclusion of a quality-of-life questionnaire as a primary endpoint in a glaucoma study—the European Quality of Life 5-Dimensional Questionnaire (EQ-5D), which includes mobility, self-care, usual activity, pain or discomfort, and anxiety or depression. This study was among the first major trials in glaucoma to include this, with LiGHT being the other notable one. IOP was the other primary endpoint.

The questionnaire scores and IOP significantly favored clear lens extraction at 36 months. (Coincidentally, this is likely why ZAP chose a 36-month primary endpoint.) The EAGLE subgroups that reached statistical significance for both of these endpoints were Chinese ethnicity, primary angle-closure glaucoma, and worse baseline visual acuity. Secondary endpoints achieving statistical significance at 36 months were the NEI VFQ-25 and Glaucoma Utility Index scores, the number of medications (60 percent of the clear lens extraction group was on zero medications vs. 21 percent of the LPI group), and visual acuity.

Interestingly, the authors found that the need for additional glaucoma surgery was much lower in the clear lens extraction group than in the LPI group. Only one patient (0.4 percent) in the clear lens extraction group required trabeculectomy vs. 24 patients (11 percent) in the LPI group that required surgery to control pressures: 16 lens extractions

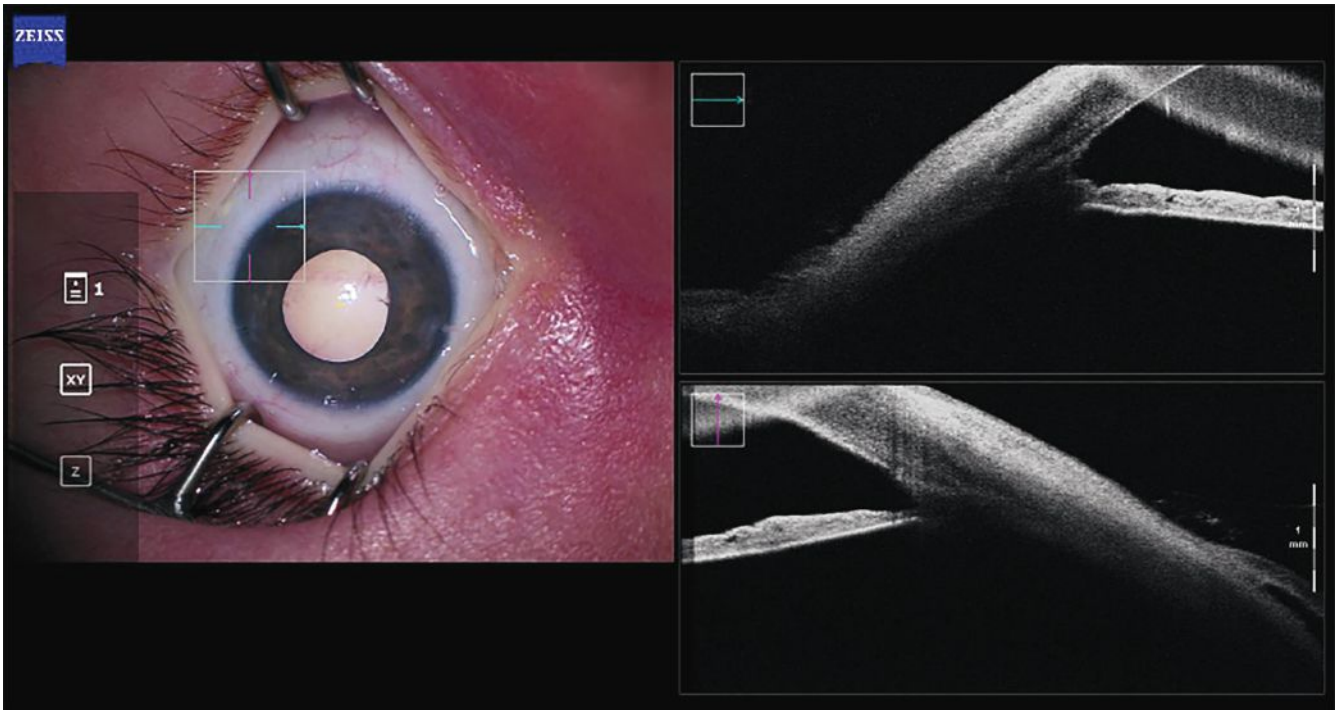

Figure 1B. An intraoperative AS-OCT image of the same patient, after goniotomy. BELL is visible, while the trabecular meshwork has been excised.

(performed for pressure control; phaco for visually significant cataracts was excluded); six trabeculectomies; one iStent and one tube shunt.

Ultimately, the EAGLE study found that initial clear lens extraction was superior to LPI in primary angle closure or primary angle-closure glaucoma. It also identified a reduced need for further medical and surgical intervention to control IOP in the clear lens extraction group as well as improved quality-of-life measures. The only disadvantage was cost. Over the 36-month time period the group analyzed, clear lens extraction wasn't deemed as cost-effective. However, when the authors modeled it out over a longer period of time on a population-based level, they found that clear lens extraction was more cost-effective than leaving patients with LPIs alone.

Based on these two studies, primary angle-closure suspects can be observed as an alternative to an LPI, and clear lens extraction may be considered for managing primary angle closure and primary angle-closure glaucoma.

Anterior Chamber Parameters

AS-OCT is able to detect narrow angles much earlier than we're able to in the clinic. Though UBM and AS-OCT devices use different technology, may of the parameters used to analyze the anterior chamber are the same. There are three categories that these parameters fall into:

1. Linear parameters such as angle opening distance (AOD), irido-trabecular contact (ITC) and anterior chamber depth (ACD);
2. Two-dimensional parameters, such as trabecular iris space area (TISA); and
3. Experimental three-dimensional parameters such as trabecular iris circumference volume (TICV), which is an integrated 360-degree measurement of TISA.

The scleral spur landmark is a key reference point for defining several of these parameters. ITC, TISA and TICV are all defined at a set distance—500 µm/750 µm—from the scleral spur landmark. While the scleral spur landmark position currently needs to be manually confirmed, several companies are working toward accurate, automated identification of it.

But what are the thresholds for each of these parameters for detecting open or closed angles? To answer this question, my colleagues and I conducted a study in 2016 to validate AS-OCT parameters.[4] We compiled images from four prospective studies (n=189 eyes), including gonioscopically confirmed open or narrow-angle patients and evaluated Youden optimal threshold values for each parameter using a training set with three random sets of 40 eyes each. We repeated this process 500 times per set and then applied optimal thresholds to a testing data set after a boot-strapping procedure to ensure accuracy. In total, 69 samples were tested to evaluate each parameter for sensitivity, specificity and kappa agreement between observers.

We evaluated AOD (mm) and TISA (mm^2) at 500 µm and 750 µm from the SSL at each of the four quadrants; TICV (µL) at 500 µm and 750 µm; ITC length (mm) at each of the four quadrants; extent of ITC

(degrees); and ITC area (mm^2). All of the absolute values of the parameters we assessed were able to distinguish between open and narrow angles (all $p<0.001$). However, nine parameters had very high sensitivities with no false negatives. These included:

- AOD500 @ temporal
- AOD500 @ nasal
- AOD500 @ inferior
- AOD750 @ nasal
- AOD750 @ inferior
- TISA500 @inferior
- TISA750 @ inferior
- TICV500
- TICV750

Overall, the best agreement with the gonioscopy (highest kappa) was the linear measurement AOD750 inferiorly (0.91), followed by the three-dimensional TICV500/750 (0.86). The fewest angle misclassifications also occurred with those same two parameters: AOD750 inferiorly (3) and TICV500/750 (5, 5). All were false positives, meaning that the angles were mistakenly classified as narrow rather than open. AOD750 is a parameter available on any UBM or AS-OCT model. The least accurate parameter was ITC length.

A New Gonio Landmark

While looking through reference data images, my colleagues and I realized that many studies were lumping in a landmark on AS-OCT with the trabecular meshwork that we in our group called the trabecular meshwork shadow. Seen on AS-OCT, it appears to cup the trabecular meshwork and run into Schwalbe's line at the insertion of the cornea. We delved deeper to find out what it was and how often it's visible on imaging.[5]

We retrospectively reviewed 303 angles of 153 horizontal images from two-dimensional angle analysis scans (Cassia SS-1000). (The mean participant age was 51.5 years, and 64 percent of patients were female, and 66 percent of patients were white.) AS-OCT images were evaluated by masked readers. We used logistic regression to analyze several potential influential factors including age, sex, race, intraocular pressure, gonioscopy grade, angle location and history or presence of surgery on the visibility of the trabecular meshwork structures.

The trabecular meshwork was found in 73 percent (220) of angles and Schlemm's canal was seen in 40 percent (120) of angles. The outer border of our mystery landmark, which we termed Band of Extracanalicular Lamina (BELL), after Nicholas P. Bell, MD who figured out the surgical correlate, was observed in 95 percent (288) of angles.

We believe that BELL represents a surgical landmark used in performing surgery for congenital glaucoma or traditional canaloplasty in an adult. In these procedures, you must cut down and dissect very deeply into the sclera. As you approach the limbus overlying Schlemm's canal, there's a compressed band of scleral fibers. These highly uniform, compressed fibers reflect light differently than the surrounding tissue on AS-OCT. BELL is visible on AS-OCT, gross pathology and histopathology staining.

The outer border of BELL was more visible in white patients than Asian patients ($p=0.02$), and in eyes with a Spaeth goniotomy grade of E vs. A ($p=0.02$). The trabecular meshwork and Schlemm's canal were more visible in temporal angles (81 percent and 49 percent, respectively) than in nasal angles (64 percent and 30 percent, respectively; both $p=0.001$). Schlemm's canal was more visible in open angles (43 percent) than narrow angles (27 percent; $p=0.02$). We verified each of these structures in a pathologic sample from enucleated eyes.

One of the challenges with UBM and AS-OCT is that the scleral spur landmark must be identified and confirmed manually each time and being a few pixels off can mean the difference between an open or a closed angle. We found that even when the scleral spur landmark or the trabecular meshwork aren't apparent, we can almost always see the outer edge of BELL. From this landmark, we can qualitatively extrapolate where the trabecular meshwork is as well as its relationship to the iris. BELL provides a quick, qualitative sense of the angle anatomy.

In 2015, Mani Baskaran, MD, of the Singapore Eye Research Institute, and colleagues demonstrated in a prospective study that baseline AS-OCT predicts gonioscopic closure, where narrower angles on AS-OCT were associated with an increased likelihood of progressing clinically at four years.[6] In the risk stratification, they found that 41 percent of patients with four quadrants of closure on AS-OCT at baseline, despite being open on gonioscopy, progressed to gonioscopic closure in four years. For patients who had only one quadrant of closure on AS-OCT, just 5 percent progressed to clinical closure on gonioscopy in the same time frame.

In the clinic, if you can't do gonioscopy on a patient for whatever reason, BELL can be used to help qualitatively figure out whether the patient's angle is narrow or open. This landmark could have future utility in population-based screening for narrow angles. ◀

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REVIEW of OPHTHALMOLOGY

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PRODUCT NEWS

Devices and drugs to improve patient care and strengthen your practice.

GLAUCOMA

The Eagle Has Landed

If you're interested in widening the array of glaucoma treatments available at your practice, a new laser may be worth a look.

The FDA recently approved the Belkin Vision Eagle, a Q-switched, 532 nm-wavelength, frequency-doubled Nd:YAG laser for selective laser trabeculoplasty.

The company says the Eagle is the first and only contactless laser for glaucoma, providing an automated and non-invasive solution for performing SLT.

The company says the Eagle has several unique features. First, the laser energy is delivered in a non-contact procedure directly through the limbus to the trabecular meshwork without the need for the use of a gonioscopy lens. In addition, the device automatically defines the target location then applies the laser treatment sequence while the eye tracker compensates for any eye movement.

For more information on the Eagle, visit belkin-vision.com.

OCULAR SURFACE THERAPY

Rooting Out Dry Eye

If you're looking to target different mechanisms of dry eye, Lumenis says its new device, OptiPlus, is a complementary device to its OptiLight technology, and is the first dual frequency radiofrequency device on the market.

While OptiLight relies on a pioneering light-based

technology to target inflammation due to meibomian gland dysfunction, the company says OptiPlus is a dedicated device that employs a RF energy to enhance clinical results. The dual-frequency RF technology enables energy penetration to different skin depths, heating the superficial layer to promote collagen formation and stimulate periorbital skin rejuvenation while also reaching into the deeper tissue to target the meibomian glands, the company says. By delivering heat across different tissue layers, Lumenis says the device increases blood circulation to "promote medical performance and aesthetic results."

For more information, visit https://information.lumenis.com/optilight.

REFRACTION TECH

Free Yourself

PlenOptika has rolled out a new portable autorefrator, the QuickSee Free.

The company says the device combines an open-view design, wavefront aberrometry and innovative measurement algorithms to produce clinically accurate autorefraction in clinics and in the field. There's also a QuickSee Free Pro available for surgical applications and contact lens fitting.

The PlenOptika Wavefront Refraction Engine precisely determines low-order refractive errors, making QuickSee Free as accurate as a desktop autorefractor, the company says.

For information, visit plenoptika.com/quicksee-free.

Transscleral Capsular Bag Stabilization Studied

While flanged iris hooks have been used off-label for capsular bag stabilization and IOL centration in complicated cases of cataract surgery in previous reports, scientists wrote of a lack of data on the optimal flange technique of iris hooks made from different materials. They aimed to assess the flange properties of different iris hooks, as part of a masked laboratory study.

The flanging properties of four different iris hooks made from polypropylene, elastic polymer and nylon were investigated with different heating distances and both with and without forceps gripping. The maximum diameter of the flanges was measured, and the shape of the flanges was evaluated.

While the flange diameters of both nylon and elastic polymer iris hooks were too-small flange diameters for intrascleral fixation, polypropylene iris hooks had a sufficient flange diameter (>330 µm) and mushroom-like shape. Furthermore, in polypropylene hooks, heating distance was directly proportional to flange diameter.

Scientists wrote that the findings suggested that only polypropylene iris hooks were suitable for flanged intrascleral fixation, which is off-label, to secure adequate fixation.

J Cataract Refract Surg 2023; Nov 23. [Epub ahead of print].
Schlatter A, Kronschläger M, Ruiss M, et al.

Days of the Week and IOP

Researchers in Japan analyzed intraocular pressure by day of the week using a "mega database" to reveal weekly patterns. They evaluated annual health checkup examinees between April 2014 and March 2015. A total of 655,818 participants (51.5 ±10.5 [range, 20 to 96] years; 40.1 percent women]) from 103 medical centers were included.

IOP was measured using a non-contact tonometer. Mean IOPs of each day of the week were compared using multiple comparison tests and multiple linear regression analysis. Wednesday was set as the reference. Weekly IOP variations stratified by sex and age were also evaluated.

Here are some of the findings:

- Mean IOPs from Monday to Sunday were: 13.19 ±2.97, 13.06 ±2.92, 13.05 ±2.91, 13.05 ±2.92, 13.12 ±2.94, 13.10 ±2.96 and 13.16±2.78 mmHg.
- IOPs were significantly higher on Monday, Friday and Saturday than those on Wednesday ($p<0.001$; $p<0.001$; and $p=0.002$).
- After adjusting for factors affecting IOP, IOPs on Monday and Saturday (β=0.097; CI. 0.074 to 0.121; $p<0.001$) were higher than those on Wednesday (β=0.032; CI, 0.005 to 0.059; $p=0.019$).
- Men had significantly higher IOPs on Monday and Saturday than on Wednesday (β=0.142; CI, 0.110 to 0.173; $p<0.001$; β=0.053; CI, 0.017 to 0.089; $p=0.004$), although women didn't have a significant trend.
- Participants ages <65 years had higher IOPs on Monday ($p<0.001$ for under 60 years; $p=0.003$ for 60 to 64 years) while those ages ≥65 years didn't ($p=0.856$).

Researchers wrote that IOP values may have a periodic weekly pattern with high IOPs on Monday more pronounced in men ages <65 years.

J Glaucoma. 2023 Nov 3. [Epub ahead of print].
Terauchi R, Wada T, Fukai K, et al.

Postural Blood Pressure's Association with POAG

Researchers evaluated whether primary open-angle glaucoma patients demonstrated abnormal postural blood pressure response to recumbency and whether such a response correlated with glaucoma severity.

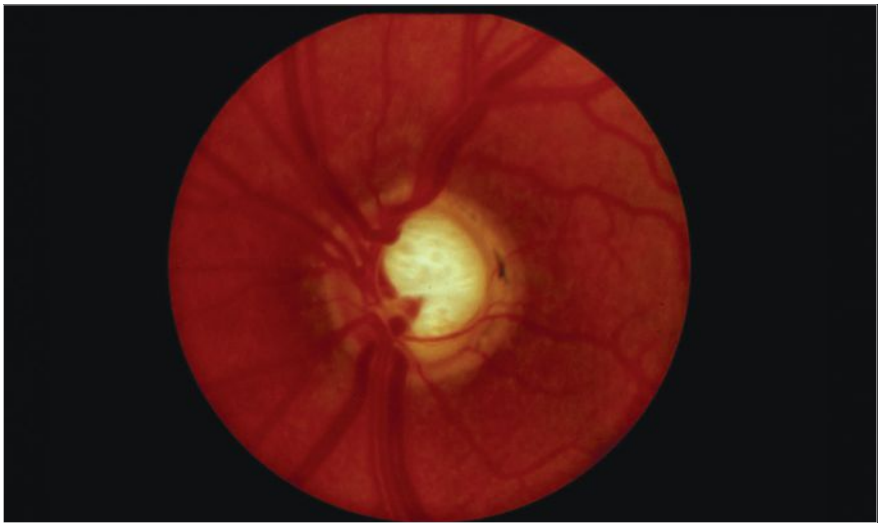
This prospective observational study included 47 POAG patients who underwent intraocular pressure; and systemic arterial (SABP), systolic (SBP) and diastolic (DBP) blood pressure measurements in seated positions and after twenty-minute recumbency positions. Mean arterial blood pressure (MABP) was calculated for seated and recumbent positions. The percentage difference between seated and recumbent SBP, DBP and MABP was calculated according to which participants were divided into three groups:

- non-dippers (percentage dips of <10 percent);
- normal dippers (percentage dips of ≥10 percent ≤20 percent); and
- exaggerated dippers (percentage dips of >20 percent).

Participants underwent optical coherence tomography of optic nerve head to measure retinal nerve fiber layer thickness, which was used as a structural biomarker of glaucoma.

Here are some of the findings:

- RNFL thickness was lower in exaggerated dippers than non-dippers and normal dippers.
- A negative correlation was



Researchers say that assessing patients' blood-pressure response to lying down vs. sitting may be a simple way to evaluate their risk for primary open-angle glaucoma.

found between postural dip and average RNFL thickness.

- Linear regression showed that postural dip was associated with lower RNFL thickness independent of age and IOP.
- Chi-square independence tests demonstrated a strong relationship between corresponding dip groups for SBP, DBP and MABP. However, it showed no significant relation between hypertension and postural dip.
- Fisher's exact test showed no relation between anti-hypertensive medication and postural dips.

POAG patients demonstrated abnormal postural blood pressure response and exaggerated recumbent dips, which was positively correlated with disease severity. Researchers wrote that postural dip assessments may serve as a simple clinic-based test of systemic vascular dysregulation as part of glaucoma risk evaluation.

J Glaucoma 2023; Nov 28. [Epub ahead of print].
Ameen Ismail A, Sadek SH, Kamal MA, et al.

Utility of Widefield OCTA for Detecting RNV in PDR

Investigators assessed the real-world clinical utility of widefield OCTA for detecting retinal neovascularization in eyes with proliferative diabetic retinopathy, as part of a retrospective cross-sectional study.

They looked at consecutive eyes clinically suspected of PDR by physicians at a tertiary eye center between March 2021 and November 2022.

All eyes underwent ultra-widefield fluorescein angiography (Optos California) and widefield OCTA (Canon S1) with a 23 × 20 mm scan area. Two independent graders detected individual RNV lesions using UWF-FA and used them as the ground truth. Widefield OCTA images were first evaluated to determine whether the images successfully illustrated retinal vasculature, regardless of the image quality index or the presence of vitreous hemorrhage. The graders then identified the RNV lesions with widefield OCTA. Investigators detected RNV by utilizing the whole retinal slab, including flow signals in the retina, and the custom vitreoretinal interface slab, defined as flow signals from 20 microns below the internal limiting membrane to 2,000 µm above the ILM. They evaluated the applicability to real-world clinical practice by not correcting segmentation errors.

Main outcome measures included the success rate of imaging and the detection rate of RNV using WF-OCTA.

Sixty-nine consecutive patients who underwent UWF-FA were identified. Of these, 114 eyes from 57 (83 percent) patients underwent both UWF-FA and widefield OCTA. Of the 114 eyes, 108 (95 percent) produced gradable widefield OCTA images. Here are some of the findings:

- Using UWF-FA, the graders identified 175 RNV lesions in 40 eyes.
- Widefield OCTA had a sensitivity of 95 percent and specificity of 88 percent for detecting eyes with RNV.
- At the level of individual RNV lesions, graders detected 156 RNV lesions with widefield OCTA, with 118 of these confirmed by UWF-FA (true positive).
- Among the 57 false negative lesions, the primary causes were being out of the scan range (26 lesions) and segmentation errors (21 lesions).

Investigators reported that widefield OCTA imaging had a high success rate for detecting eyes with retinal neovascularization in a real-world clinical setting. Despite a 67 percent detection rate for individual retinal neovascularization lesions, they suggested that the imaging modality may serve as a valuable non-invasive method for detecting retinal neovascularization detection in eyes with diabetic retinopathy.

Ophthalmol Retina 2023; Nov 24. [Epub ahead of print].
Hamada M, Hirai K, Wakabayashi T, et al.

Optic Disc Drusen in RP

Researchers wrote that studies of patients with retinitis pigmentosa have reported an increased prevalence of optic disc drusen (ODD) compared with ODD prevalence in the general population. They added that the diagnostic gold standard method for identifying ODD is enhanced-depth imaging optical coherence tomogra-

phy (EDI-OCT) but that the modality hasn't previously been used systematically for identifying ODD in patients with RP. This study aimed to estimate the prevalence of ODD in patients with RP using EDI-OCT.

In this cross-sectional study, 40 patients with clinically diagnosed RP, ages 18 or older were included. All patients underwent an ophthalmic exam, including kinetic perimetry, EDI-OCT of the optic nerve head and fundus photography. Genetic testing with a next-generation sequencing panel of retinal dystrophy genes was performed on the RP patients without a prior genetic diagnosis. Here are some of the findings:

- Twelve patients (30 percent) had at least one ODD.
- Six patients had bilateral ODD.
- No significant differences between patients with and without ODD were found according to age, refraction, best-corrected visual acuity, Bruch's membrane opening or visual field.
- The genetic variation causing RP was found in 11 of 12 cases in the ODD group, and in 17 of 28 cases in the group without ODD.

Researchers say the prevalence of ODD in patients with RP was 15 times higher than in the general population and much higher than previously estimated, potentially indicating that the two conditions might be pathogenically related.

J Neuroophthalmol 2023; Nov 17. [Epub ahead of print].
Steensberg AH, Schmidt DC, Malmqvist L, et al.

Angle Kappa and Power Calcs

Scientists evaluated the effect of ocular biomechanics on the prediction error of IOL power calculation in an ophthalmology department at Centro Hospitalar Universitário do Porto in Portugal, as part of a prospective longitudinal study.

Before cataract surgery, the subjects underwent biometry with IOL Master 700 (Zeiss) and biomechanical analysis with Corvis Scheimpflug Technology (Oculus). The targeted spherical equivalent was calculated with SRK-T and Barrett Universal II.

This study included 67 subjects. Here are some of the findings:

- Using the SRKT formula, an association was found between:
  – PE and Corvis Biomechanical Index (CBI, B=-0.531; p=0.011); and
  – AE and the horizontal offset between the center of the pupil and the visual axis (angle kappa, B=-0.274; p=0.007).
- Using the Barrett Universal II formula:
  – PE was independently associated with anterior chamber depth (B=-0.279; p=0.021); and
  – CBI (B=-0.520; p=0.013) and AE were associated with angle kappa (B=-0.370, p=0.007).

Scientists concluded that a large angle kappa may reduce the predictability of IOL power calculation and that ocular biomechanics likely influence the refractive outcomes after IOL implantation. They added that eyes with softer corneal biomechanics had more myopic prediction error, which may relate to anteriorization of the effective lens position, and suggested that dynamic measurements may pave the way for future formulas.

J Cataract Refract Surg 2023; Nov 13. [Epub ahead of print].
Marques JH, Baptista PM, Ribeiro B, et al.

OCT/OCTA for Tracking Glaucoma Progression

Researchers examined event-based glaucoma progression using optical coherence tomography and OCT angiography, as part of a retrospective study.

Glaucoma eyes with ≥two- and four-visits with OCT/OCTA imaging were included. Peripapillary capillary density (CD) and retinal nerve fiber layer thickness were obtained from 4.5 × 4.5 mm optic nerve head scans. Event-based OCT/OCTA progression was defined as decreases in ONH measurements exceeding test-retest variability on ≥two consecutive visits. Visual field progression was defined as significant VF mean deviation worsening rates on ≥two consecutive visits.

Here are some of the findings:

- Among 147 eyes (89 participants), OCTA identified 33 progressors (22 percent) and OCT identified 25 progressors (17 percent).
- They showed slight agreement (κ=0.06), with 7 eyes (5 percent) categorized as progressors by both.
- When incorporating both instruments, the rate of progressors identified increased to 34 percent.
- Similar agreement was observed in diagnosis- and severity-stratified analyses (κ<0.10).
- Compared to progressors identified only by OCT, progressors identified only by OCTA tended to have thinner baseline RNFL and worse baseline VF.
- VF progression was identified in 11 eyes (7 percent).
- OCT and VF showed fair agreement (κ=0.26), with six eyes (4 percent) categorized as progressors by both.
- OCTA and VF showed slight agreement (κ=0.08), with four eyes (3 percent) categorized as progressors by both.

Researchers found that OCT and OCTA showed limited agreement on event-based progression detection, with OCT showing better agreement with visual field. Researchers concluded that OCT and OCTA may provide valuable, yet different and complementary, information about glaucoma progression. ◀

Eye (Lond) 2023; Nov 11. [Epub ahead of print].
Wu JH, Moghimi S, Nishida T, et al.

A man is referred to Wills Eye Hospital for progressive vision loss over months after an injury to his right eye.

ERIC B. LEE, MD, AND CHRISTOPHER J. RAPUANO, MD
PHILADELPHIA

Presentation

A 52-year-old male with several months of decreasing vision in the right eye is referred to the Wills Eye cornea clinic. He was struck in the right eye by a tree branch while hiking five months prior, for which he was treated with antibiotic drops. After the initial healing, he noted a progressive decline in his vision. He denied any pain, redness, discharge or other ocular symptoms.

History

The patient had an ocular history notable for LASIK in both eyes more than 20 years ago. He also underwent a basal cell carcinoma excision of the left lower eyelid two weeks prior to presentation. Past medical history was only notable for hyperlipidemia, managed with rosuvastatin. Family history was non-contributory. The patient never smoked or used alcohol. Review of systems was unremarkable.

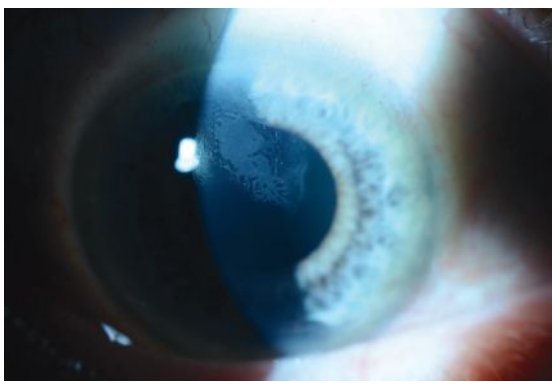


Figure 1. Slit lamp exam photograph of the patient's right eye showing a superior opacity extending from the superior LASIK flap edge.

Examination

At presentation, uncorrected visual acuity was 20/50 in the right eye and 20/60 in the left. His pupils were round and reactive in both eyes without an afferent pupillary defect in either eye. Intraocular pressures were 12 mmHg and 14 mmHg in the right and left eyes, respectively. Extraocular motility and confrontation visual fields were full bilaterally.

Slit lamp examination of the right eye revealed a 4 mm (width) by 3.7 mm (height) creamy-white opacity extending from the superior flap edge *(Figure 1)*. High magnification slit-beam view revealed the opacity was in the LASIK flap interface. There was no cleft at the LASIK flap edge. The remainder of the anterior exam of the right eye was unremarkable. Anterior segment examination of the left eye was notable for a well-healing lower lid excision with intact sutures in place, and a nasal-hinge LASIK flap well-positioned and without opacities. Topography of the right eye showed irregular astigmatism in the area of the corneal opacity *(Figure 2)*.

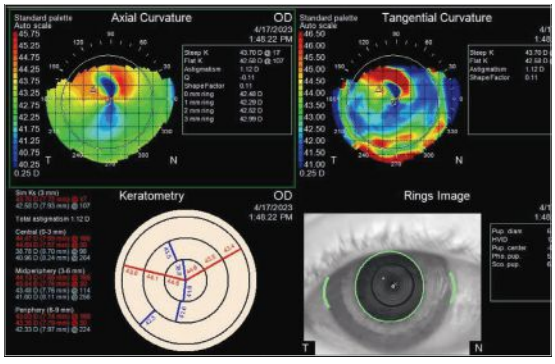


Figure 2. Topographic report of the right eye showing irregular astigmatism in the area of the corneal opacity.

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

Work-up, Diagnosis and Treatment

The differential diagnosis includes epithelial basement membrane dystrophy, epithelial ingrowth in the LASIK flap interface, diffuse lamellar keratitis and infectious keratitis. Given the patient's clinical history, unilaterality, slit lamp examination and otherwise quiet anterior segment exam, post-LASIK epithelial ingrowth (PLEI) secondary to flap-dislocation from recent trauma was the diagnosis. Given the extent of the epithelial ingrowth and progressive decreasing vision, treatment was recommended.

The patient underwent flap lift in the right eye with mechanical debridement of the ingrowth, followed by suturing of the flap edge. Histopathology of a surgical specimen demonstrated partially degenerated corneal epithelium compatible with epithelial ingrowth *(Figure 3)*. On postoperative day one, the patient's uncorrected visual acuity was 20/60 in the right eye. He started on besifloxacin four times daily and prednisolone acetate 1% four times daily for one week. At the patient's postoperative week one visit, the besifloxacin was stopped, and the prednisolone acetate 1% was tapered over the course of two weeks. His anterior segment exam remained stable with a well-positioned LASIK flap with no epithelial interface or stromal infiltrate and seven intact sutures in place *(Figure 4)*. The sutures were removed over two visits at postoperative months two and three. At postoperative month four, the patient's uncorrected visual acuity in the right eye was 20/30 -1. Anterior segment exam showed a well-positioned LASIK flap without epithelial cells centrally but with a few cells at the superior flap edge extending < 0.3 mm. At postoperative month six, the patient's uncorrected visual acuity was 20/30 +3 and his anterior segment exam was stable without changes.

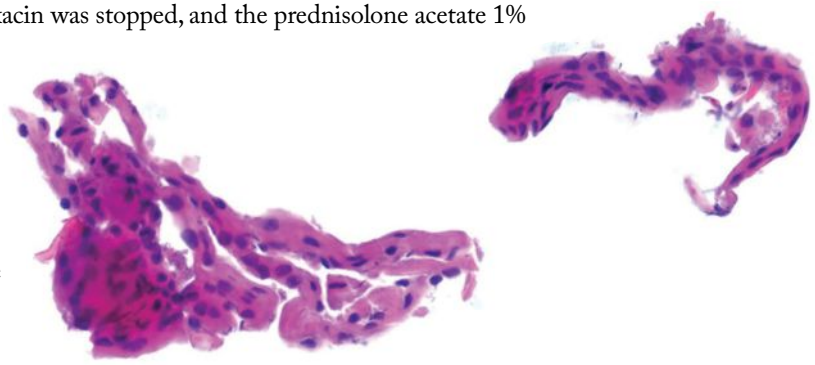


Figure 3. Histopathology of a surgical specimen from mechanical debridement of the lifted LASIK flap showing corneal epithelium compatible with epithelial ingrowth.

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Discussion

Post-LASIK epithelial ingrowth is a rare complication following LASIK surgery, with an incidence measuring between 0 to 3.9 percent.[1] Though most cases are generally detected within two months of surgery, rare cases of late-onset PLEI have been reported following traumatic injuries.[2,3] Risk factors for the development of PLEI can be broadly divided into modifiable and non-modifiable factors. Modifiable risk factors are largely related to operative technique and include surgical instrumentation, method of flap manipulation and conformation of the flap edge. Non-modifiable risk factors are less well-studied but may include patient factors such as age and diabetes status, type of refractive correction and flap lifts for retreatment.[1,4,5]

The management of PLEI can be guided using the Probst/Machat grading system, which considers the appearance and location of the epithelial ingrowth *(Table 1)*. Indications for treatment include decreased vision, often from irregular astigmatism, and damage to the LASIK flap. Damage can result from dense ingrowth impeding nutrients from getting to the flap causing injury ranging from punctate epitheliopathy to epithelial defect to flap melting. Grade 1 cases aren't visually significant, rarely progress and can be managed with observation. Grade 2 cases may slowly progress and eventually impact vision, warranting non-urgent treatment within weeks or months. Grades 3 and 4 cases often significantly impact vision and can rapidly progress, requiring urgent treatment.

When treatment is indicated, the most common and well-studied intervention is mechanical debridement. In studies with greater than 10 treated eyes, surgical debridement achieved uncorrected distance VA ≥ 20/60 in 74 to 80 percent of cases and ≥ 20/25 in 45 to 53 percent of cases, and corrected distance VA ≥ 20/60 in 78 to 91 percent of cases and VA ≥ 20/25 in 78 to 85 percent of cases.[1] During debridement, care is taken to scrape both the exposed stroma and the posterior side of the flap free of epithelial cells. Adjuvant ethanol, isopropyl alcohol, mitomycin C and excimer laser phototherapeutic keratectomy have all been described in various case studies, without statistically significant differences in outcomes.[2,7-9] At Wills, mechanical debridement without adjuvant therapy with or without suturing of the flap edge is the standard practice. Some cases of PLEI can also be treated with non-invasive neodymium:yttrium aluminum garnet (Nd:YAG) laser, though outcomes are less consistent compared to mechanical debridement.[10,11]

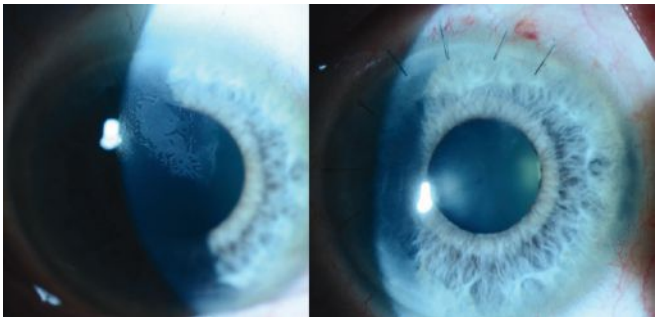

Figure 4. Slit lamp exam photographs of the patient's eye before (left) and one week after (right) mechanical debridement of epithelial ingrowth, showing resolution of the interface opacities.

In conclusion, PLEI is a rare but potentially visually significant complication following LASIK surgery that can present years after surgery, often in the setting of flap-lift LASIK enhancements and traumatic LASIK flap displacement. We describe a patient with months of gradual vision loss after a traumatic injury to his eye 20 years after LASIK surgery. Mechanical debridement with or without flap edge suturing remains the standard of care at Wills and often results in excellent outcomes. ◀

Grade	Exam	Progressive	Location	Management
I	Thin growth (1-2 cells), well-delineated demarcation line at advancing edge, no flap change	No	2 mm within flap edge	None required
II	Thicker growth, discrete cells within epithelial nest, no demarcation line, rolled or grey flap edge with no melt	Slowly	2 mm within flap edge	Non-urgent
III	Significant growth, opaque ingrowth, geographic areas of necrotic cells with no demarcation line, rolled flap edge with peripheral confluent haze	Yes	> 2 mm from flap edge	Urgent
IV	Aggressive growth, strands of epithelial cells invading visual axes, may have flap melt	Yes	Involving visual axes	Urgent

Table 1. Probst/Machat grading system for PLEI (adapted from Ting et. al., modified from Neff and Probst).[1,6]

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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.

Neovascular AMD

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

Intraocular Inflammation

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

Increased Intraocular Pressure

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

ADVERSE REACTIONS

Clinical Trials Experience

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

A total of 839 patients with GA in two Phase 3 studies (OAKS and DERBY) were treated with intravitreal SYFOVRE, 15 mg (0.1 mL of 150 mg/mL solution). Four hundred nineteen (419) of these patients were treated in the affected eye monthly and 420 were treated in the affected eye every other month. Four hundred seventeen (417) patients were assigned to sham.

The most common adverse reactions (≥5%) reported in patients receiving SYFOVRE were ocular discomfort, neovascular age-related macular degeneration, vitreous floaters, and conjunctival hemorrhage.

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

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

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

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

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

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

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

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

Lactation

Risk Summary

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

Females and Males of Reproductive Potential

Contraception

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

Pediatric Use

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

Geriatric Use

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

PATIENT COUNSELING INFORMATION

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

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

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

SYF-PI-17Feb2023-1.0

7/23 US-PEGGA-2200163 v3.0

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

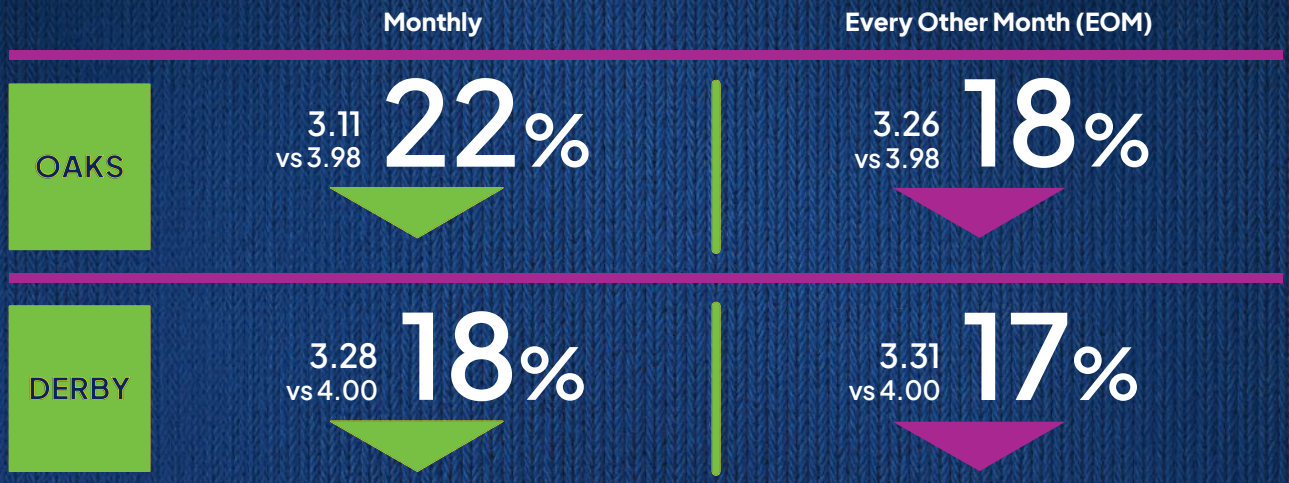
CONTRAINDICATIONS

- 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.
- **Neovascular AMD**
  - In clinical trials, use of SYFOVRE was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (12% when administered monthly, 7% when administered every other month and 3% in the control group) by Month 24. Patients receiving SYFOVRE should be monitored for signs of neovascular AMD. In case anti-Vascular Endothelial Growth Factor (anti-VEGF) is required, it should be given separately from SYFOVRE administration.
- **Intraocular Inflammation**
  - In clinical trials, use of SYFOVRE was associated with episodes of intraocular inflammation including: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, and anterior chamber flare. After inflammation resolves, patients may resume treatment with SYFOVRE.

SYFOVRE achieved continuous reductions in mean lesion growth rate* (mm^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)

- **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

iStent infinite®

Go with the Flow

Give patients with glaucoma who have failed prior medical and surgical intervention a powerful new direction with iStent infinite®—a first-of-its-kind **standalone** implantable alternative designed to deliver **up to 8 clock hours (240°)** of outflow coverage while minimizing tissue disruption.[1]

The interventional glaucoma revolution is here.

REFERENCE:

1. Sarkisian SR Jr, Grover DS, Gallardo M, et al; iStent infinite Study Group. Effectiveness and safety of iStent infinite trabecular micro-bypass for uncontrolled glaucoma. *J Glaucoma.* 2023;32(1):9-18.

iStent infinite® IMPORTANT SAFETY INFORMATION

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

PM-US-0908

GLAUKOS®