Wills Eye Resident Series: A case of fluctuating vision in a young patient, *p. 63*

REVIEW of OPHTHALMOLOGY®

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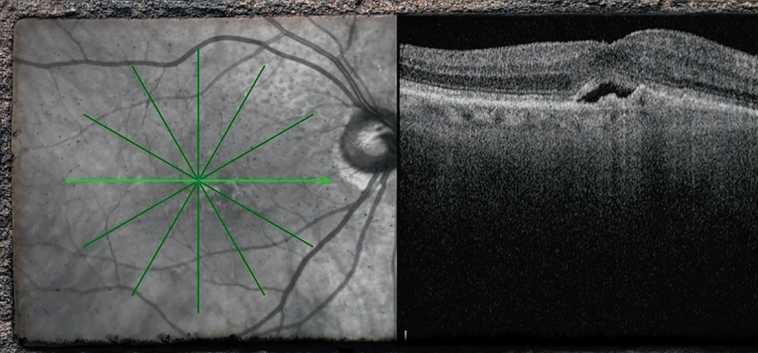
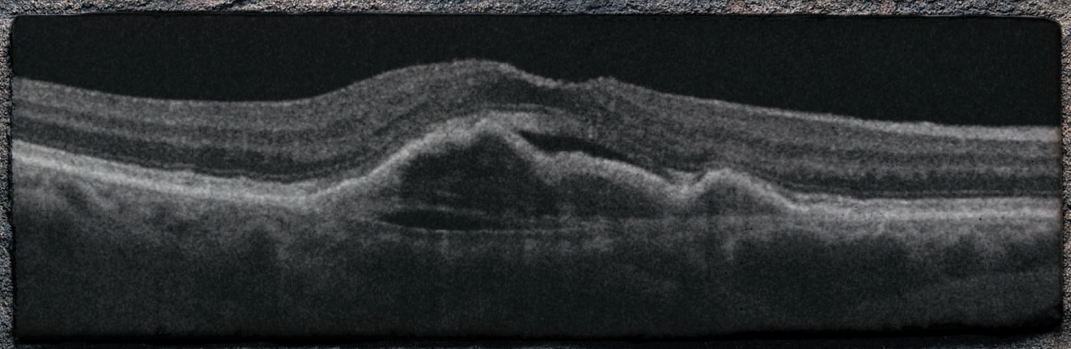
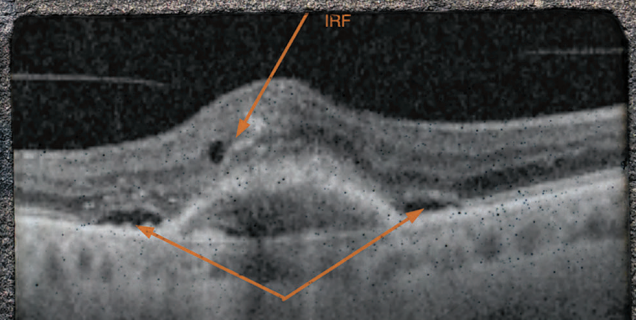
WHEN YOUR AMD TREATMENT HITS A WALL

Experts weigh in on how to deal with treatment resistance in wet AMD. **P. 30**







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†In a chronic dry eye patient usage study, participants from a variety of socioeconomic backgrounds answered questions about their experience with iVIZIA lubricant drops. In the study, 203 chronic dry eye patients, 28-80 years old, switched from their dry eye artificial tears to iVIZIA for a month.[1]
‡To limit blurriness when using contact lenses, remove contacts, apply drops, then insert contacts.

Reference: 1. Thea Data on File.

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AUGUST 2024

Susvimo Implant to Return to Market Following Recall

After voluntarily recalling Susvimo (ranibizumab injection) in October 2022, Genentech announced in July the reintroduction of the ocular implant for the treatment of wet age-related macular degeneration.

Susvimo is implanted surgically and refilled once every six months with a needle designed specifically for the implant. It was initially approved by the FDA in 2021 for the treatment of wet AMD in eyes with at least two prior anti-VEGF injections.

"We're pleased to reintroduce Susvimo, a unique therapeutic approach shown to provide an effective alternative to regular eye injections by preserving vision with two refills per year in Phase III study patients with wet AMD," the company announced in a formal statement.[1]

Genentech took the implant and tool assembly kit, including the drug vial and initial fill needle, off the market after it investigated reports of septum dislodgement in the port delivery system in patients during the Phase III trial program. The recall didn't include the Susvimo 100 mg/ml drug vial or refill needle in order to allow retina specialists to continue refill-exchange procedures in those patients with an existing implant.

In a letter sent to health-care providers first announcing the recall, Genentech said, "During an investigation into septum dislodgement cases in the port delivery system with ranibizumab Phase III clinical trial program, we identified a need for additional testing of the commercial implant supply. This additional testing of our commercial supply involved repeatedly puncturing Susvimo implants with a needle, to evaluate performance of the septum of the implant over the long-term via multiple refills. The results showed that some implants did not perform to our standards. Hence, a pause in all new implantations is required."[2]

According to Jason Hsu, MD, a retina surgeon at Wills Eye Hospital in Philadelphia, who was part of the Phase III trials for Susvimo, as the company alluded to in its statement, the implant includes a septum for the needle to penetrate. "The septum creates a barrier to prevent any efflux of the drug into the subconjunctival space," he explains. "However, in the reports of dislodgement, the glue of the septum wasn't holding, essentially causing the septum to drop into the tip of the implant and preventing any refills."

Among the changes to the implant were the doubling of the bonding strength of the septum component, as well as lubrication of the refill needle, which allows it to be inserted more smoothly and reduces the insertion force, notes Dr. Hsu.

"In my experience inserting these devices, septum dislodgement wasn't a major issue," he says. "We did see it happen in a couple of patients, but we witnessed dislodgement of the entire implant into the eye during the refill procedures. Some of that had to do with the amount of pressure it took to insert the needle into the device for refills. The changes made to the refill needle add a little bit more reassurance that it won't require as much pressure, so this should hopefully make it much safer for the long term."

The U.S. Food and Drug Administration has given a post-approval supplement to the Biologics License Application for Susvimo, reflecting these updates. Genentech also said it will work to make Susvimo available in the United States in the coming weeks.

"As for those who did have the original Susvimo implant, now that a new device is FDA approved, they'll need to have it exchanged at some point, which is a bit of an inconvenience to undergo another surgery," continues Dr. Hsu. "But I think these long-lasting, anti-VEGF options are a huge benefit to everyone, patients and clinicians, in terms of burden of care. I'm happy to see it's back on the market because I think it will allow us to have another option for patients who need very frequent treatments. This potentially means they don't need to come back to the office as often for repeated intravitreal injections."

1. Genentech to Reintroduce Susvimo for People With Wet Age-Related Macular Degeneration (AMD). https://www.gene.com/media/press-releases/15031/2024-07-08/genentech-to-reintroduce-susvimo-for-peo. Accessed July 18, 2024.
2. Voluntary recall of the SUSVIMO Ocular Implant. https://www.gene.com/download/pdf/Susvimo_DHCP_Important_Prescribing_Information_2022-10-18.pdf. Accessed July 18, 2024.

Eye Length's Relation to Glaucoma Severity, Progression

Research has suggested a clear relationship between myopia and glaucoma; axial elongation in myopic eyes stretches posterior ocular structures, resulting in progressive thinning of the retina, choroid and sclera and a higher susceptibility of lamina cribrosa deformation. In turn, these patients are subjected to a greater likelihood of glaucomatous optic disc changes. With the knowledge that axial length and glaucoma are related, a recent study aimed to determine whether there is a difference in inter-eye glaucoma severity and progression in patients with asymmetric axial length.[1] The results revealed that glaucoma tended to be more severe and to progress faster in the longer eye.

The long-term observational study included 190 eyes of 95 glaucoma patients with asymmetric axial length (>1 mm difference between eyes) from a university hospital in Korea. The researchers classified each person's eyes as the "longer eye" and "shorter eye" then performed an analysis on baseline and follow-up clinical data. The mean patient age was 51 years, and the mean follow-up period was just over 10 years.

Here are some of the main findings from the study:

- There was no difference in baseline intraocular pressure or central corneal thickness between longer and shorter eyes.
- Several baseline disc parameters were greater among longer eyes, including ovality index, beta-zone and gamma-zone parapapillary atrophy.
- In baseline OCT data, the thickness of the RNFL and ganglion cell-inner plexiform (GCIPL) layer was reduced in longer eyes vs. short eyes.
- The mean deviation and visual field index values were significantly lower in the longer eyes according to a baseline visual field test.

The researchers also reported differences in glaucoma progression between longer and shorter eyes. The following rates of change were greater in longer eyes: superior GCIPL (longer eyes: -0.65 µm/yr, shorter eyes: -0.40 µm/yr), mean deviation (longer eyes: -0.40 dB/yr, shorter eyes: -0.21dB/yr) and visual field index (longer eyes: -0.92 percent/yr, shorter eyes: -0.46 percent/yr).

"The greater the difference between the mean IOP and beta-zone parapapillary atrophy area between inter-eyes, the greater the difference in the rate of change of RNFL and GCIPL," the study authors pointed out. Furthermore, they added, "the greater the difference in IOP fluctuation, the greater the difference in the rate of change between mean deviation and visual field index."

All these observed differences between clinical parameters of longer vs. shorter eyes "provide insights into the nuanced nature of glaucomatous changes associated with axial length dissimilarities," the authors noted. When evaluating patients with an inter-eye axial length difference of more than 1 mm, it may behoove ophthalmologists to consider that—based on the findings of this study—the longer eye may experience structural differences in the optic nerve head (larger ovality index and parapapillary atrophy area), greater thinning of the RNFL and GCIPL and more rapid change in mean deviation and visual field index.

"Longer eyes, as characterized by structural variations at baseline and an accelerated rate of glaucomatous change, exhibit a higher susceptibility to disease severity and progression," the researchers concluded in their paper.

1. Huh MG, Jeong Y, Shin YI, et al. Assessing glaucoma severity and progression in individuals with asymmetric axial length: An intra-patient comparative study. Ophthalmology. July 15, 2024. [Epub ahead of print].

Bilateral, Same-day Surgery Safe According to U.K. Study

Increased efficiency at surgical centers and negligible risk argue for the adoption of same-day dual cataract removal in regions where demand far outstrips supply. However, widespread adoption of such a practice would require dramatic logistical and financial changes that are not in the offing any time soon. The Centers for Medicare and Medicaid Services have yet to bless such a protocol, all but stopping it in it tracks.

Nevertheless, the experience of surgeons outside the U.S. gives us a window into outcomes we could anticipate if circumstances change. In the U.K., immediate sequential bilateral cataract surgery (ISBCS) was introduced into

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Excellent tolerability[1,4-6]‡

- Low rate of burning or stinging on instillation
- Blurred vision and conjunctival redness were reported in 1%-3% of individuals

***The exact mechanism of action for MIEBO in DED is not known.[1]**

†**Study design:** Two 57-day, multicenter, double-masked, saline-controlled studies (GOBI and MOJAVE) were conducted in adults ≥18 years old with a self-reported history of DED in both eyes. Across GOBI and MOJAVE, 614 patients received MIEBO and 603 patients received control with 591 and 575, respectively, assessed on Day 57. **Primary endpoints were change from baseline in tCFS and change from baseline in eye dryness score at Day 57.** Day 15 was the earliest time point at which signs and symptoms were evaluated in the trials. Day 57 was the last.[1,5,6]

‡In 2 pivotal studies of >1200 patients (614 patients received MIEBO), there were no incidences of serious ocular AEs with MIEBO. Most AEs were considered mild. The discontinuation rate for MIEBO was comparable to control (pooled: 0.2% vs 0.5%; GOBI: 0.3% vs 1.0%; MOJAVE: 0% vs 0%). 0.5% (pooled) of patients experienced instillation site pain AEs, such as burning or stinging (GOBI: 1.0%; MOJAVE: 0%). Blurred vision (pooled: 2.1%; GOBI: 3.0%; MOJAVE: 1.3%) and conjunctival redness (pooled: 0.8%; GOBI: 0%; MOJAVE: 1.3%) were reported in 1%-3% of individuals.[1,4-6]

AE, adverse event; DED, dry eye disease; tCFS, total corneal fluorescein staining.

INDICATION

MIEBO™ (perfluorohexyloctane ophthalmic solution) is a semifluorinated alkane indicated for the treatment of the signs and symptoms of dry eye disease.

IMPORTANT SAFETY INFORMATION

- MIEBO should not be administered while wearing contact lenses. Contact lenses should be removed before use and for at least 30 minutes after administration of MIEBO
- Instruct patients to instill one drop of MIEBO into each eye four times daily
- The safety and efficacy in pediatric patients below the age of 18 have not been established
- The most common ocular adverse reaction was blurred vision (1% to 3% of patients reported blurred vision and conjunctival redness)

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see accompanying Brief Summary of full Prescribing Information for MIEBO.

References: 1. MIEBO. Prescribing Information. Bausch & Lomb, Inc; 2023. **2.** Sheppard JD, Nichols KK. Dry eye disease associated with meibomian gland dysfunction: focus on tear film characteristics and the therapeutic landscape. *Ophthalmol Ther*. 2023;12(3):1397-1418. doi:10.1007/s40123-023-00669-1 **3.** Vittitow J, Kissling R, DeCory H, Borchman D. In vitro inhibition of evaporation with perfluorohexyloctane, an eye drop for dry eye disease. *Curr Ther Res Clin Exp.* 2023;98:100704. doi:10.1016/j.curtheres.2023.100704 **4.** Data on file. Bausch & Lomb, Inc; 2023. **5.** Tauber J, Berdy GJ, Wirta DL, Krösser S, Vittitow JL; GOBI Study Group. NOV03 for dry eye disease associated with meibomian gland dysfunction: results of the randomized phase 3 GOBI study. *Ophthalmology*. 2023;130(5):516-524. doi:10.1016/j.ophtha.2022.12.021 **6.** Sheppard JD, Kurata F, Epitropoulos AT, Krösser S, Vittitow JL; MOJAVE Study Group. NOV03 for signs and symptoms of dry eye disease associated with meibomian gland dysfunction: the randomized phase 3 MOJAVE study. *Am J Ophthalmol*. 2023;252:265-274. doi:10.1016/j.ajo.2023.03.008

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BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use MIEBO safely and effectively. See full Prescribing Information for MIEBO.

MIEBO™ (perfluorohexyloctane ophthalmic solution), for topical ophthalmic use

Initial U.S. Approval: 2023

1 INDICATIONS AND USAGE

MIEBO™ (perfluorohexyloctane ophthalmic solution) is indicated for the treatment of the signs and symptoms of dry eye disease (DED).

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

MIEBO should not be administered while wearing contact lenses. Advise patients that contact lenses should be removed prior to and for at least 30 minutes after administration of MIEBO.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in 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 patients with DED, 614 patients received at least one dose of MIEBO in two randomized controlled clinical trials across 68 sites in the United States. The most common ocular adverse reaction was blurred vision. Blurred vision and conjunctival redness were reported in 1-3% of individuals.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well controlled studies with MIEBO in pregnant women.

In animal reproduction studies with oral administration of perfluorohexyloctane during the period of organogenesis, no adverse maternal or developmental effects were observed in rats at doses up to 162 times the recommended human ophthalmic dose (RHOD) (*see Data*). Maternal toxicity, miscarriages and reduced fetal weights were observed in rabbits at all doses tested, with the lowest dose as 41 times the RHOD.

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 is 2 to 4%, and of miscarriage is 15 to 20%, of clinically recognized pregnancies.

Data

Animal Data

An embryofetal study was conducted in pregnant rabbits administered perfluorohexyloctane by oral gavage on gestation days 6 to 19, to target the period of organogenesis.

Perfluorohexyloctane produced maternal toxicity, characterized by reduced body weight gain and food consumption, and miscarriages at all doses tested, with the lowest dose as ≥ 250 mg/kg/day (41 times the RHOD based on body surface area). Reduced fetal weights were also observed at ≥ 250 mg/kg/day but no fetal mortality or malformations. A no observed adverse effect level (NOAEL) for maternal toxicity was not established in rabbits.

An embryofetal study was conducted in pregnant rats administered perfluorohexyloctane by oral gavage on gestation days 6 to 17, to target the period of organogenesis. There was no evidence of embryofetal toxicity or teratogenicity at doses up to 2,000 mg/kg/day (162 times the RHOD).

8.2 Lactation

There are no data on the presence of perfluorohexyloctane in human milk, the effects on the breastfed infant, or the effects on milk production. The lack of clinical data during lactation precludes a clear determination of the risk of MIEBO to an infant during lactation; however, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for MIEBO.

8.4 Pediatric Use

The safety and effectiveness of MIEBO in pediatric patients below the age of 18 years have not been established.

8.5 Geriatric Use

No overall differences in safety and effectiveness have been observed between elderly and younger patients.

12 CLINICAL PHARMACOLOGY

12.3 Pharmacokinetics

The pharmacokinetics of perfluorohexyloctane following topical ocular administration of MIEBO has not been quantitatively characterized in humans. A single pharmacokinetic (PK) study was conducted that showed low systemic perfluorohexyloctane blood levels after topical ocular administration. Perfluorohexyloctane was not metabolized by human liver microsomes in vitro.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals have not been conducted to evaluate the carcinogenic potential of perfluorohexyloctane.

Perfluorohexyloctane was not mutagenic or clastogenic in a standard battery of genotoxicity tests, including a bacterial mutagenicity assay (Ames assay), an in vitro chromosome aberration assay using human peripheral lymphocytes, and an in vivo bone marrow micronucleus assay in rats.

17 PATIENT COUNSELING INFORMATION

Use with Contact Lenses

Advise patients that contact lenses should be removed prior to and for at least 30 minutes after administration of MIEBO.

Administration Instructions

Advise patients to instill one drop of MIEBO four times daily into each eye as depicted in the Administration Instructions.

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Patented. See https://patents.bausch.com for US patent information.

MBO.0046.USA.23 Issued: 5/2023

FEATURES

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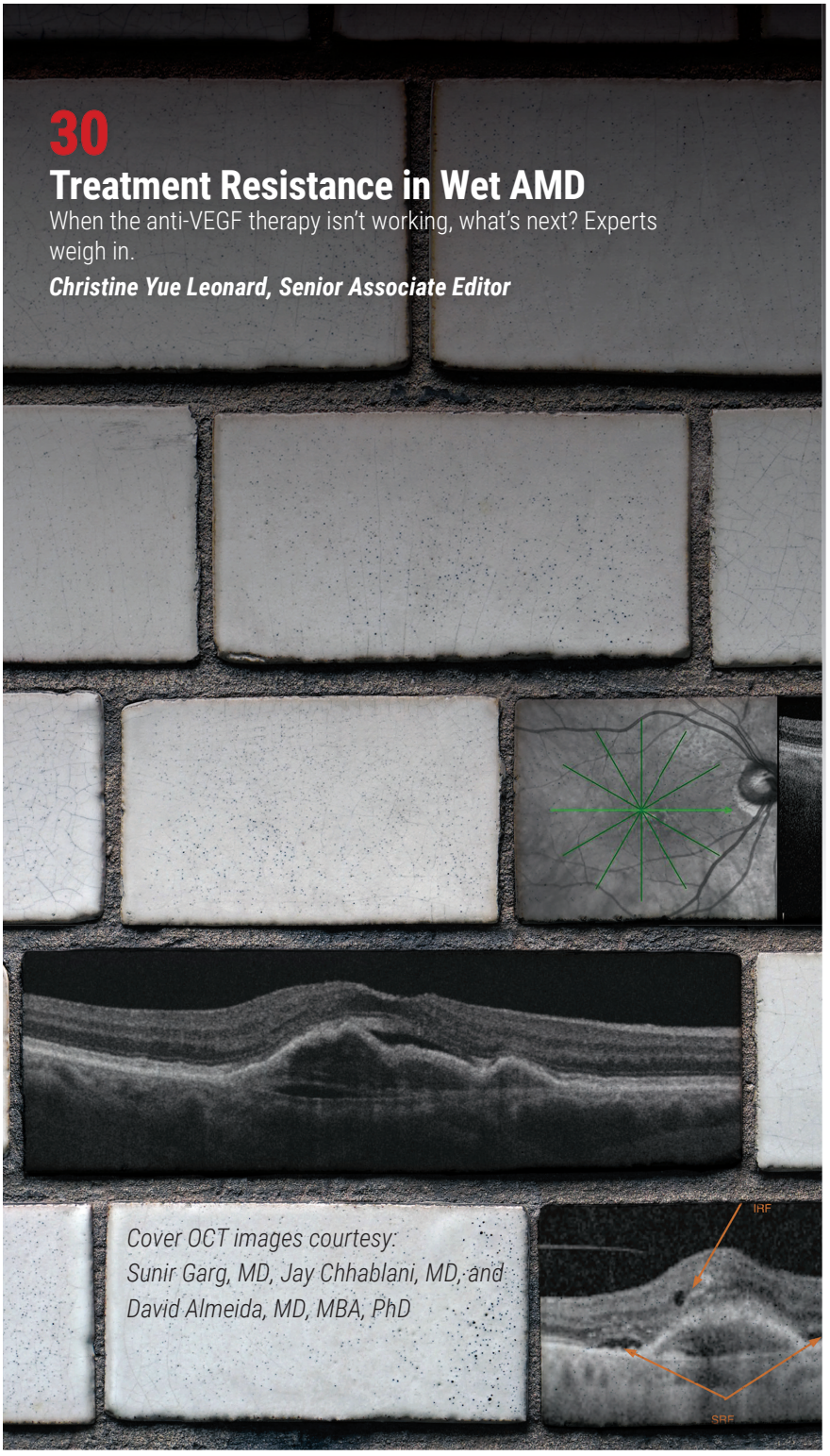

Cover OCT images courtesy: Sunir Garg, MD, Jay Chhablani, MD, and David Almeida, MD, MBA, PhD

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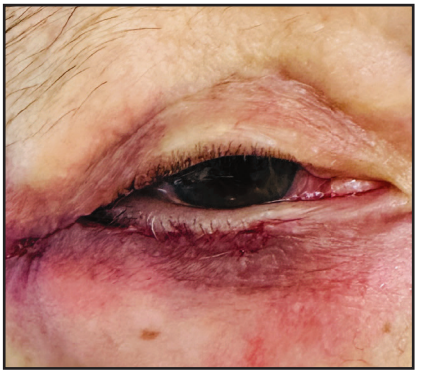
August 2024



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government-sanctioned guidelines in 2017 and has become increasingly popular there, but still only comprises 0.5 percent of all cataract operations performed nationally.

The Buckinghamshire Healthcare NHS Trust redesigned its service to routinely offer ISBCS and is now considered a leading provider of the service in the U.K. As such, it audited its cataract operations performed in 2022 to gain greater insight on the spread of the newer approach. In total, 4,652 cataract operations were performed; 10.7 percent (n=498) were operations using the ISBCS approach on 249 patients. Trainees performed 32.5 percent of these cases, and there were only two intraoperative complications, which both occurred during the second eye operation. One of these was a suspected suprachoroidal hemorrhage while the other was a posterior capsular rupture post lens implantation. Postoperative complications included one retinal detachment needing a vitrectomy following uncomplicated ISBCS and five instances of Irvine-Gass syndrome managed medically.

In a recent article for the journal *Eye*, the study authors relay that, "from this data, ISBCS does not pose a greater risk to patients in terms of complications" and note that "with appropriate preoperative counseling, patients listed for unilateral surgery can be converted to ISBCS on the day of operation to fully utilize theatre capacity. Patients listed for ISBCS can also be converted to unilateral surgery on the day of operation when surgeons need time to deal with complications safely."

In their discussion, the researchers further elaborate on the benefits this dual procedure may provide. They explain how doing ISBCS is quicker to perform on one patient than doing two separate cataract operations on differing patients due to preoperative review, patient maneuvering, setup times and postop counseling, which are all quicker on the day, potentially meaning that "this time saving could allow for more operations to be carried out in a single theatre session," the authors point out.

A number of patients seem to prefer this method, too, as one study found 45 percent of patients on NHS cataract surgery waiting lists would undergo ISBCS if offered, while another study reported 36 percent of NHS patients accepting ISBCS when offered.

The investigators also argue that the one patient who experienced a macula-on rhegmatogenous retinal detachment six weeks after operation had a better outcome than she would have receiving the surgeries separately. This is because the detachment likely would have occurred before the second eye operation, thus causing a long delay before operation on that eye, which would result in worse vision and greater morbidity while recovering from the detachment. As well, this may have caused her to decline the operation in the second eye, resulting in long-term increased morbidity.

However, the authors highlight that "perhaps the greatest impact of ISBCS in years to come will be the flexibility it provides to adapt surgical lists in real-time with no additional administrative burden." As they outline, a surgical list may consist of ISBCS cases but given any complications, surgeons may modify the procedures for the day to accommodate for increased time, dropping the procedures to only perform on one eye. Conversely, patients may be given the opportunity to opt out of the second operation on the day either before the operation or after the first eye's completion, offering greater patient choice.

1. King, C., Botcherby, E.J., Adams, M. et al. Implementing immediate sequential bilateral cataract surgery at Buckinghamshire Healthcare NHS Trust. Eye (2024). https://doi.org/10.1038/s41433-024-03202-1.

Ophthalmology Groups Respond to GLP-1/NAION Data

Earlier this month, researchers at Harvard University published the results of their recent study, which observed an increased risk of nonarteritic anterior ischemic optic neuropathy in patients taking semaglutide for type 2 diabetes or weight loss. Semaglutide, a glucagon-like peptide receptor agonist (GLP-1 RA), is the active ingredient in Ozempic and Wegovy, two medications being prescribed with increasing frequency across the United States, adding to a cause for concern about the study's findings.

The American Academy of Ophthalmology and the North American Neuro-Ophthalmology Society recently released a statement responding to the study and commenting on its potential implications for clinical practice. The stance of the two organizations is that, while the observed association between semaglutide and NAION of this study is "interesting," more research is warranted to confirm whether the relationship is causal.

"The type of study conducted here helps identify potential links between GLP-1 treatment and NAION, but it's not the type of study that can show the treatment caused NAION," states Andrew Lee, MD, a clinical spokesperson for the American Academy of Ophthalmology and a neuro-ophthalmologist at Houston Methodist Hospital, in a recent *Vision Monday* article. Until more research is conducted, he says "patients should be aware of this information and, in consultation with their care team, make a careful, informed choice based on their individual risk profile."

(Continued on p. 16)

References: 1. St. Peter et al. Reduction of Eyedrop Volume for Topical Ophthalmic Medications with the Nanodropper Bottle Adaptor. *Med Devices (Auckl).* 2023. **2.** Steger et al. An Evaluation of the Efficacy and Safety of Timolol Maleate 0.5% Microdrops Administered with the Nanodropper®. *Ophthalmology*. 2024. **3.** https://nanodropper.com/whitepaper. **4.** Nanodropper, Inc. data on file.

REVIEW of OPHTHALMOLOGY

WALTER C. BETHKE, EDITOR IN CHIEF

EDITOR'S PAGE

The Annual Insult

Do you ever get the sneaking suspicion everyone's having fun but you? Everyone's leading an exciting life? And, of course, everyone's making more money. It's the feeling you get when you scroll through other people's social media feeds: "Courtney's sharing a panini with J.Lo?! I never do anything fun."

I wouldn't blame ophthalmologists if they got this feeling after reading various news items from the past month.

First came the "annual insult," also known as the proposed cut in Medicare reimbursement for 2025. While other workers get cost-of-living increases and the cost for things like staffing and utilities continue to rise, cataract surgeons' reimbursement gets cut. The proposed decrease is around 2.8 percent.

Next came a *Wall Street Journal* investigative report of Medicare Advantage plans that alleged insurers were diagnosing patients with conditions they didn't have in order to get more money from the government, because sicker patients with certain conditions are allowed more funds for their treatment.[1] The story hits close to home, too, as some of the diagnoses were ophthalmic, specifically diabetic cataracts. So, you're getting less money for removing actual cataracts, while insurers are allegedly making millions off of cataracts that don't even exist. Makes you wonder if you're in the wrong racket.

The *Journal* found that members of one particular Medicare Advantage plan were 15 times more likely to have diabetic cataracts than a patient in Medicare. "Eye doctors interviewed by the *Journal* said it was implausible that such a large share of UnitedHealth's patients could have the relatively rare disease," the article reports.

To add insult to the alleged financial injury, the paper's analysis found that more than 66,000 Medicare Advantage patients were diagnosed with diabetic cataracts *after* they'd already had cataract surgery! Now, I'm no doctor—I don't even play one on YouTube—but that just doesn't seem possible.

All in all, the *Journal* reports, the government paid Medicare Advantage insurers more than $700 million from 2019 to 2021 for the historically rare diagnosis of diabetic cataracts. "Most of the diagnoses were added by insurers," the report adds.

When all diagnoses were taken into account, the charges for diseases that patients may not have even had add up to around $50 billion.[1]

As has been mentioned before in this space, if the government could just eliminate the waste, and potential fraud, from its programs, then Medicare reimbursement cuts could be reduced or even eliminated for a year or longer, giving ophthalmologists some much needed financial relief. Until then, I guess physicians will just have to operate at a "Medicare Disadvantage."

— Walter Bethke
Editor in Chief

1. Weaver C, McGinty T, Matthews AW, Maremont M. Insurers Pocketed $50 Billion From Medicare for Diseases No Doctor Treated. WSJ. https://www.wsj.com/health/healthcare/medicare-health-insurance-diagnosis-payments-b4d99a5d?mod=health_trendingnow_article_pos5. Accessed July 28, 2024.

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(Continued from p. 12)

The AAO and the North American Neuro-Ophthalmology Society offered several other comments and concerns regarding the design and limitations of the study. For one, they point out that prior to its 2017 FDA approval, semaglutide was rigorously studied in multiple randomized controlled trials around the world. Notably, this is the first study to report an association between semaglutide and NAION.

They also noted that subjects in this study were either overweight, obese or had type 2 diabetes, the latter of which is an established risk factor of NAION, with others including heart disease, history of heart attack, high blood pressure and sleep apnea. However, the study authors did assert that they controlled for these potential confounders in their analysis.

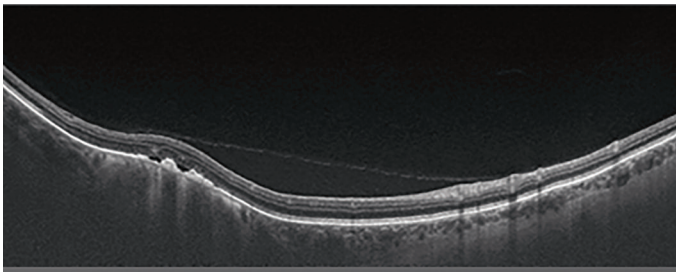
Another potential limitation of the study according to the AAO and the North American Neuro-Ophthalmology Society was that all patients included were seen at Massachusetts Eye and Ear in Boston. Because the specialty hospital sees a large percentage of NAION patients in the region, this could limit the generalizability of the findings.

The two organizations point out that semaglutide has previously been linked to other vision changes, such as blurred vision, worsening of diabetic retinopathy and macular complications, though these effects typically subside within three or four months.

Though the AAO and the North American Neuro-Ophthalmology Society don't recommend that people stop taking semaglutide at this time, they reiterate that further research will help clarify the relationship between the drug and ocular events such as NAION.

Drugs and Systemic Diseases May Alter OCT Findings

Comparing inner retinal measurements against a reference database is vital to diagnosing and monitoring certain pathologies, including primary eye conditions like optic neuropathies, as well as visual pathway lesions and systemic diseases. Researchers recently performed a study that used optical coherence tomography to conduct measurements of the inner retina in a large sample of normal, healthy eyes. Furthermore, it assessed the association between various inner retinal measures, such as peripapillary RNFL, and physiological factors, demographics, non-ocular pathology and pharmaceutical drug use.



A recent analysis found that certain systemic diseases and drugs were significantly associated with deviations in standard OCT inner retinal measures, underscoring the importance of considering systemic health when assessing OCT data.

The study employed a retrospective, cross-sectional analysis of 705 consecutive participants with bilateral normal, healthy optic nerves and maculas. Mean age was 46.6 and 59 percent were women. One-third (33.1 percent) were white, 24.2 percent were Asian, 15.7 percent were categorized as "other" and 26.8 percent did not disclose their group. The mean refractive error was mildly myopic (-0.92 D). The most prevalent non-ocular pathologies were hypertension (10.5 percent), migraine (7.2 percent) and asthma (5.4 percent), while the most prevalent drugs were lipid-lowering agents (15.7 percent), ACE inhibitors (9.5 percent) and diabetes drugs (7.4 percent).

Data such as vertical cup/disc ratio, cup volume and macular ganglion cell layer-inner plexiform layer thicknesses were extracted from Cirrus OCT scans. These measures were then regressed against predictor variables that included participants' physiology, demographics, non-ocular pathology and pharmaceutical drug use following the World Health Organization classifications.

The results showed that several non-ocular pathologies and pharmaceutical drug uses were significantly associated with deviations in standard OCT inner retinal measures, which exceeded the impact of other factors like age and intraocular pressure. Specifically, the use of systemic corticosteroids or sex hormones/modulators and the presence of diseases like vasomotor or allergic rhinitis were linked to thinner inner retina and larger optic nerve cup measures. Conversely, antineoplastic agents and the presence of liver or urinary diseases were associated with thicker inner retina and smaller optic nerve cup measures.

"Relatively novel findings included that the use of sex hormones/modulators were associated with compromised inner retinal integrity, while unspecified liver or urinary diseases and antineoplastic agents were associated with diffuse macular GCL-IPL thickening," the researchers wrote. ◀

1. Trinh M, OK, La M, Ly A. Linking physiology and demographics, non-ocular pathology and pharmaceutical drug use to standard OCT measures of the inner retina: The PPP project. Ophthalmic Physiol Opt. July 7, 2024. [Epub ahead of print].

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REFERENCES:
1. Data on File. 2024DOF4002 **2.** Data on File. DOF2023CT4052 **3.** Data on File. 2024DOF4005 **4.** Data on File. DOF2023CT4023 **5.** Data on File. DOF2023CT4007 **6.** Data on File. DOF2019OTH4002

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WARNINGS: Intraocular lenses may exacerbate an existing condition, may interfere with diagnosis or treatment of a condition or may pose an unreasonable risk to the eyesight of patients. Patients should have well-defined visual needs and be informed of possible visual effects (such as a perception of halo, starburst or glare around lights), which may be expected in nighttime or poor visibility conditions. Patients may perceive these visual effects as bothersome, which, on rare occasions, may be significant enough for the patient to request removal of the IOL. The physician should carefully weigh the potential risks and benefits for each patient. Patients with a predicted postoperative residual astigmatism greater than 1.0 diopter may not fully benefit in terms of reducing spectacle wear. The lens and delivery system should be discarded if the lens has been folded within the cartridge for more than 10 minutes. Not doing so may result in the lens being stuck in the cartridge. 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.

PRECAUTIONS: Interpret results with caution when using autorefractors or wavefront aberrometers that utilize infrared light, or when performing a duochrome test. Confirmation of refraction with maximum plus manifest refraction technique is strongly recommended. The ability to perform some eye treatments (e.g., retinal photocoagulation) may be affected by the IOL optical design. The surgeon should target emmetropia, as this lens is designed for optimum visual performance when emmetropia is achieved. The TECNIS Odyssey™ IOLs should not be placed in the ciliary sulcus. Patients with a predicted postoperative astigmatism greater than 1.0 D may not be suitable candidates for implantation with the TECNIS Odyssey™ IOLs, as they may not obtain the benefits of reduced spectacle wear or improved intermediate and near vision seen in patients with lower predicted postoperative astigmatism.

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

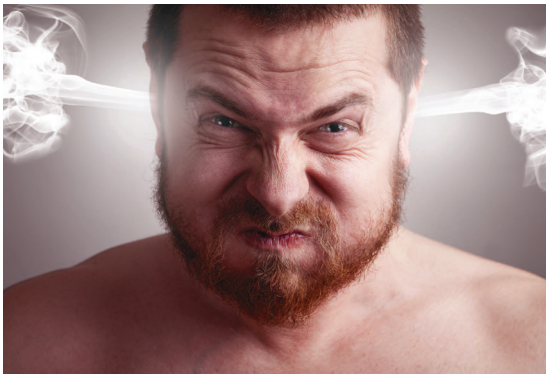
The Angry Ape

Musings on life, medicine and the practice of ophthalmology.

MARK H. BLECHER, MD
CHIEF MEDICAL EDITOR

The recent attempt on the life of former President Donald Trump has had an outsized effect on many Americans and on the body politic. But why? Thousands of people are shot in the United States every day and it doesn't even make a splash on the local news. Even shooting deaths have become so common that the thoughts and prayers don't even have a chance to become inconsequential. So why was this event more noteworthy? Should it be more noteworthy? Obviously, I know the answer, or rather the many answers. He's a past president. He's the nominee to run again. He is both famous and infamous. He's a symbol of the American political system, and of a subset of political thought held by a large number of Americans. So, it's both right to have this event command the national consciousness, at least for a while, and it's very wrong. After all Trump did say all lives matter, but with apologies to George Orwell, some lives matter more apparently.

In case you were worried this column would descend into partisan politics, I've said what I wanted about the event that caused me to think about why violence in this world seems to continue unabated. High-profile violence, especially. While crime statistics indicate some decrease in violent crime over the last two years in many U.S. cities, it certainly doesn't feel that way. And I'm not just talking about violent crime here, but the tendency for violence around the world. Are we as a species becoming more or less violent, and why? It would seem to be more violent, but I keep asking myself if that is real or is it simply because social media has put each episode in our face?



There are many reasons for why we're a violent, aggressive species. It's inherent in our genes, originating from self-preservation and procreation. Like all animals, we want to live and reproduce. And to do that we have to defend our person, our resources and our mates. This can require violence—or at least it did. The reflexive response of the amygdala and hippocampus can be moderated by our subcortical and cortical inputs. The rational human can decide not to fight, or at least fight less and with less physical violence. So why don't we? Isn't that the point of civilization, to achieve a society that provides the resources and structure to not need to kill to survive? That leads to the question as to whether we've achieved that and, if we have, why isn't that sufficient? What are the other reasons we remain aggressive and violent at the drop of a hat? OK, not all of us, but way too many. Is it fun/satisfying to be violent? Are these tendencies enhanced by a modern stressful society? Is drug use central to this? The answer is likely a combination. It seems that despite our evolution, it's very easy to trigger aggression and violence. Especially in males. That implicates testosterone, as do the statistics of who commits violent crime.

So, with violence and aggression so prevalent in humans, what's the basis of an increased incidence of high-profile violence such as mass shootings and assassinations? Is this any different than inner-city gang violence, drug trafficking violence or war in the Middle East? I submit that it is. The kind of violence I'm calling out is less about anger in the moment, than it is about a baseline of anger. An anger of vengeance, and grievances long held but unresolved, of people walking around every day with a smoldering level of anger. If it isn't of the moment, you would think that our higher processes would have a better chance of intervening. And the aggressive response could possibly be mitigated. It's tough to suppress a reflex. It shouldn't be as difficult to defuse a grudge. But here we are with another high-profile violent episode to contend with and as of this writing, no idea where it came from. We say that there is no role for violence in American politics, but why don't we say that about American life? It seems, as a species, we have a long way to go. ◀

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

A New Way to Track Refractive Outcomes

Use this application to graph outcomes for your refractive surgery procedures.

ANDREW BEERS
ASSOCIATE EDITOR

Mathieu Gauvin, MD, and Avi Wallerstein, MD, principal investigators from the McGill University Refractive Surgery Research Unit in Quebec, Canada, have developed a free software program called mEYEstro that automatically graphs refractive surgery outcomes. Here's how the two physicians created the program and what their technology can offer refractive surgeons.

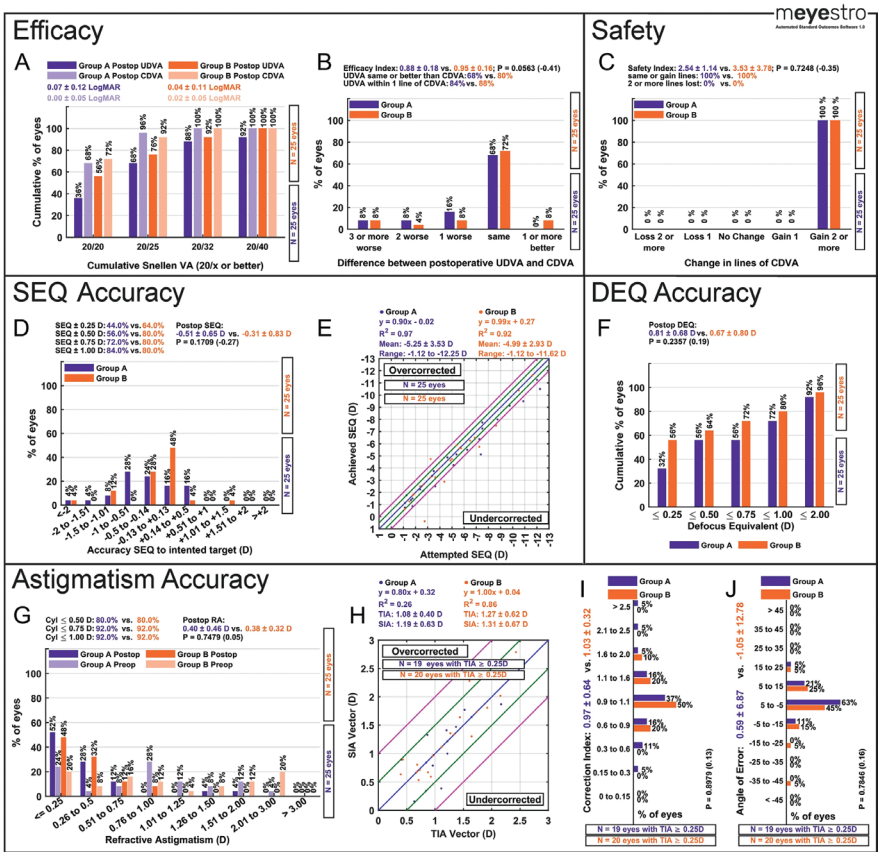
Intro to mEYEstro

"Initially we noticed that many published articles weren't adhering to the standards recommended by the journals for outcomes reporting," says Dr. Gauvin when explaining how he and Dr. Wallerstein came up with the concept for mEYEstro. In 2023, the team of physicians published a study to show the efficacy, safety, accuracy and stability of their software.[1] They explained in their paper how other available online tools could help with graphing, but nothing streamlined the process while meeting the academic standard needed.

"We then identified a significant gap in the available tools for refractive surgery outcome analysis," continues Dr. Gauvin. "Existing software solutions were either too expensive, required manual data entry, were prone to user error or weren't comprehensive. We wanted to create a user-friendly, automated tool that would simplify and expedite the process of generating standardized refractive surgery graphs and performing statistical analyses."

During the development process, Drs. Gauvin and Wallerstein encountered some obstacles. "One major challenge was ensuring that the software could perform accurate and automated statistical analyses and generate high-resolution graphs with minimal user input," says Dr. Gauvin. "We also had to ensure compatibility with widely used data formats and maintain user data security and confidentiality. Overcoming these challenges required rigorous testing and iterative improvements and 'beta user' feedback."

In their 2023 study, the team of physicians cited the works of Dan



An example of graphs produced by mEYEstro. This dataset was used to investigate the outcomes of surgery between two groups.

This article has no commercial sponsorship.

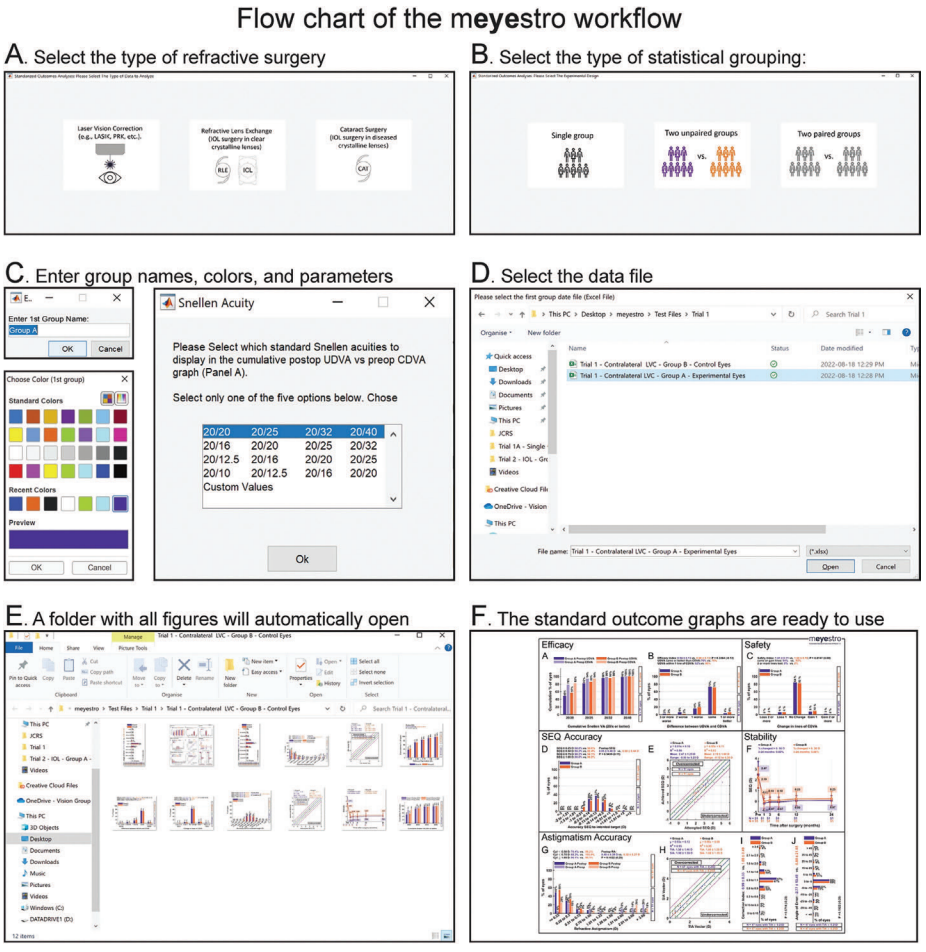
Dr. Colvard is a surgeon at the Colvard-Kandavel Eye Center in Los Angeles and a clinical professor of ophthalmology at the Keck School of Medicine of the University of Southern California. **Dr. Charles** is the founder of the Charles Retina Institute in Germantown, Tennessee.

Z. Reinstein, MD, and George O. Waring III, MD, whose studies set the standards for graphing refractive surgery results. The mEYEstro software was developed to adhere to Drs. Waring and Reinstein's terminology, calculations and graphical representations. Additionally, when comparing two groups in a study, the software automatically selects and plugs the data into the appropriate hypothesis test. The software can run tests such as the Kolmogorov-Smirnov test, unpaired sample T-tests, paired sample T-tests, non-parametric Mann Whitney U-tests and non-parametric Wilcoxon signed-rank tests.

When conducting their study, Drs. Gauvin and Wallerstein designed three data files to upload to the software in order to test the efficacy, safety, accuracy and stability of their software. "The data files were designed to be straightforward and compatible with Microsoft Excel, a widely used program in both clinical and research settings," explains Dr. Gauvin. "We defined 20 columns, including 15 mandatory ones for the essential preoperative and postoperative refractive data, and five optional columns for additional stability data points. This design ensures that the software can automatically generate accurate and comprehensive graphs based on standardized input formats."

According to the study, mEYEstro is capable of generating 11 standard graphs for the following:

- cumulative UDVA and CDVA;
- difference between UDVA and CDVA;
- change in lines of CDVA;
- spherical equivalent to intended target;
- attempted vs. achieved SEQ;
- defocus equivalent accuracy;
- refractive astigmatism accuracy;
- target-induced astigmatism vs. surgically induced astigmatism;
- correction index histogram; and
- angle of error histogram and SEQ stability overtime.



The software is easy to use and provides physicians with a host of customization options. Above are simple steps for creating graphs for refractive outcomes. A detailed tutorial is available on the Refractive Surgery Research Unit's YouTube channel (https://www.youtube.com/watch?v=NFlRRHx6Zal).

Each graph can be downloaded individually or combined as a TIFF image file.

"Currently, mEYEstro works exclusively with Excel spreadsheets due to their widespread use and simplicity," says Dr. Gauvin. "Implementing compatibility with Google spreadsheets or other programs would require additional development and testing. While there are no immediate plans to add this feature, we're open to user feedback and may consider it for future updates based on demand. To date we haven't had such a request. It's also our understanding that Google users can save their spreadsheet as an Excel file; so technically this shouldn't be a big hurdle."

Interfacing with mEYEstro

While there are tutorials on YouTube that explain how to use the mEYEstro software, the 2023 study provides in-depth instructions on how to download and use the program. The software runs using the MATLAB runtime compiler, which allows the software to run independently on the desktop. This installation program will download along with mEYEstro.

Physicians interested in downloading the mEYEstro software can find the link in the 2023 study or search for the file on https://www.lasikmd.com/media/meyestro. Once

the program is installed, the user can open it up on their desktop and begin uploading their data.

The mEYEstro software begins by asking what type of refractive surgery procedure was performed. Then, the user can choose whether their study analyzed a single group, two unpaired groups or two paired groups. Following this step, the software will ask the user to customize their study's group names and colors, and set parameters for the study's outcomes. This is when the user uploads their dataset from Excel. Afterwards, the software shares a ZIP file containing multiple TIFF images of accurately graphed outcomes.

"The most unique feature of mEYEstro is its ability to automatically generate all required graphs and perform statistical analyses within 30 seconds with minimal user inputs," says Dr. Gauvin. "This automation saves time and reduces the risk of user error, making the analysis process efficient and reliable."

Before downloading mEYEstro, physicians will need to agree to the terms and conditions expressed by Lasik MD. Basically, they want physicians to acknowledge the developers of the software when publishing mEYEstro's graphs in any publication or presentation. Simply cite the 2023 study or use the citation in the footnotes below if mEYEstro is used for outcomes graphing.

"We have seen a significant number of downloads since the release of mEYEstro," adds Dr. Gauvin. "Our published article is approaching 2,000 views since its release, and many have downloaded mEYEstro and viewed our tutorial video. We expect this number to start increasing significantly as more people become aware of its availability, as was the case with our other software, AstigMATIC, which has now been used in nearly 75 peer-reviewed papers since 2018, with 30 of those in the last year alone. The positive feedback and widespread interest suggest that the software will eventually be widely adopted by the ophthalmology community."

Continuously Developing

There's always room for improvement and Drs. Gauvin and Wallerstein are already working on the next updates for mEYEstro.

> **We wanted to create a user-friendly, automated tool that would simplify and expedite the process of generating standardized refractive surgery graphs and performing statistical analyses.**
>
> ***— Mathieu Gauvin, MD***

"Users can expect enhancements that provide more detailed corneal cross-linking specific analyses, direct LogMAR data entry and advanced nomogram features so they can easily improve their future outcomes," shares Dr. Gauvin. "These updates will improve the software's capability to provide comprehensive and precise refractive surgery outcome analyses. We're also working on providing a web-based version of mEYEstro. Practitioners could then choose between the downloadable or web format.

To broaden their footprint in ophthalmology, the team of physicians have developed AstigMATIC, a tool that automatically generates advanced standard vector graphs. But mEYEstro and AstigMATIC aren't the only endeavors Drs. Gauvin and Wallerstein want to share with the public. There are plans in the future to continue developing and updating programs.

"Currently, mEYEstro and AstigMATIC are our primary contributions to the field of ophthalmology," mentions Dr. Gauvin. "However, we're currently exploring opportunities to develop new tools that can address other needs within eye care and potentially other medical specialties. User feedback and emerging needs in the field will guide our future projects. For example, we're working on making a new tool called TxFix that'll be available to the community. This tool will allow surgeons that had unfortunately treated the wrong script to immediately calculate the expected refraction while the patient is still on the bed, allowing them to immediately treat the error."

While TxFix is still under development, physicians can use mEYEstro and AstigMATIC in a clinical setting to improve procedural outcomes. "By providing standardized graphs and statistical analyses, clinicians can quickly understand the efficacy, safety, accuracy and stability of their procedures, identify trends, and make evidence-based decisions to optimize patient outcomes," shares Dr. Gauvin. "For busy surgeons, mEYEstro simplifies the process of analyzing and presenting clinical outcomes on a single page view, which is crucial for improving our understanding of surgical results.

"We invite the community to share their experiences and suggestions to help us make mEYEstro even better," continues Dr. Gauvin. "We're excited to see how mEYEstro will continue to contribute to the field of ophthalmology and improve patient care." ◀

1. Gauvin M, Wallerstein A. mEYEstro software: An automatic tool for standardized refractive surgery outcomes reporting. BMC Ophthalmology 2023;23:171.

DISCLOSURES

Drs. Gauvin and **Wallerstein** have no financial interests to disclose.

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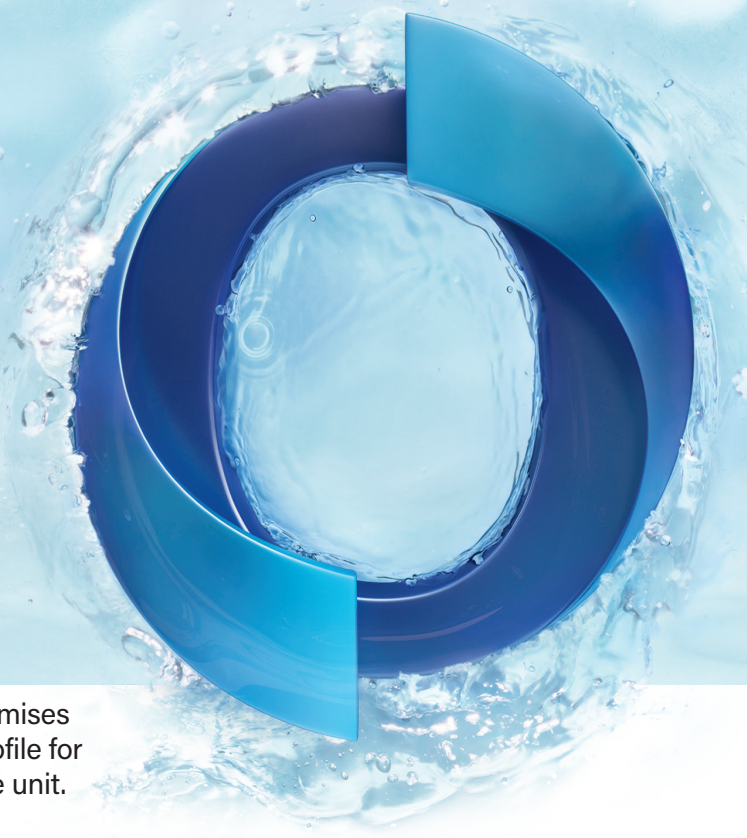

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*In the clinical trial, no patient undergoing routine cataract surgery receiving IHEEZO required supplemental treatment to maintain anesthesia; this was not the case for patients receiving tetracaine. Supplemental treatment was defined as general anesthesia, intraoperative systemic analgesia, or local anesthesia. Though supplemental administration was not required by any patient in the clinical trial, IHEEZO may be reapplied as needed to maintain anesthesia.[1,2]

†Sufficient anesthesia with IHEEZO lasted an average of 21.5 minutes in the clinical trial, while mean total surgical time was 13.9 minutes.[2]

APPROVED USE

IHEEZO is indicated for ocular surface anesthesia.

IMPORTANT SAFETY INFORMATION

IHEEZO is contraindicated in patients with a history of hypersensitivity to any component of this preparation.

IHEEZO should not be injected or intraocularly administered.

Patients should not touch the eye for at least 10 to 20 minutes after using anesthetic as accidental injuries can occur due to insensitivity of the eye.

Prolonged use of a topical ocular anesthetic may produce permanent corneal opacification and ulceration with accompanying visual loss.

Do not touch the dropper tip to any surface as this may contaminate the gel.

IHEEZO is indicated for administration under the direct supervision of a healthcare provider. IHEEZO is not intended for patient self-administration.

The most common adverse reactions in studies following IHEEZO administration (incidence greater than or equal to 5%) were mydriasis, conjunctival hyperemia, and eye irritation.

You are encouraged to report suspected adverse reactions to the FDA. Visit **www.fda.gov/medwatch**, or call **1-800-FDA-1088**.

Please see Brief Summary of Full Prescribing Information for IHEEZO on adjacent page.

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References: 1. Iheezo. Prescribing information. Harrow IP, LLC; 2022. **2.** Data on File. Harrow IP, LLC; 2023.

IHEEZO™

(chloroprocaine HCl ophthalmic gel) 3%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

IHEEZO™ (chloroprocaine hydrochloride ophthalmic gel) 3% is a preservative-free ester anesthetic indicated for ocular surface anesthesia.

4 CONTRAINDICATIONS

IHEEZO is contraindicated in patients with a history of hypersensitivity to any component of this preparation.

5 WARNINGS AND PRECAUTIONS

5.1 Not for Injection or Intraocular Administration

IHEEZO should not be injected or intraocularly administered.

5.2 Corneal Injury Due to Insensitivity

Patients should not touch the eye for at least 10 to 20 minutes after using anesthetic as accidental injuries can occur due to insensitivity of the eye.

5.3 Corneal Opacification

Prolonged use of a topical ocular anesthetic may produce permanent corneal opacification and ulceration with accompanying visual loss.

5.4 Risk of Contamination

Do not touch the dropper tip to any surface as this may contaminate the gel.

5.5 For Administration by Healthcare Provider

IHEEZO is indicated for administration under the direct supervision of a healthcare provider. IHEEZO is not intended for patient self-administration.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

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

The data described below reflect 201 patients undergoing various surgical ocular procedures in two placebo-controlled trials (Study 1 and Study 2). Patients in Study 1 were randomized to receive a single instillation of 3 drops of IHEEZO or placebo. Patients in Study 2 were randomized to receive a single or multiple instillations of 1, 3, or 3+3 drops of IHEEZO or placebo.

The most common adverse reactions in these studies (incidence greater than or equal to 5%) following IHEEZO administration were mydriasis, conjunctival hyperemia, and eye irritation.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies of IHEEZO use in pregnant women to inform a drug-associated risk. There are no animal reproduction studies for chloroprocaine.

8.2 Lactation

Risk Summary

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

8.4 Pediatric Use

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

8.5 Geriatric Use

No overall differences in safety or effectiveness of IHEEZO have been observed between elderly and younger patients.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Chloroprocaine, like other local anesthetics, blocks the generation and the conduction of nerve impulses, presumably by increasing the threshold for electrical excitation in the nerve, slowing the propagation of the nerve impulse, and reducing the rate of rise of the action potential. In general, the progression of anesthesia is related to the diameter, myelination, and conduction velocity of affected nerve fibers. Clinically, the order of loss of nerve function is as follows: (1) pain, (2) temperature, (3) touch, (4) proprioception, and (5) skeletal muscle tone.

12.3 Pharmacokinetics

The systemic exposure to chloroprocaine following topical ocular administration of IHEEZO has not been studied.

Elimination

Metabolism

Chloroprocaine is metabolized by plasma pseudocholinesterases and nonspecific esterases in ocular tissues. Chloroprocaine is rapidly metabolized in plasma by hydrolysis of the ester linkage by pseudocholinesterase. The hydrolysis of chloroprocaine results in the production of ß-diethylaminoethanol and 2-chloro-4-aminobenzoic acid, which inhibits the action of the sulfonamides.

Excretion

Chloroprocaine plasma half-life in vitro is approximately 25 seconds in adults and approximately 43 seconds in neonates. The kidney is the main excretory organ for most local anesthetics and their metabolites. Urinary excretion is affected by urinary perfusion and factors affecting urinary pH.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Long-term studies in animals to evaluate carcinogenic potential of chloroprocaine have not been conducted.

Mutagenesis

2-chloroprocaine and the main metabolite, ACBA, were negative in the in vitro bacterial reverse mutation test (Ames assay) and the in vitro chromosome aberrations assay.

Impairment of Fertility

Studies in animals to evaluate the impairment of fertility have not been conducted with chloroprocaine.

14 CLINICAL STUDIES

14.1 Study 1 and Study 2

Study 1 (NCT04779606) and Study 2 (NCT04753710) were randomized, double-blinded, placebo-controlled studies conducted to evaluate the efficacy, safety, and local tolerability of IHEEZO in 145 healthy volunteers.

In Study 1, 85 healthy males and females were randomized in a 4:1 ratio to receive a single ocular instillation of IHEEZO (n=68) or placebo (n=17). The double-blinded treatment included an IHEEZO or a placebo dose of 3 drops instilled at 1-minute (±15 seconds) intervals in the right eye of each volunteer. The median age was 39 years (range 19 to 55 years); 59% female and 41% male.

In Study 2, 60 healthy males and females were randomized (40:20) to receive single or multiple ocular instillations of an IHEEZO dose of 3 drops in the right eye. The median age was 25 years (range 18 to 59 years); 54% female and 46% male.

The efficacy in Study 1 and Study 2 was determined by proportion of patients achieving full conjunctival anesthesia evaluated by conjunctival pinching 5 minutes after administration.

Efficacy results of Study 1

The proportion of subjects with successful anesthesia was 90% in the IHEEZO group and 12% in the placebo group ($P<0.01$). The median time for the IHEEZO group achieving anesthesia was 0.67 minutes. The median duration of anesthesia was 14.3 minutes.

Efficacy results of Study 2

The proportion of subjects with successful anesthesia was 95% in the IHEEZO group and 20% in the placebo group ($P<0.01$). The median time for the IHEEZO group achieving anesthesia was 0.67 minutes. The median duration of anesthesia was 19.3 minutes.

14.2 Study 3

Study 3 (NCT04685538) was a randomized, prospective, multicenter, active-controlled, observer-masked study conducted to evaluate the efficacy and safety of IHEEZO (n=166) versus tetracaine ophthalmic solution 0.5% (n=172) in patients undergoing cataract surgery.

The primary endpoint was defined as the proportion of patients in each treatment group gaining successful anesthesia without any supplementation. On average, patients needed 1 to 1.5 minutes to obtain sufficient anesthesia to successfully perform the surgical procedure, which lasted on average 22 minutes.

No patient treated with IHEEZO required supplemental treatment to complete the intended surgical procedure.

17 PATIENT COUNSELING INFORMATION

Eye Care Precaution

Do not touch the dropper tip to any surface as this may contaminate the gel. Advise patients that their eyes will be insensitive for up to 20 minutes due to the effect of the anesthetic, and that care should be taken to avoid accidental injuries.

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Oculoplastics and Cataract Involvement

A discussion of the diseases to address prior to cataract surgery, and the ones that may be able to wait.

N. GRACE LEE, MD, FACS
BOSTON

Cataract surgery and oculoplastics are interconnected. It's important that we respect each other's skills and specialties because the eyelids are, frankly, the protectors of the globe. What's happening to the eyelids plays a huge role and impact on the health of the eyeball itself. The surface of the eye is directly affected by how well the eyelids close and how well they hug the surface in order to protect it from the external elements. There are many facets of oculoplastics aside from the eyelids, including lacrimal drainage and thyroid eye disease, which are also sometimes interwoven in cataract surgery patients.

There's a joke that the eyelids get in the way of cataract surgeons operating on the eyeball, but for us as oculoplastic surgeons, the globe gets in the way of operating in the orbit. It's important for cataract surgeons to be aware of the status of the eyelids when discussing surgery with their patients. If the eyelids aren't in optimal position or shape, or if the patient has complaints of tearing, it's important to consider an evaluation to see if there's an obstruction of the nasolacrimal drainage system, which should be addressed before cataract surgery.

In this article we'll cover some of the most common oculoplastic presentations, such as eyelid malpositions, eyelid lesions, lacrimal drainage and TED, and whether they should be addressed before or after cataract surgery.

Ptosis

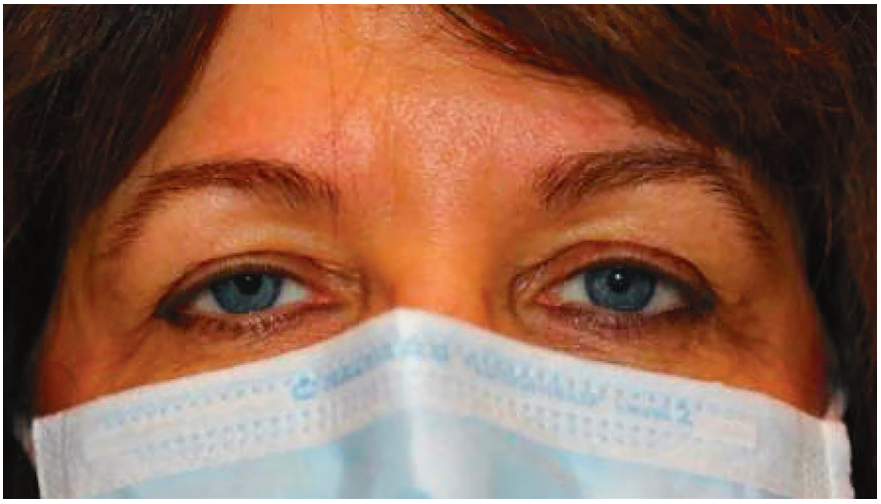
Ptosis is one of the most prevalent eyelid malpositions and it can also occur post-cataract surgery.

If you're evaluating a patient for cataract surgery and they have a significant amount of ptosis, this may affect your IOL calculations (i.e., if the lid is pressing down on the eye to a degree that's actually changing the curvature of the cornea).

A recent paper in the oculoplastics literature looked at the degree of astigmatism change with keratometry after lifting an eyelid with ptosis surgery (not involving cataract). According to the study, the mean axial change of corneal astigmatism was 17.4 degrees after ptosis surgery, and the average axial change of corneal astigmatism in a cohort with *severe* blepharoptosis after surgery was 22.7 degrees.[1] So it turns out that a good amount of astigmatism can be induced by the eyelid.

The common teaching has been to proceed with cataract surgery before eyelid surgery (ptosis repair, blepharoplasty) because cataract surgery can sometimes induce ptosis from 1 to 20 percent of the time. Usually it's a wait-and-see approach to prevent the patient from needing two eyelid surgeries, but I think what this new paper shows is that some of these patients might end up with a refractive surprise after lid surgery if their IOLs were calculated based on the astigmatism that might have been induced by the severely ptotic lid.

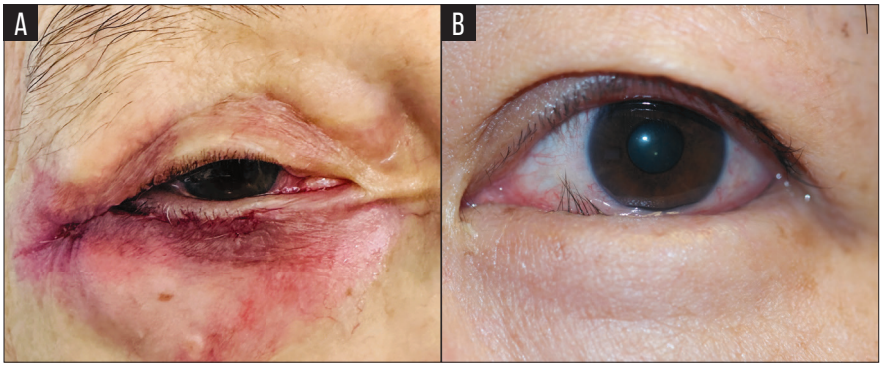
Therefore, there are cases of severe ptosis covering the pupil where I



One of the most common eyelid malpositions, ptosis can typically wait to be addressed until after cataract surgery, however, some research suggests that significant ptosis may induce astigmatism, leaving patients with a refractive surprise after eyelid surgery.

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.



Entropion (A) and ectropion (B) surgery should occur ahead of cataract surgery due to their interference with the ocular surface. It's recommended to wait at least three to four months before proceeding with cataract surgery to ensure accurate IOL calculations.

might recommend that ptosis surgery occur first to optimize accuracy of IOL measurements. It would be important to counsel the patient that ptosis may recur after cataract surgery, however.

Ptosis following cataract surgery is not uncommon in my practice. There are different thresholds of when cataract surgeons will refer these patients to me. Sometimes it's only a couple of months after their cataract removal because patients are significantly bothered. Unfortunately, if they come too early postop, I might tell the patients to wait a little longer as the height of the eyelid may improve gradually over time—similar to traumatic ptosis. I have seen post-cataract ptosis go away after a few months and if a surgical decision was made too early, the patient may have undergone unnecessary surgery. In the meantime, I do like to offer patients the possibility of prescription eye drops to help elevate the eyelid temporarily.

Some other factors also play into the determination of addressing ptosis before or after cataract surgery, including:

• ***Vision impairment.*** How impaired are they by their vision vs. their ptosis? If the patient is in their 90s, they may not want to undergo multiple surgeries. With ptosis surgery in particular, it's prudent to suspend all blood thinners, which temporarily increases the risk of heart attack or stroke. The benefits of ptosis surgery may not outweigh the risks of suspending all anticoagulation in some patients. In that case, it would be best to proceed with the cataract surgery just to enable the patient to get around and successfully complete their activities of daily living.

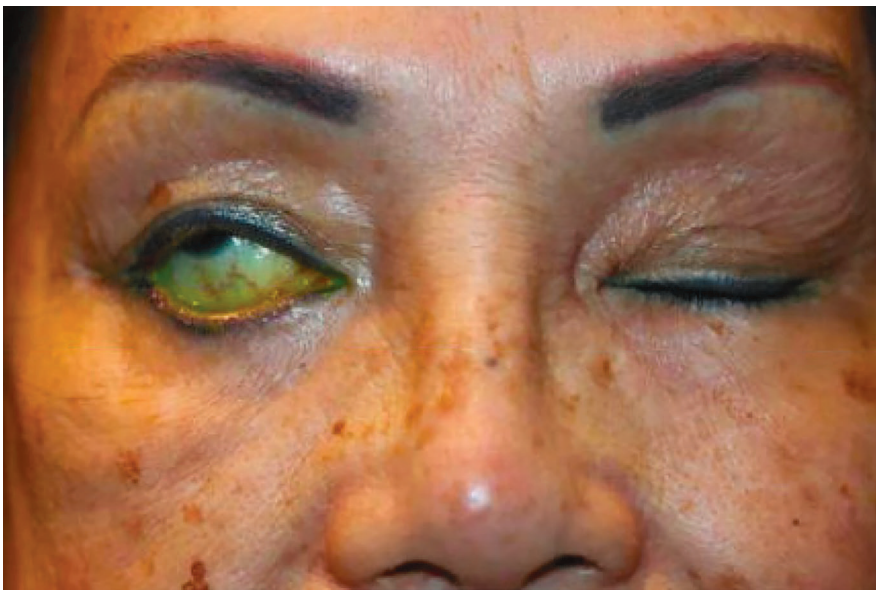
• ***Creating or aggravating dry eye.*** I'm very conservative when it comes to eyelid surgery in the setting of dry eye. If a patient has background dry eye that isn't optimized, then I almost always turn them away from ptosis surgery or even blepharoplasty because any upper eyelid-elevating surgery has the potential to make dry eye worse. I usually send them back to their ophthalmologist to work on helping their ocular surface and once the clinical signs and symptoms of dry eye have improved, I can proceed with upper eyelid surgery.

Entropion and Ectropion

Cataract surgeons are more likely to refer entropion patients for correction before surgery because in these cases, the lower eyelid has become so lax that it's actually rolling inward, causing that skin and the eyelashes to rub across the surface of the eye. It's very irritating. However, one of the biggest risks with this is endophthalmitis. When you think about the amount of bacteria on our lashes and if that were to be wiping across or near a cataract incision or the wounds, it's very unnerving.

With that said, one study showed a four-times higher risk of developing entropion of the lower eyelid in eyes that had undergone cataract surgery, compared with the fellow unoperated eye.[2] I've heard anecdotally from colleagues that they've seen new onset entropion happen even within the first week or month postop.

One caution with entropion is that sometimes it's not always there. Sometimes it's the way that the patient moves their eye around or squeezes their eyes shut that causes or induces the entropion. Applying the speculum for cataract surgery can cause worsening of pre-existing looseness or laxity



In cases of lagophthalmos/facial palsy, oculoplastics surgeons will perform a workup to determine if the condition is temporary or permanent. If temporary, eyelid surgery may not be necessary.

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ABOUT RICK

Rick Bay served as the publisher of *The Review Group* for more than 20 years.
To those who worked for him, he was a leader whose essence was based in a fierce and boundless loyalty.
To those in the industry and the professions he served, he will be remembered for his unique array of skills and for his dedication to exceeding the expectations of his customers, making many of them fast friends.

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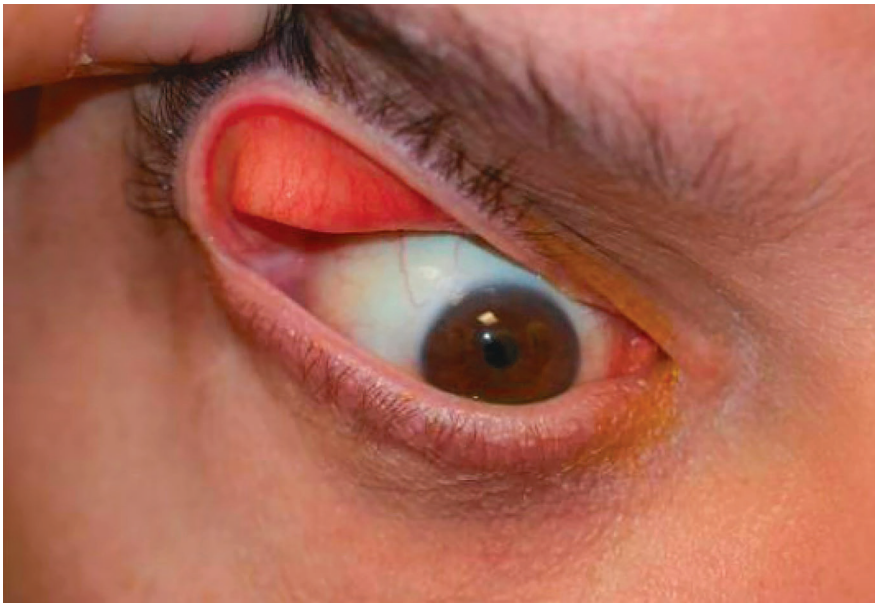
of the eyelid and that might theoretically generate the entropion or even ectropion later on.

In the case of ectropion, if the lid is loose and flipped inside out and you can see the inside of the eyelid facing out into the air, then you're probably not going to have a healthy ocular surface or maintain important eye drops that are required after cataract surgery to prevent infection and inflammation. This could decrease the efficacy of post-cataract eye drops and it's probably best to have the ectropion corrected prior to cataract surgery.

In order to correct entropion or ectropion, we sometimes over-tighten the eyelid knowing that in a few months or a few years, it's likely to loosen back up again. In this over-tightening, it's possible that the lower eyelid could push against the cornea—similar to ptosis—to a degree that causes an irregular astigmatism. I'd recommend waiting at least three or four months before cataract surgery just to make sure that the eyelid isn't so taut up against the globe that it's causing irregular astigmatism when IOL calculations are performed.

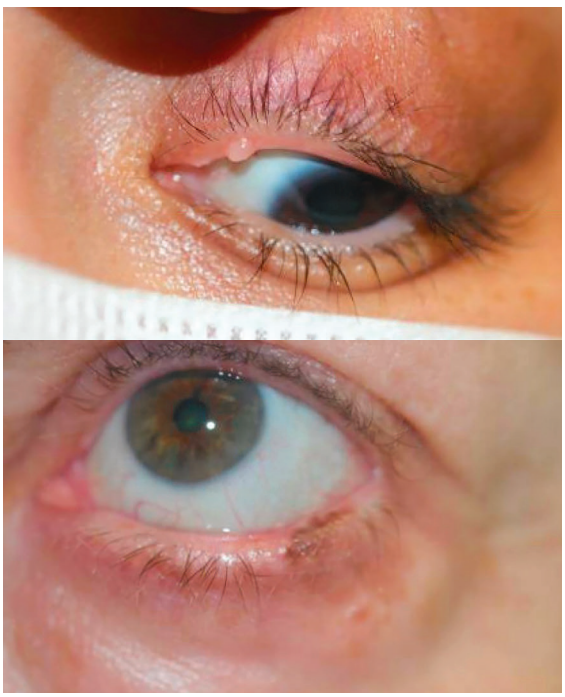


Floppy eyelid syndrome is highly correlated to sleep apnea, often unbeknownst to the patient. A sleep study is recommended and if sleep apnea is confirmed, it should be under accurate management before proceeding with any surgery.

Lagophthalmos and Floppy Eyelid Syndrome

In facial palsy/lagophthalmos, the eyelids don't close so they're not protecting the globe. First, the patient should get worked up, and when the workup is complete, it may be necessary to improve the position of the eyelids with surgery. As oculoplastic surgeons, we perform any of the following surgeries: placement of an eyelid weight into the upper eyelid to weigh down the eyelid and improve closure; we can also tighten up the paralyzed lower eyelid to aid with closure. It's also important to know the tempo of recovery—is this permanent or will it eventually improve? If temporary, eyelid surgery may not be necessary.

Floppy eyelids are highly correlated with sleep apnea. If the patient doesn't know if they have sleep apnea, it's imperative that they have a sleep study test to make sure it's diagnosed and treated before having cataract surgery. When a person has sleep apnea, they tend to toss and turn and some people actually sleep on their face. This could lead to rubbing their eyelids and their face which continues to stretch them out. We do hesitate to perform floppy eyelid surgery unless the patient is controlled with their sleep apnea, uses a CPAP machine and is able to get a full night's sleep without tossing and turning.



Benign lesions (top) don't always need to be removed before cataract surgery, but doing so may help in IOL calculations. Alternatively, suspicious lesions (bottom) such as basal cell carcinoma, should be biopsied, diagnosed and treated ahead of time.

Lesions: Benign and Suspicious

I see a good number of referrals for benign lesions that occur right on the edge of the eyelid at the waterline or margin, which can cause distortion in the ocular surface tear film. Benign lesions don't always need to be removed before cataract surgery, but I have excised them to help cataract surgeons achieve more accurate calculations.

The approach is much different if the lesion is suspicious. I believe ophthalmologists are very good at identifying the warning signs. They look for madarosis (loss of lashes); they can look at ulceration; and they look at the telangiectasias. The most common suspicious lesion is basal cell

carcinoma followed by squamous cell carcinoma, sebaceous carcinoma, and melanomas. These should be biopsied and diagnosed and treated before their cataract surgery.

Lacrimal Drainage Issues

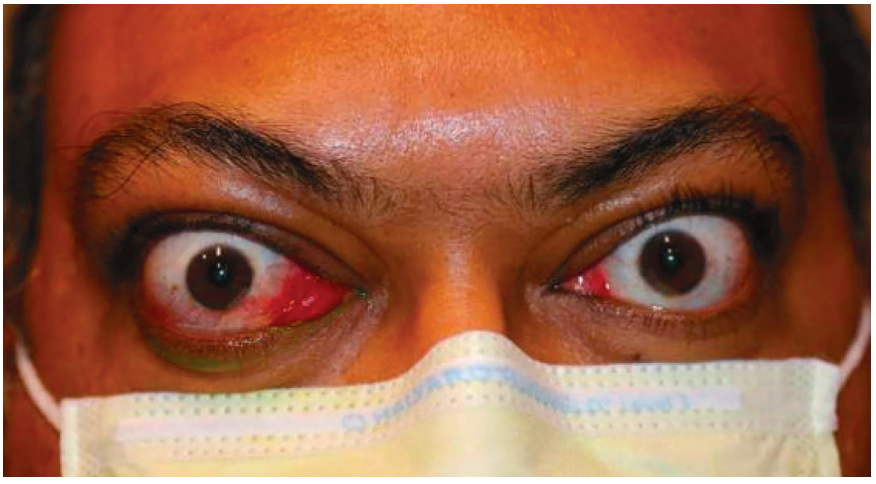
These often get underdiagnosed and overlooked. In the case of dacryocystitis, an infection of the lacrimal sac, that would clearly need to be treated because the patient has an abscess near the eye that excretes pus. Obviously cataract surgery should be placed on hold until the infection is cleared. We would treat this with systemic and topical antibiotics followed by definitive DCR (dacryocystorhinostomy) surgery with stent placement. This stent is typically left in place for two to three months, but it shouldn't interfere with cataract surgery.

Now, if the patient doesn't have an infection and has simply an acquired nasolacrimal duct obstruction, the risk of dacryocystitis is still on my mind. The lacrimal sac is accumulating tears and harboring all of the blinked-off bacteria. Even if it's not an overt infection, I wonder if there must be an in-and-out seeping of potential organisms.

In this instance, it's probably a better idea to at least have a discussion with the patient regarding whether they want to proceed with an oculoplastic surgery first or if they want to accept the risks of potential infection. I think in some countries they do preoperative antibiotic drops and potentially oral antibiotics if they have a confirmed nasolacrimal duct obstruction, and they continue that through perioperative and postoperative courses. You could also consider DCR surgery prior to cataract surgery.

Thyroid Eye Disease

Thyroid eye disease is challenging because there's such a wide spectrum. You may see a TED patient who has just a little bit of dry eye and may see another TED patient who has so much proptosis and compression of the optic nerve that they're actively losing vision. Sometimes there's some mild eyelid retraction.



Thyroid eye disease runs a wide gamut of presentations among patients. If in its active state with fluctuating amounts of orbital pressure, TED should first be stabilized before proceeding with cataract surgery.

Recently, a study that I came across looked at the refractive surprise in TED patients.[3] They analyzed more than 5,000 eyes that underwent cataract surgery in their cohort, of which 1.1 percent had TED. Postoperatively, 13.8 percent of patients with TED had a refractive prediction error greater than ±1 D. The study didn't specify if these patients had active or inactive TED, proptosis and orbital congestion, any eyelid signs or just dry eye—TED is a big bucket term—so it's unclear what exactly was happening. I'd take that study with a grain of salt.

Theoretically, if there was significant pressure in the orbit and the globe from active inflammation of TED, your measurements of the length of the globe can be distorted. In the active state, TED is volatile and patients can have fluctuating amounts of orbital pressure, which could affect your IOL calculations. If TED isn't in the active state, cataract surgery can very rarely reactivate TED.

In Summary

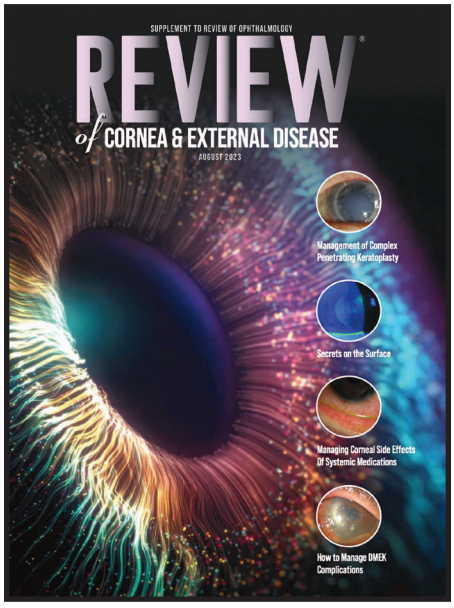
When facing oculoplastics issues in cataract patients, keep these points in mind:

- Upper eyelid malpositions can usually wait until after cataract surgery unless ptosis is very severe and can impact keratometry or corneal topography
- Laxity of the lower lids (entropion or ectropion) should generally be addressed before cataract surgery as the position of the lower eyelids impacts the health of the ocular surface
- Malignant or suspicious lesions should undergo biopsy and treatment before cataract surgery.
- Consider repairing lacrimal drainage problems before cataract surgery.
- Consider counseling TED patients about refractive surprise after cataract surgery.
- In general, allow two to three months of healing from oculoplastic surgery before scheduling cataract surgery. ◀

1. Chen PJ, Lee YK, Lai CC. Significant changes of corneal astigmatism after levator muscle surgery for acquired blepharoptosis. Ophthalmic Plast Reconstr Surg. March 21, 2024. Epub ahead of print.
2. Schulz CB, Fallico M, Rothwell A, Siah WF. Lower eyelid involutional entropion following cataract surgery. Eye (Lond) 2022 Jan;36:1:175-181.
3. Strong Caldwell A, Patnaik JL, Ackerman M, Christopher KL, Lynch AM, Singh JK. Risk of refractive prediction error after cataract surgery in patients with thyroid eye disease. Clin Ophthalmol 2021;11:15:4431-4438.

ABOUT THE AUTHOR

Dr. Lee is an associate professor of ophthalmology at Harvard Medical School and an ophthalmic plastic surgeon at Massachusetts Eye and Ear.



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TREATMENT RESISTANCE IN WET AMD

When the anti-VEGF therapy isn't working, what's next? Experts weigh in.

CHRISTINE YUE LEONARD
SENIOR ASSOCIATE EDITOR

Despite the success of anti-VEGF injections for stabilizing visual acuity and slowing progression in patients with wet age-related macular degeneration, there remains a subset of patients who experience inadequate treatment response. Fortunately, retina specialists have a number of therapeutic options at their disposal when alternative modes of treatment are required.

Here, experts discuss treatment resistance, how they monitor and treat patients who aren't responding to the initial therapy, and exciting wet AMD therapies on the horizon.

Understanding Treatment Resistance

Resistance in wet AMD may arise from a number of factors, such as genetic predisposition, variation in VEGF expression or disease characteristics. It's a difficult term to define in the wet AMD space because there isn't a set of standardized criteria for retina specialists to use when judging treatment response. According to David Almeida, MD, MBA, PhD, of Erie Retinal Surgery and director of clinical research of Erie Retina Research in Pennsylvania, differing interpretations of clinical data and subjective thresholds for inadequate response and true resistance creates variability and, he says, "leaves a lot of vision on the table."

"The substantial majority of patients respond to treatment, but some patients don't respond at all, and others don't respond as well as we'd like them to," says Sunir Garg, MD, a professor of ophthalmology at Sidney Kimmel Medical College at Thomas Jefferson University and an attending surgeon at Wills Eye Hospital in Philadelphia. "As a community of doctors, we've struggled with where to draw the line when assessing whether a patient has a complete or incomplete response. What one doctor considers to be a pretty good response, another may view as a glass half empty and call it an inadequate response."

"Each of us has our own definitions. What we typically do in the clinic is start the patient with a loading dose and assess the response," says Jay Chhablani, MD, a professor and vitreoretinal surgeon at the University of Pittsburgh School of Medicine and director of clinical research at UPMC Vision Institute. "If they don't respond after three injections of the same agent, we try to switch drugs. If they don't respond to that, we may label them as resistant or recalcitrant wet AMD."

Diagnostics and Biomarkers

When evaluating treatment response, retina specialists employ OCT and assess vision function. "Sometimes I'll get fluorescein angiography and occasionally indocyanine green angiography. Seldom I'll get OCT angiography," Dr. Garg says. "These additional modalities help us to better understand what's happening in the disease process. They can also be

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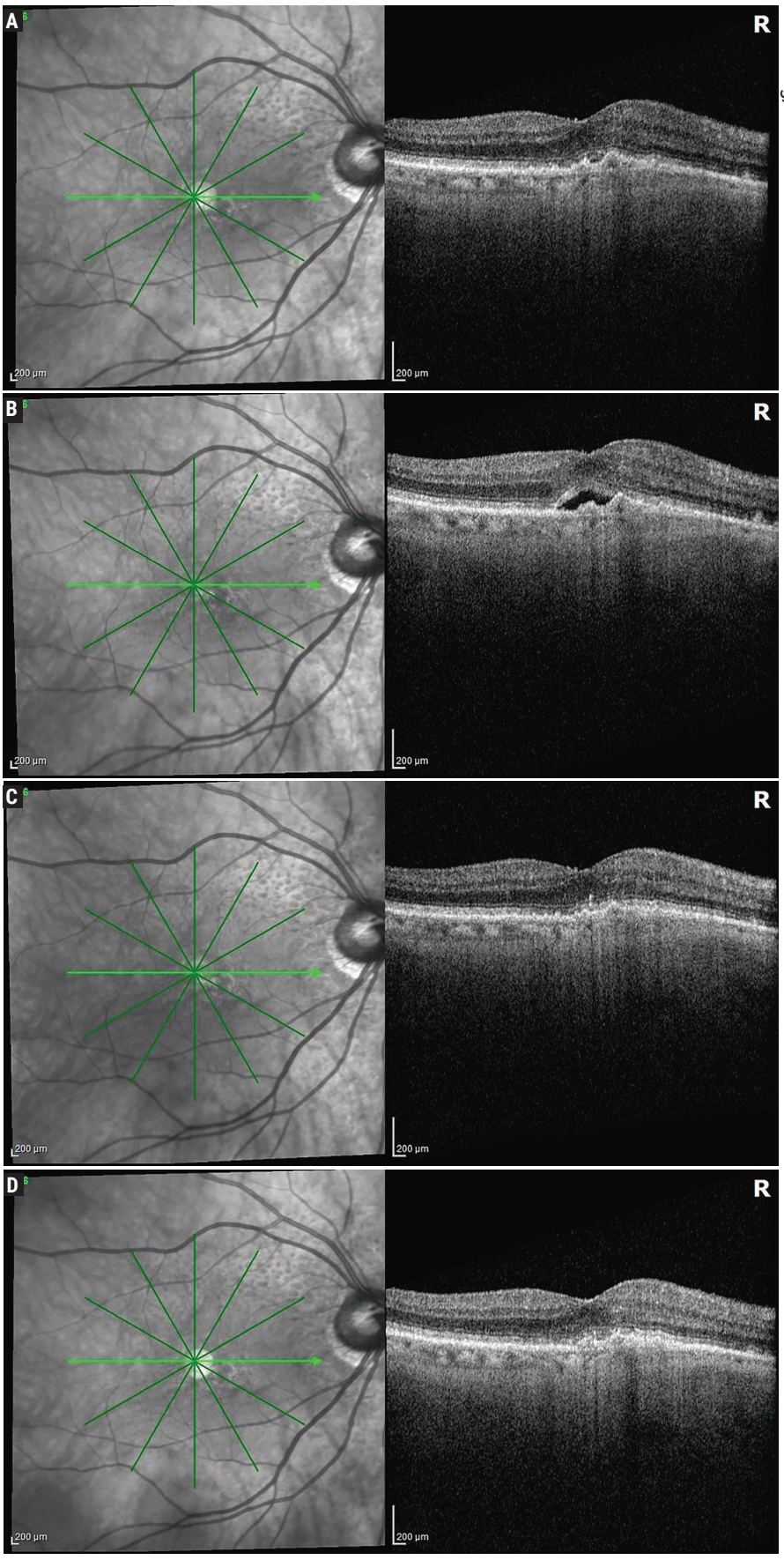
Dr. Garg is a consultant for Apellis, Bausch + Lomb and Boehringer Ingelheim and performs research for Boehringer Ingelheim, Regeneron, Roche/Genentech, Kodiak Biosciences, Apellis, Iveric Bio, NGM Bio and RegenxBio. **Dr. Starr** is an advisor for Roche/Genentech, AbbVie/Allergan, Alimera Sciences and Gyroscope Therapeutics. **Dr. Chhablani** discloses relationships with Eye Point and Iveric Bio. He has stock in Ocular Therapeutix and AbbVie, which owns RegenXBio. **Dr. Almeida** is a consultant for Roche and Boehringer Ingelheim and is a speaker for Regeneron and Genentech.



Sunir Garg, MD

useful to educate the patient in terms of what's happening, but I don't often get these additional tests.

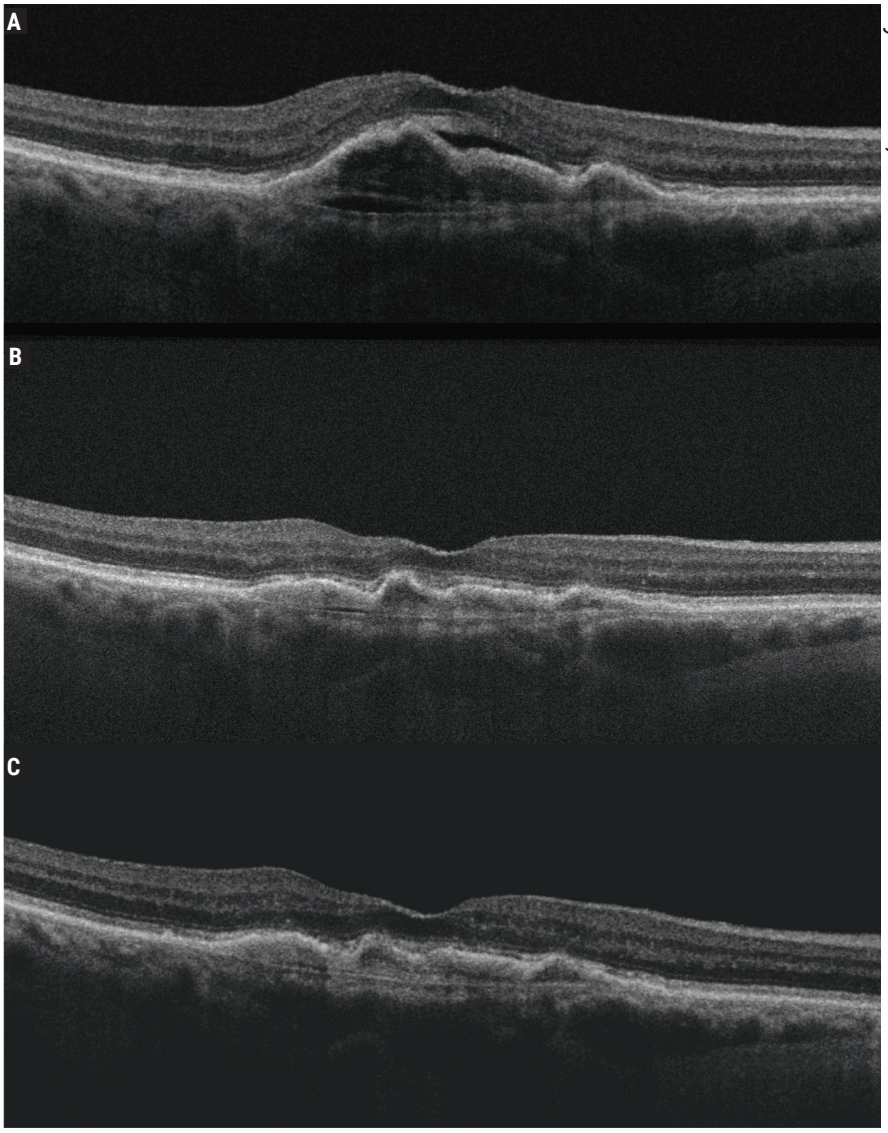
"Intraretinal fluid, subretinal fluid and subretinal fibrosis are some of the main things I look for on OCT," he continues. "I also look at fluctuations in the macular edema. One of the things we've learned from recent studies is that patients who have more consistent control of their macula edema tend to do better over the long term, compared to patients who have fluctuations in their edema, where the drug starts to wear off toward the tail end of their treatment interval, then macula thickness increases and then goes back down [with the next injection]. That seems to take a toll on vision as time goes by."

Dr. Chhablani says, "Some of the research-driven criteria I consider are pigment epithelial detachment, choroidal cleft, sub-RPE fluid and subretinal hyperreflective material or SHRM. Many of these patients present with SHRM, and when we start treatment, it's important to look at these SHRM characteristics to see whether there's a good response or not."

Dr. Almeida adds that "a good prognostic indicator that a patient may have more severe disease is if you can't make out all of the ellipsoid zone in the macula. Also look for areas of concomitant atrophy with big PED. Big PEDs and atrophy are common causes of rips, which can cause vision loss."

"It's important to always ask the patient how they're doing, because

An 82-year-old patient had a two-year history of exudative AMD in the right eye. She remained essentially fluid-free (A) with an aflibercept 2 mg injection every four weeks but had a decrease in vision and increase in subretinal fluid at five weeks (B). She then received faricimab at four weeks and was fluid-free (C), and she was able to remain fluid-free on faricimab at an eight-week interval (D).



Jay Chhablani, MD

The right eye of an 85-year-old female patient who had persistent activity with Eylea for wet AMD (A, 20/60) and after undergoing Vabysmo treatment showed a significant reduction in activity (B). The right eye was maintained at six-weekly Vabysmo with no activity (C, 20/30).

at the end of the day, my goal is to make the patient as happy as I can with their vision," says Dr. Garg. "Be sure to ask patients about their visual needs and what they're experiencing. Vision on the eye chart is an imprecise indicator of what the patient's vision is actually doing."

Management Strategies

Anti-VEGF agents are currently the mainstay of wet AMD treatment. For patients exhibiting treatment resistance, switching drugs or increasing the dosage in certain cases and shortening the treatment interval may get patients back on track.

"There are many options available in our armamentarium for patients who develop resistance to medication, whether it's a different class of drug or a biosimilar," says Matt R. Starr, MD, an assistant professor of ophthalmology and vitreoretinal surgeon at the Mayo Clinic. "We usually start with bevacizumab in my practice, and switch to faricimab or aflibercept 8 mg if needed. We've also had pretty good success jumping back to something like Cimerli and then trying something different. The Mayo Clinic has a good track record of using biosimilars for oncologic disorders, and we haven't had any problems. If I start to see a decline in visual acuity or a worsening of fluid, especially intraretinal fluid, those are two reasons I'd want to switch agents."

"When patients seem to be resistant to treatment, sometimes you just need to do the treatments more frequently, then go back to every four weeks," Dr. Garg says. "I've had a few patients who we've brought back in a two-week interval, though that's not covered by insurance. That can sometimes help to get a better anatomic response and sometimes a better visual response. In other resistant patients, I'll look to see if they have idiopathic polypoidal choroidal vasculopathy because that can respond well to photodynamic therapy and verteporfin. I'll also look for PED or subretinal hemorrhage. Typically, I can see those changes on OCT, but sometimes I'll get ICG angiography. In other patients, we'll try different drugs. Some patients do better with one particular drug over another."

The protocols for switching drugs are in part dictated by the step therapy requirements of individual insurance companies. "If I have the luxury of being able to choose drugs for patients, I'll often start them off with ranibizumab or aflibercept 2 mg, and if I don't get the response I want, sometimes I'll switch them to another agent or look into switching to one of the newer drugs," Dr. Garg continues. "Faricimab and aflibercept 8 mg weren't looked at for patients who are resistant to treatment; the studies were done on treatment-naïve patients, so we're not following the Phase III studies when doing this, but I've had really good responses. I may not be able to extend their intervals out as much as what patients see on the TV commercials, but even extending it out from five weeks to seven weeks really does alleviate a lot of the treatment burden. It's great to see."

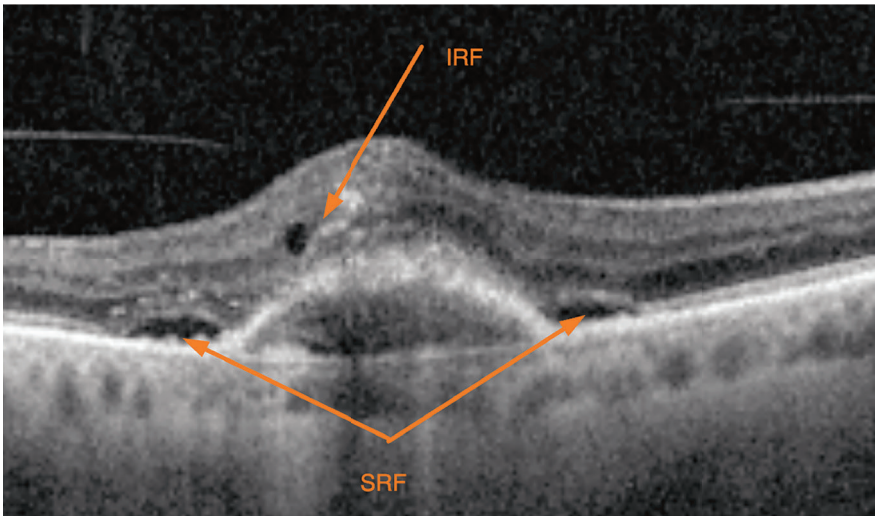
Dr. Chhablani says he has a very low threshold for switching drugs since switching in the early stage of the disease often yields a greater response than switching later in the disease stage. "Say I start a patient with a loading dose of bevacizumab," he says. "I get OCTs monthly. When they come for injections, even in the loading dose, I like to get their OCTs done and I want to evaluate how the response has been, even on one injection. If the response isn't good after two injections, I'd send the requisition for approval of faricimab, for the dual mechanism, so by the time they come for their fourth injection, they're already approved and are set to get switched to something else. Considering that faricimab is now approved by more insurances, I tend to switch patients to faricimab more frequently."

Dr. Chhablani adds that for patients who are doing well with aflibercept 2 mg but aren't able to extend out beyond four to six weeks, he'll offer them aflibercept 8 mg to extend them out to eight to 10 weeks.

Combined Therapies

For cases of PCV, combining photodynamic therapy with anti-VEGF may help. "This is the only scenario in which I'd do a combination treatment," says Dr. Garg, who combines PDT with aflibercept. "I haven't found combinations of different anti-VEGFs to be helpful clinically to me. I haven't found that adding steroids to my anti-VEGFs is very helpful either. So, it's either anti-VEGF monotherapy or occasional additional verteporfin for PCV cases."

If PCV is suspected, Dr. Chhablani says it's important to get the patient's FA-ICG done right away and consider a combination therapy in the early stages of the disease. "In cases where the patient starts on anti-VEGF, is responding and then slowly becomes resistant, get FA-ICG done. There may be a suspicious PCV network," he says. "For monocular patients who aren't responding to anything and have no PCV, I'd still consider doing a combination therapy just because sometimes they don't respond to any anti-VEGF. Doing a combination therapy gives you a double edge to work on. I definitely consider PDT as an option.



David Almeida, MD, MBA, PhD

Intraretinal and subretinal fluid, pictured here, along with other potential findings such as pigment epithelial detachment, choroidal cleft, subretinal fibrosis, sub-RPE fluid or subretinal hyperreflective material, are important indicators of a patient's disease state and are used to subjectively assess treatment response.

"One other combination I use sometimes is a steroid combination if I suspect a massive amount of SHRM or if the PED height is very high and there's a risk of RPE rip," he continues. "In those cases, I try to do steroids and anti-VEGF at baseline and then continue anti-VEGF monotherapy. I've seen good results with that."

Tips for Success

Overall, managing treatment intervals, dosage and potential different agents is a balancing act. Here are some key points to keep in mind:

• ***Reset to the loading dose.*** "For a patient exhibiting treatment resistance, one thing that works very nicely and gives both of you some time is resetting to a loading dose," Dr. Almeida says. "Going to a second-generation drug such as aflibercept 8 mg or faricimab and doing two or three loading doses gives you that continuity of seeing the patient every month for two or three months. It gives you time to see how the pathology changes, and it helps the patient understand the idea of teamwork and that you understand what's important to them. This helps you align the goals of treatment with the patient."

"Staying engaged with the patient and on top of the disease process is key," Dr. Garg says. "Sometimes I'll see patients two weeks after the injection just to better understand what their anatomic response is to the drug, when the drug is at its full strength. Keep trying different things. As long as you have your patient's best interest at heart and are working to improve their quality of life, the patients will be interested in working with you."

• ***Change the method of drug delivery.*** "If you see early on that a patient is getting worse on a second-generation product, it's a good idea to engage in a different way in order to prevent the patient from losing more vision," Dr. Almeida continues. "You have to change the pharmacodynamics of that patient. The port delivery system or Susvimo allows you to go from interrupted drug delivery to continuous drug delivery, which is completely different. This can

(Continued on page 60)

TREATING WET AMD PATIENTS WHO ALSO HAVE GA

GA can be treated after wet AMD treatment, concurrently with wet AMD treatment, or not at all.

MICHELLE STEPHENSON
CONTRIBUTING EDITOR

If patients have both wet age-related macular degeneration and geographic atrophy, the wet AMD almost always needs to be treated because it can significantly affect vision. Whether or not the GA requires treatment and whether it should be treated concurrently with wet AMD treatment depends on several factors. Here, retina experts explain how they approach these cases.

Background

Anti-VEGF injections are highly effective for treating wet AMD, while two new drugs—Syfovre (pegcetacoplan) and Izervay (avacincaptad pegol)—were approved in 2023 for the treatment of geographic atrophy.

"Wet AMD is a greater risk to vision, not so much in terms of quantitative impact, but in terms of timeline, meaning that you lose vision more quickly from wet AMD than dry AMD," explains J. Sebag, MD, who is in practice at the Doheny Eye Institute at UCLA and president of VMR Consulting, in Huntington Beach, California. "Additionally, the evidence supporting the efficacy of treatment for wet AMD is far superior to the evidence supporting the efficacy of geographic atrophy treatment. Yes, treatment slows the rate of GA progression, but there's no proof that slowing the rate of progression translates to better vision. In fact, that's the reason the EMA in Europe has twice rejected approval for those drugs because they don't believe that there is sufficient evidence of efficacy to merit approval in Europe, in spite of what the FDA did."

Dr. Sebag's approach to treating patients who have both of these conditions is to treat the wet AMD and, once that has stabilized, then direct his attention to the geographic atrophy. "In the OAKS and DERBY trials of geographic atrophy, a percentage of patients developed wet AMD," he notes. "It ranged from 2 to 11 percent in the OAKS study and from 4 to 13 percent in the DERBY study. Those patients were treated for both conditions concurrently. And that was driven by the clinical trial protocol, meaning they had to continue treating the geographic atrophy because they were in the study, but they were also obligated to treat the new problem, that being the wet AMD, concurrently. But that doesn't necessarily translate to clinical practice, and I think that there will be a variance of treatment approaches amongst practitioners."

According to David Boyer, MD, in practice in Beverly Hills, treating these two conditions isn't a one-size-fits-all treatment. "Let's assume you have a patient with geographic atrophy, and you're treating him or her every four to eight weeks. Then, that patient develops a choroidal neovascular membrane. Do you want to treat that patient? Should you be treating both conditions at the same time to avoid the patient coming up and back? Some patients may not want to stay around to have the treatment, so if you do both eyes, you're treating with the anti-VEGF first, and then you're treating with your choice of geographic atrophy medication," Dr. Boyer says.

Dr. Boyer normally does treat-and-extend. "In that patient, you may be able to extend the anti-VEGF to a much longer time period," he says. "Where does the patient live? How inconvenient is it for him or her to come in? You may settle at eight weeks even though you know that you probably can go longer with your anti-VEGF as long as they remain dry. If the patient has glaucoma,

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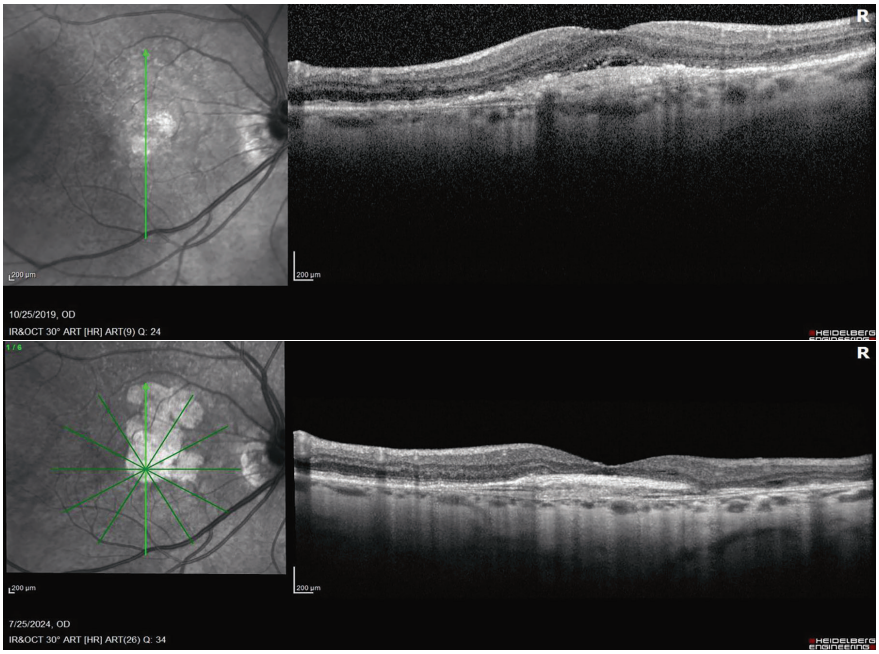
Dr. Regillo is a consultant to and receives research support from Apellis and Astellas. **Dr. Sebag** has no financial interests to disclose. Pertaining to products or product categories mentioned in this article, **Dr. Csaky** has a financial interest in Genentech, Heidelberg Engineering and Regeneron. **Dr. Boyer** is a consultant to Bayer, Genentech, Optos, OptoVue, Regeneron and Roche.

his or her pressure probably won't come down in 15 to 20 minutes. So, it's going to be much harder for them to wait around the office. They're already waiting for a considerable period of time just to get the one injection."

Another scenario is a patient who has neovascularization and then develops geographic atrophy. "You think you've got the wet under control, but the geographic atrophy is now starting to cause the patient problems," Dr. Boyer says. "You're already out two months or three months in treating the patient with anti-VEGF, so now you've got to taper. You might go six and 12 weeks. In other words, at six weeks, you would treat the patient with an anti-geographic atrophy drug, and at 12 weeks, you would treat them with both. A lot of my patients don't like two injections given at the same time. Other patients want to minimize the number of visits. Sometimes, they're wet in one eye and dry in the other eye, and you can work it out in the schedule so they get two different medications. You've got to use two different lots of medications if you're doing both eyes, and it's not easy on the patient to have two injections plus a tap if necessary."

He lets patients choose whether they want to be treated concurrently or separately. "Most of the time, they don't want to spend an extra 15 minutes here. Most of my patients don't like two injections, for some reason, especially when you're doing a tap. Additionally, you're adding one extra chance of getting an infection, one extra needle in the eye. So, for me, I try to minimize as much as I can, but you have to listen to the patient and what the patient's needs are," he says.

Carl D. Regillo, MD, director of the Retina Service at Wills Eye Hospital in Philadelphia, agrees that the active wet AMD needs to be treated and stabilized before considering GA treatment. An example is a patient who is undergoing treatment for geographic atrophy, and it turns wet. "In that scenario, I will sometimes continue the GA treatment, and sometimes I won't," he says. "However, I'll be treating the wet AMD for sure. So, in other words, if I'm treating the dry, and I usually treat every six to eight weeks with one of the two GA drugs, and the patient's affected eye turns wet, I factor in vision, symptoms, GA lesion size and location, fellow eye status, and how often the patient will need to come in to treat the wet AMD. There are a lot of variables, but at the very least, we know we must treat the wet AMD optimally and it'll take months to know how often the patient will need to come in to control the wet component of the AMD."



First visit (top), the patient has wet AMD. At the most recent visit (bottom), the wet AMD is well-controlled with anti-VEGF injections, but the GA has really grown, and the patient is now on complement inhibitors. The treatment alternates between anti-VEGF and anti-complement, once a month.

Dr. Regillo doesn't treat the same eye on the same day with both treatments. "Continuing the treatment for GA depends a lot on the patient's preferences, how often he or she needs the wet AMD treatment, and how easy it is for him or her to get to the office," he says.

Another scenario is a patient with wet AMD, who's been treated and stabilized, and he or she starts developing geographic atrophy that's affecting or threatening vision. "I will occasionally treat those patients for their GA in addition to their wet AMD," Dr. Regillo says. "I have patients who have been on wet AMD treatment and are doing really well. Then, over time, they start to have problems with geographic atrophy affecting their vision. I'll speak to them about potentially treating their GA, too. I'll treat the wet AMD, and then I'll treat the GA on different days, not the same day, and coordinate the office visits to be the least burdensome as possible. So, for example, let's say the patient is on wet AMD treatment every 12 weeks, I'll treat that same eye halfway in-between at six weeks with the GA treatment, and then have him or her come twice around the 12-week point. However, these aren't common scenarios. Usually, I'll treat an eye with one condition or the other, very rarely both. At this time, I only have a handful of these types of patients where I'm treating both conditions in the same eye."

Dr. Sebag notes that some cases of GA don't require treatment at all. "If patients have geographic atrophy that's not threatening the fovea, it shouldn't be treated," he says. "And if patients have geographic atrophy that's already wiped out the fovea, that also doesn't require treatment. There is a big difference between clinical trials and clinical practice. In practice, I have concerns that a lot of patients with chorio-retinal atrophy are

being treated, and they shouldn't be. So, in my use of those drugs, I limit it to patients who have geographic atrophy threatening the fovea. If the experience in the clinical trials is borne out in clinical practice, then that's a useful treatment, but only in a subset of patients, and I have concerns that people may not be adhering to the criteria that I just described."

Dr. Regillo agrees and says he doesn't treat cases of geographic atrophy that are at the ends of the spectrum. "I wouldn't treat geographic atrophy if it's mild, and I wouldn't treat it if it's severe," he notes. "If GA has already knocked the vision down, patients aren't very likely to benefit from that treatment. Wet AMD is always a threat. Wet AMD almost always needs to be treated."

Dr. Boyer adds that age also plays a role in the treatment decision. "If patients are successfully being treated with an anti-VEGF medication, and they develop some atrophy, do they really need to be treated if they're 90-something years old?" he muses. "The medicines only reduce the progression; they don't stop it. You don't want to stop the anti-VEGF because that will cause a significant loss of vision. It's a difficult decision."

Dallas' Karl Csaky, MD, PhD, says he doesn't use anti-complement therapy extensively as a standalone approach. "The majority of our patients who are being treated with anti-complement are usually in a clinical trial," he says. "A handful of our patients have wanted anti-complement therapy, and then I treat but it's not something that I do routinely. We're a big clinical research practice where we have probably four or five geographic atrophy trials, and most of our patients typically fit into one of those trials."

Dr. Csaky has had several cases of choroidal neovascularization in the setting of anti-complement therapy. "One of the clinical points to consider is that the appearance of CNV in the context of anti-complement therapy may present somewhat differently than the usual appearance of the CNV," he says. "Unlike our typical CNV patients, who develop excessive exudation, hemorrhage, and lots of fluorescein leakage, many of the classic features that we see in AMD patients who come into the clinic with CNV, for the patients who are on anti-complement therapy and develop some activity, the appearance can be more subtle in the cases that I've seen, albeit it has only been a handful of cases. In one case, for example, the patient presented with minimal thickening of the retina without frank intraretinal fluid."

Dr. Csaky adds that performing fluorescein angiography may not be helpful because it's very difficult to discern in a patient with GA what is just window defect, what is just noise, and what is a signal. "We know from lots of studies and experience that patients with GA tend to develop less active CNV," he says. "The choroid and choriocapillaris can be thinner, so they don't have the vascular hydraulic push that's seen when someone has a normal-appearing choroid or choriocapillaris and then develops CNV. Those CNVs are much more active; there's more exudation, it's very clear."

For this reason, he says that OCT-angiography has been particularly useful as it can help, in some cases, clearly delineate an area of CNV that may be otherwise difficult to diagnose. This can be especially helpful in determining if a small area of intraretinal fluid is simply due to the ongoing degenerative process or indeed CNV activity.

In these cases, Dr. Csaky has done both treatments on the same day, depending on patient preference. "Then, it's just more of a logistic issue of what's the best way to treat both. We typically don't necessarily stop the anti-complement therapy, because there's no reason to," he explains. "We might hold one injection while we do the first anti-VEGF, as there may be other issues that come into play when you start doing two injections in the same day. So sometimes, we'll hold off the anti-complement treatment and just do the anti-VEGF and then have the patient come back."

Dr. Csaky says that, in his limited experience, the CNV tends to respond quite well. "We have done, for example, only one anti-VEGF, and we see improvement in vision. We have seen a prompt resolution of the disease, and then these cases don't require frequent anti-VEGF injections," he says. ◀

RETINA INDUSTRY NEWS

Cholesterol-lowering Drug May Slow Vision Loss in Diabetes Patients
Findings from the LENS Trial revealed fenofibrate, a medication used for many years to reduce blood fat levels, significantly reduced the progression of diabetic retinopathy.

Vabysmo Prefilled Syringe's New Indications
The FDA has approved the Vabysmo 6 mg single-dose prefilled syringe for use in the treatment of wet AMD, diabetic macular edema and macular edema following RVO. Vabysmo will continue to be available in a 6-mg vial. Vabysmo PFS will become available to U.S. retina specialists in upcoming months, the company says.

MacTel Treatment Gets Priority Review
Neurotech Pharmaceuticals announced the FDA determined that the Biologic License Application for NT-501, an investigational encapsulated cell therapy for the treatment of MacTel, warrants a substantive review. The application has a prescription drug user fee act goal date of December 17.

Dry AMD Treatment Reaches Phase III
Stealth BioTherapeutics enrolled and dosed its first patient in the ReNEW trial for elamipretide in patients with dry AMD.

Ocugen Retinal Trials Advance
Ocugen announced the first patient was dosed in its Phase III liMeliGhT clinical trial for OCU400, a gene therapy candidate being developed for retinitis pigmentosa. The company also announced it will proceed with a high dose of OCU410ST, a gene therapy candidate for Stargardt disease.

Cohort III and Phase II Approved for Simultaneous Enrollment in ArMaDa Study
Ocugen announced a positive outcome of the Data and Safety Monitoring Board Review for its Phase I/II ArMaDa clinical trial for OCU410 (AAV5-hRORA), a modifier gene therapy candidate in development for geographic atrophy. Six subjects with GA were dosed in the Phase I/II clinical trial to date—three with the low dose and three with the medium dose. An additional three patients will be dosed with the high dose of OCU410 in the dose-escalation phase.

ACIOLS: FUNDAMENTAL OR FADING OUT?

Although these lenses haven't had the best reputation, some surgeons continue to believe in their utility and say they should remain in the cataract armamentarium.

LIZ HUNTER
SENIOR EDITOR

The choice a cataract surgeon makes when confronted with an eye that has little to no capsular support is the source of one of ophthalmology's most heated debates. Should an anterior chamber lens be inserted, or would one of the many posterior chamber lens fixation techniques work better? These days, most surgeons would probably opt for the latter option, leaving the humble ACIOL fighting to maintain relevance in a fixation-friendly world.

We asked cataract surgeons to discuss the risks associated with ACIOLs, the instances when they may actually be preferred over a posteriorly fixated lens and why all anterior segment surgeons—including residents—should continue to keep this technique in their toolkit. Read on for what they had to say.

The Risks vs. Reality

There are a few reasons ACIOLs carry some inherent risks, according to surgeons.

Physiologic location is one. "Some of the issues that surround the use of ACIOLs are related to the placement of the lens in the anterior chamber in front of the iris that puts it in closer proximity to the cornea," says Mark Kontos, MD, a cataract and refractive surgeon in Washington state. "In patients who may have initial weaknesses to the cornea, such as Fuchs' dystrophy, having an anterior chamber lens close can sometimes precipitate problems with the cornea to where they develop cloudiness that's unable to resolve. There's also a risk of developing a persistent corneal edema or other issues that could be problematic for the vision. In patients who are younger, having an anterior chamber lens could be a problem for them as far as the health of their cornea as they grow older."

Others highlight the design of the lens as its biggest fault. Early ACIOL designs featured rough edges on the haptics, which caused damage to the cornea and gave rise to the flexible-loop ACIOL. Uveitis-glaucoma-hyphema syndrome was one of the most common complications associated with ACIOLs due to its contact against the iris, although the condition has become more rare as phaco techniques have evolved.[1]

"With the evolution of PCIOLs and extracap, ACIOLs were reserved for use in the event of complications—broken capsule, displaced nucleus, vitrectomy," says Douglas K. Grayson, MD, who is a cataract and glaucoma specialist practicing in New Jersey, as well as an attending surgeon at New York Eye and Ear Infirmary. "Surgeons would implant an ACIOL as a last resort. The cornea was already obscured, the patient was uncomfortable and it was more about getting a lens in and finishing the case. In those scenarios, ACIOLs were suboptimal—they caused synechiae, UGH syndrome, CME and secondary glaucomas. Those were situations where a lens probably shouldn't have been placed at all. The patient should have been left aphakic and brought back another day under control to have a lens implanted."

Dr. Kontos says incision size also contributes to complications. "In order to place this lens, you have to

This article has no commercial sponsorship.

Dr. Grayson consults for Alcon, Glaukos and Johnson & Johnson Vision. **Dr. Kontos** is a consultant for Alcon. **Dr. Packard** has no relevant disclosures. **Dr. Shen** has no financial disclosures.

make a pretty large incision—5.5 to 6 mm," he explains. "That can create irregular astigmatism to the cornea or create difficulties with the wound, such as wound leaks. Because the lens rests on the iris, it can sometimes cause abnormalities in the shape of the pupil that aren't necessarily a functional problem, but cosmetically they could be an issue for the patient. Sometimes you can get persistent inflammation because of the haptics touching on the iris in such a way that creates an inflammatory response."

ACIOL sizing is another concern of Richard Packard, MD, FRCS, FRCOphth, who now consults for Arnott Eye Associates in London. "If it's too small the lens can propeller inside the eye and damage the endothelium ," he says. If your peripheral iridectomy doesn't work well, the iris can bulge around the IOL. The iris could also fixate around the haptics so it decenters the pupil. All manner of things could happen.

"However, if you compare the results in outcomes, there isn't that much of a difference," he continues. "It's a moot point."

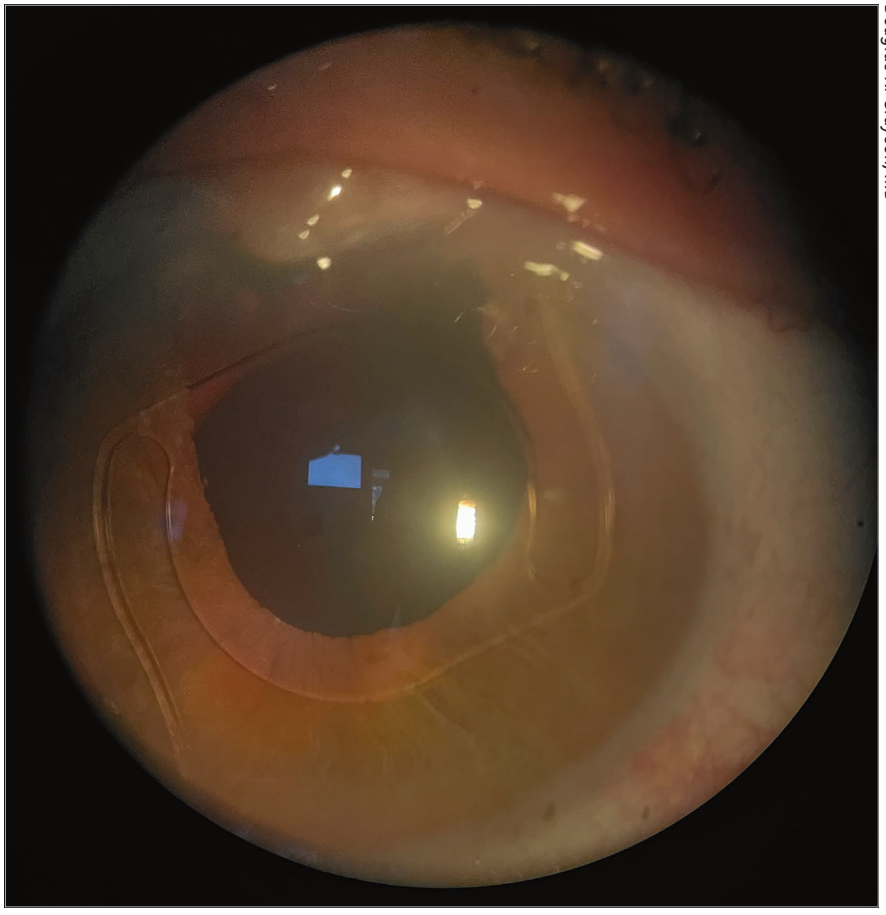
Several studies support this. In 2005, researchers at Bascom Palmer Eye Institute compared the clinical outcomes and complications of patients who received an ACIOL vs. a sutured PCIOL after cataract surgery resulting in poor capsular support. They concluded that there were no significant differences in outcomes and went as far as to say that "a reconsideration of ACIOL condemnation is warranted" and "placement of an ACIOL may be considered a comparable, or even favorable, alternative [to transsclerally sutured PCIOLs] depending on the surgeon's training and patient characteristics."[2]

Approximately 15 years after that was published, an updated study reinforced the continued safety profile of ACIOLs. Published in 2020, a retrospective case study of 45 peer-reviewed pieces of literature evaluated eight different types of IOL fixation techniques:

- ACIOL;
- iris-claw IOL;
- retropupillary iris-claw IOL;
- 10-0 polypropylene iris-sutured posterior chamber IOL;
- 10-0 polypropylene scleral-sutured PCIOL;
- 8-0 polypropylene scleral-sutured PCIOL;
- CV-8 polytetrafluoroethylene; and
- intrascleral haptic fixation.

Evidence showed no superiority of any single technique, and researchers determined each one had equivalent visual acuity outcomes, safety profiles and its own risks of postoperative complications.[3]

Joanne Shen, MD, an ophthalmologist at the Mayo Clinic in Scottsdale, Arizona, and a coauthor of that study, says the current ACIOL design available is the least traumatic in its evolution. "Our study did show that there may be some higher association of cystoid macular edema and anterior chamber inflammation with an ACIOL," she notes. "This is obviously because of where the IOL sits, and this research wasn't a clinical trial so we'll never have definitive data to say ACIOLs are unsafe or safe. You can't say it across the spectrum."



Douglas K. Grayson, MD

A well-positioned ACIOL with superior iridectomy and filtering bleb.

Appropriate Times to Use an ACIOL

Despite the increasing popularity of PCIOL fixation techniques, the cataract surgeons we spoke with say there are plenty of reasons to keep ACIOLs in the realm of options for patients lacking capsular support.

"I've always maintained that in a controlled circumstance, anterior chamber lenses of modern design are excellent if you measure for the correct size," says Dr. Grayson. "They're put in as a secondary procedure where

the person's already aphakic, and they're very well-tolerated. If they're placed in the angle correctly, they don't cause corneal decompensation. Any problem that may be related, such as CME, which can't be resolved with medications or injections, you have a very clear-cut source you can look with and say, 'Aha, see this one haptic may be a little bit off and that may be causing it.' So you could do a secondary procedure to rotate the anterior chamber lens and relieve that source of irritation. So, the AC lens is a very useful tool."

For Dr. Kontos, any decision depends on the situation, and often age is a large part of it. "Every case is going to be a unique scenario, and in certain scenarios, I think using an anterior chamber lens is perfectly fine," he says. "As long as the patient has a relatively healthy cornea, has a large or deep anterior chamber, and there aren't any other issues going on, such as vitreous in the anterior chamber, you can probably use an ACIOL and do fine with it, especially in older patients. In a patient who's in their late 70s or 80s, doing a simple surgery with an ACIOL can sometimes be a lot easier than going through the more complex surgery when you have to suture a posterior chamber lens. There can be situations where, during cataract surgery, the case can become complicated and perhaps you have no capsular support and have lost the lens into the back of the eye or something, you could place an anterior chamber lens if everything else is okay. This way you at least get a lens in the patient so that they could be functional. It's important to have ACIOLs available in the operating room area, just in case of that emergency situation."

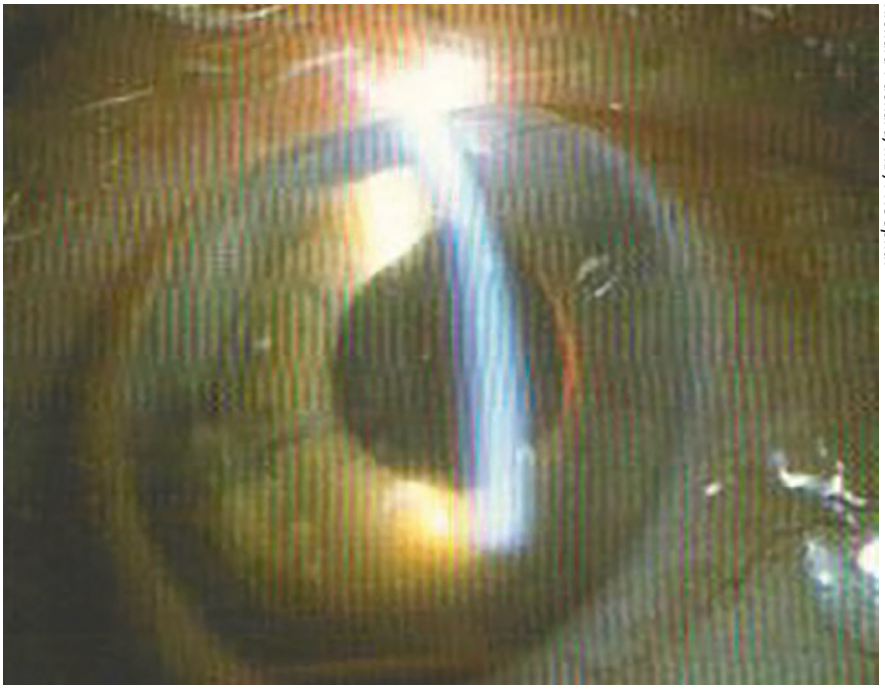
Dr. Grayson poses an example of a scenario when an ACIOL could be the best option. "If a patient had a displaced PCIOL that had been in place for 15 years," he says, "and, say, due to pseudoexfoliation, the one-piece lens had to explanted. So, the lens is explanted, you wait about a month until the cornea is clear and everything's calm. Now you can put in an ACIOL, after measuring carefully and picking the right size. That's one clinical scenario where it was an uncomplicated removal of a displaced one-piece lens, and they just have a nice AC lens and they can move on."

Dr. Shen says she also considers the patient's proximity to the clinic. "If you practice in a rural area, you may never see that patient again," she says. "It's likely they're going to go back and see their local optometrist or other non-surgeon. This is important because the downside of some of these newer fixation techniques is they have erosions of the sutures or the haptic. This requires monitoring.

"On the other hand, with an ACIOL, you don't have to monitor them as closely to make sure nothing's peeking out of the surface that might allow bacteria to enter into the eye and cause endotheliitis and blindness," she continues. "I personally have some patients who live about three to four hours away. I'm probably not going to be able to see them every six months, realistically. I also think about if they're in a nursing home; if they have dementia. These are things that we as surgeons have to factor in."

ACIOLs also require very few instruments to insert, Dr. Shen notes. "We have to factor in what our operating room has," she says. "Do we have all the instruments and the technology to do some of these newer techniques of suturing, such as the Yamane technique and scleral fixation? You can't just perform those with the bare bones like the ACIOL, which doesn't require much technical equipment. It's pretty straightforward."

"There's much more that has to take place for choosing a PCIOL," says Dr. Kontos. "It requires more skill on the part of the surgeon and there's a lot of variability that can occur. There can be problems with erosion of the haptics, or other issues that can create problems and the need to go back and do revision surgery. If you can avoid all of those things by doing a simpler surgery that the patient can tolerate, then I think it's a perfectly appropriate course of action."



Richard Packard, MD, FRCOphth

Uveitis-glaucoma-hyphema syndrome was a common complication caused by ACIOLs and is often cited as a reason to avoid implanting them.

PCIOLs and the various fixation techniques have their own drawbacks. "We're seeing a lot of these fixation techniques creating some of the same problems as the first generation of PCIOLs did, including tilt, CME, erosions, UGH syndrome," says Dr. Grayson. "There are a fair number of Yamane revision cases that have been sent to me."

Dr. Shen says the scleral-fixated techniques don't work well if a patient has had trauma, leaving the wall of their eye damaged and thinned. "If the sclera has been damaged, you may not have anything to sew to," she says. "Imagine you're trying to hang a picture on a wall, but every stud has been eaten by termites, so you don't know where to hang it on the wall."

She's also concerned about the amount of torque these PCIOLs are undergoing. "These lenses aren't designed to be torqued in this manner with the haptics that are typically supposed to be in one plane being bent forward," says Dr. Shen. "What are we going to see in 10 years? Time will tell. Ultimately, none of these IOLs have been FDA labeled for these insertion techniques, including the sutured IOLs. If you look at the FDA labeling, there isn't anything that says, 'This is how you sew it on, this is what you use to sew it on.' That was never discussed in the labeling."

Surgeon Skills and Access

Even though surgeons can make the case for ACIOLs, they acknowledge the gap in training and access to the product.

"When I was training in the '90s, ACIOLs were the standard," says Dr. Shen. "If you couldn't put a lens in the bag or in the sulcus, you did an ACIOL. I'm in my 50s now, so for me and others in this generation and above, we're still comfortable with this procedure. But the newer generations, they're also learning eight different types of IOL fixation techniques, with different types of sutures and lenses."

It's also not incredibly common to run into this type of complication during residency.

"It's probably difficult to learn in residency because the opportunities to place an anterior chamber lens are limited, and in a lot of residencies, you may not see one because of just how advanced cataract surgery has gotten over the years," Dr. Kontos says. "The need to place an ACIOL is so much more rare than it used to be. When I was a resident, it was just something you were definitely going to see and do at some point. But now it's really not quite that way. It's very conceivable to imagine an ophthalmology resident going through their entire residency without seeing an ACIOL placed. If that's the case, it behooves you to learn and have some sense of it because I think it's a skill that's important to have. Just like anything, there's going to be a time or two where that makes the most sense for the patient, and it's a good idea to be able to have the ability to do it."

> **It's never going to be commonplace, but I think there's always going to be a place where an ACIOL is an appropriate option for a patient, as opposed to the sutured IOL.**
>
> ***— Mark Kontos, MD***

"Younger ophthalmologists in training who have a complication where parts of the nucleus are going posteriorly, the previous generation would have maybe converted to an extracap procedure and tried to remove that nucleus in total to prevent posterior displacement, and possibly have them put in an ACIOL if things were calm enough, or we'd come back and do the AC lens two or three weeks later," says Dr. Grayson.

"But what happens now is, when a complication occurs with the nucleus going posteriorly, they'll close and defer to retina," he continues. "In the previous days, retina would remove the nucleus and then send it back to the anterior segment surgeon to do some form of a lens. Now, retina specialists are trained in doing these sutured secondary lenses. I try to get my residents at New York Eye and Ear to at least become familiar with it so they know how to use it. But I think the anterior segment surgeons are losing their secondary lens skills."

There's also the matter of keeping ACIOLs on hand for surgeries. Currently, only Alcon and Bausch + Lomb manufacture these lenses. Dr. Packard says surgeons should have a bank of them ready, with at least three sizes for each IOL power.

"It's never going to be commonplace, but I think there's always going to be a place where an anterior chamber lens is an appropriate option for a patient, as opposed to the sutured IOL," says Dr. Kontos. "When you're doing cataract surgery and you're not really anticipating the need for one, it's a good idea to just use them as part of your planning process to say, 'Okay, if something catastrophic were to occur here and I can't get a lens into the posterior chamber or posterior capsule area or sulcus fixed, can I put an anterior chamber lens in this patient? Do we have them available in the surgery center if I need it?'"

"Pre-planning for an AC lens will lead to successful use of the lens," seconds Dr. Grayson. "In a complicated cataract procedure that's gone on for an hour, don't try to just jam in a lens. Leave the patient aphakic, let everything clear, let the cornea clear, let the eye heal, and then another day you can do an AC lens with a vitrectomy if you need to, or you could do a pre-planned sutured lens.

"But the point of it is, and I teach residents this, if things have gone badly and it's an extended period of time, never be afraid to just hold off on the lens, wait until things cool down, and then go on and do your

lens later," he continues.

Surgical Pearls

Technique is important for ACIOL success, so we asked these surgeons to share their top tips:

• ***Sizing and lens power***. Dr. Packard says correct lens sizing is critical. "If it's too small it could be more dangerous because it will propeller inside the eye and damage the endothelium," he says. "You could use standard calipers to measure white to white and wound size, Stahl caliper, Kelman dip stick or OCT. You also need to remember to recalculate your A-constant."

• ***Wound construction***. Dr. Kontos says it's best to make a temporal wound for these lenses. "It's important to be able to have good wound construction," he says. "You want to make sure that you don't have a shallow wound that can allow the haptic of the anterior chamber lens to get caught into the wound. You want to make sure that you've gone into the cornea a little ways so you have a posterior lip when you insert the lens, that it's going to be wedged back into the proper place in the angle, and it doesn't have an easy way to slip right up into the wound. Make sure that the wound is well-sealed at the completion of the surgery."

"I use a 6-mm, peripheral clear corneal incision for the AC lens, rather than doing a scleral tunnel," says Dr. Grayson. "It gives you better visibility, placement and angulation to put the lens in. Close the wound with three sutures, and on a peripheral corneal wound, you don't induce astigmatism, and patients do very well."

• ***Constrict the pupil***. "Another pearl involves constricting the pupil so that the iris is somewhat taut when you insert the lens," says Dr. Kontos. "It's a good idea to use Miochol for these cases to try and constrict the pupil as much as you can. It makes it a much easier process, and it's less likely to get the iris hung up on the haptics as you're sliding the lens in."

• ***Visualization***. Dr. Kontos says to make sure the placement of the haptics are in the angle above the iris and not rubbing up against the cornea or caught up and entangled into the iris itself. "The haptics should be resting on the surface of the iris and not embedded in the iris in any way," he says. "It's helpful to use a Sheets glide, which acts as a scaffold by which you can slide the lens into place, and then you can remove that fairly easily. That's a good technique and a good piece of equipment to have handy if you're going to be using an anterior chamber lens."

• ***Peripheral iridectomy/iridotomy***. Dr. Grayson says, "In any secondary lens procedure, a peripheral iridectomy is important, whether it's done by laser or surgically."

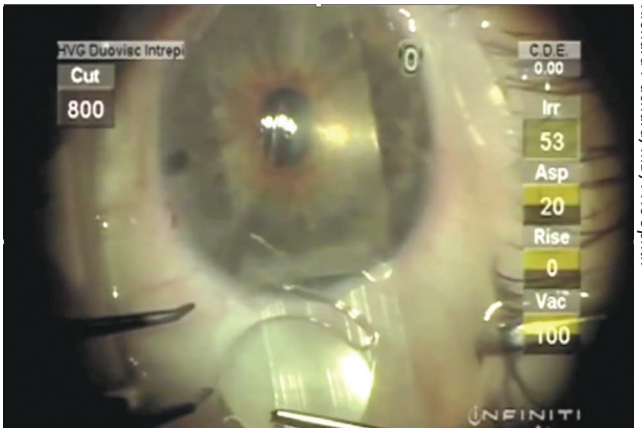
"It's something that can be simply done at the temporal wound area," adds Dr. Kontos. "You can just grab a piece of proximal iris that's close to the angle and make a small little cut with Van Ness scissors, and that gives you a peripheral iridectomy to eliminate any possibility of angle closure."

"You can do your peripheral iridectomy quite easily with a vitreous cutter," suggests Dr. Packard. "You just turn the cut rate down to as low as you possibly can, use a bit of suction on the iris for a split second on the foot pedal, and you've got your iridectomy."

• ***Lens orientation***. If placing the lens temporally, rotating it with the haptics oriented vertically is a good idea, suggests Dr. Kontos. "That also helps to make sure that the lens haptics are seated properly, making sure that you're placing the lens in the right configuration," he says. "It does have a right-side up. The lens is vaulted slightly anteriorly. So it's important that when the lens is being inserted, that you're inserting it in such a way that the anterior vault is facing outward towards the surface of the cornea. If you place it inverted in the other way, then it's going to be pressing down into the iris, and that's going to create some problems over the long term."

• ***Check for vitreous***. Before completing the case, use triamcinolone to ensure no vitreous is left in the anterior chamber, recommends Dr. Packard.

In conclusion, Dr. Packard says, "Whoever you are as a surgeon, you should have your 'Get Out of Jail Free' technique for when things have gone significantly pear-shaped, and you don't have anything to support a lens by way of the capsule. You should feel competent and comfortable with this technique so when things go bad, you know you can still end up giving the patient a satisfactory outcome." ◀



Richard Packard, MD, FRCOphth

Surgeons say a Sheets glide is a handy tool for ACIOL insertion as it helps create a scaffold to slide the lens into place.

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

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

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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.

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THE PRESBYOPIA DROP PIPELINE

For physicians and patients open to pharmaceutical treatments for presbyopia, new options may be arriving soon.

ANDEW BEERS
ASSOCIATE EDITOR

Miotic eye drops are traditionally used for the treatment of glaucoma, but many pharmaceutical companies are developing their drugs with a different approach in mind. Since these solutions constrict the pupil, ultimately creating a pinhole effect, researchers and clinicians have found the topical therapy useful for the treatment of presbyopia. Now, the presbyopia eye drop market is open, and companies are racing to get their product approved for commercialization.

Here's a breakdown of what's available and what's to come for presbyopia eye drops.

Miotic Agents

Vuity (AbbVie) was the first presbyopia eye drop to be approved by the U.S. Food and Drug Administration. This is a 1.25% pilocarpine solution, which is one of the miotic solutions commonly used in other presbyopia eye drops. What researchers have found is that the most frequently used miotic agents for glaucoma are essentially the easiest approach for treating presbyopia.

"Pilocarpine and carbachol are the two miotic drops that were most commonly used in glaucoma," says Richard Lindstrom, MD, the founder of Minnesota Eye Consultants in Minneapolis. "They increased the facility of outflow of the aqueous reducing eye pressure and these drops were showing efficacy in that regard. But there were others as well that were in a different category called acetylcholinesterase inhibitors. Nobody's really tried to bring those to the market for presbyopia because they're very powerful. They have a relatively high side effect profile, and they last a very long time, sometimes 24 to 48 hours."

Besides pilocarpine and carbachol, there are other miotic agents currently under investigation for the treatment of presbyopia. One solution, aceclidine, has been around since the 1960s to treat glaucoma and, at the time, was considered a safer, but slightly weaker, alternative to pilocarpine.[1] Another solution, brimonidine tartrate, has been available since 1996 and was approved for managing ocular hypertension and glaucoma.[2] It's also been found in over-the-counter products to reduce redness from minor ocular irritations.

When it comes to using miotics for presbyopia, doctors should consider the concentration of the solution before prescribing it. "The higher the level of concentration of any miotic, the smaller the pupil," explains Dr. Lindstrom. "And my bias is something in the low twos, or 1.8 to 2.4 mm, as a pupil size that I personally as a clinician think is a good target. You can get even better near vision in a bright light if you go smaller than that. There's also the possibility of getting longer durability, if you will, meaning longer duration of action with the higher concentrations or with other compounds."

Interestingly, one off-label indication for miotic solutions is for treating other refractive errors in tandem with presbyopia. "The interesting thing about miotics is that in the bright light, they're good both for near and distance vision," states Dr. Lindstrom. "And I think one thing that hasn't been talked about a lot is the fact that on a bright sunny day, besides helping you see better up close, they also improve your distance vision, right? So, if you have

This article has no commercial sponsorship.

Dr. Lindstrom is on the Medical Advisory Board and an equity owner of Orasis Pharmaceuticals.

higher order aberrations or if you have low levels of refractive error, maybe a little astigmatism or a little myopia or hyperopia, miotic drops improve your vision."

Also, miotics have been considered to reduce pupil size in patients who struggle to drive at night. "If you're a young person wearing contact lenses, which have optical zones in the 6 mm zone or so, if your pupil dilates at night beyond that, then you tend to get halos," mentions Dr. Lindstrom. "Also with certain intraocular lenses, you sometimes get unwanted visual images at night. Miotic drops can help many of those patients as well by basically reducing the impact of higher-order aberrations and the astigmatism that go along with those situations."

Latest Market Approval

In 2023, the FDA approved Orasis Pharmaceuticals' low-dose, preservative-free eye drop, Qlosi. Originally CSF-1, this eye drop uses a 0.4% pilocarpine solution for the treatment of presbyopia.

The pooled results from Qlosi's NEAR Phase III trials demonstrated how the solution is safe and effective for presbyopes.[3] Researchers from two Phase III trials enrolled a total of 613 subjects between October 2020 and February 2022. Patients were excluded from the trials if their distance-corrected near visual acuity at 40 cm in one eye wasn't approximately between 20/50 to 20/160 Snellen at baseline. Each of the subjects, ages 45 to 64, were selected randomly to either receive Qlosi (n=309) or the vehicle (n=304). In order to be successful, the subjects had to achieve at least a three-line gain from baseline in DCNVA at 40 cm without losing one or more lines of CDVA at 4 m on the eighth follow-up day after an hour has passed since their first dose was administered.

According to the results, 40.1 percent of subjects in the Qlosi group achieved the studies' primary endpoint compared to 19.1 percent of subjects in the vehicle group. When testing each group at different times on day eight of the trials, the researchers discovered that the percentage of subjects who responded positively to Qlosi was significantly more than those in the vehicle group. Subjects from the Qlosi group reported ocular treatmentrelated adverse events such as instillation site pain (5.8 percent), vision blur (3.6 percent) and conjunctival hyperemia (1.6 percent) as well as non-ocular adverse events such as headache (6.8 percent), instillation site/facial pain (1.9 percent; described as brow ache) and nausea (1.3 percent). Additionally, no serious adverse events were reported.

"The most common side effect that we've known for decades when you apply a miotic drop is brow ache or headache," says Dr. Lindstrom. "There are still some patients who can get a brow ache or a headache when they take even the lower concentration pilocarpine drops. Now, what we've learned from years using them for the treatment of glaucoma is that if patients use them regularly, then those side effects tend to diminish or even disappear. The other thing we've learned, interestingly enough, is that if you just take an aspirin or an Advil 30 minutes before you put the drop in your eye, that tends to reduce the frequency of that type of side effect significantly as well. But the main thing that reduces the frequency is the use of lower concentration of pilocarpine.

"The thing that's unique about Qlosi is it has a very comforting vehicle as far as the solution that the pilocarpine is placed in," continues Dr. Lindstrom. "So, the vehicle is basically a topical lubricant. It has hydroxypropyl methylcellulose and sodium hyaluronate, and it's really comforting when you put it in the eye. The quality topical lubricant tends to enhance your vision rather than reduce it because many patients also have a little bit of a dry eye. In a sense, you're applying a pilocarpine plus an artificial tear when you put Qlosi in your eye."

Make sure to explain to patients that Qlosi has been approved for

For safe use, instruct patients to administer Qlosi at least five minutes apart from other topical ophthalmic medications and avoid contacting the ocular surface with the eye dropper.

PRESBYOPIA-CORRECTING EYE DROPS APPROVED AND IN THE PIPELINE

Name	Company	Active Ingredient	Mechanism of Action	Approval Status
Vuity	AbbVie	Pilocarpine 1.25%	Miotic	FDA approved
Qlosi	Orasis Pharmaceuticals	Pilocarpine 0.4%	Miotic	FDA approved
Microline	Eyenovia	Pilocarpine 2%	Miotic	Phase III trials completed
LNZ100	Lenz Therapeutics	Aceclidine 1.75%	Miotic	Phase III trials completed
Brimochol	Visus Therapeutics	Carbachol + Brimonidine Tartrate	Miotic	First of two Phase III trials completed
Nyxol +low-dose pilocarpine	Ocuphire Pharmaceuticals	Phentolamine ophthalmic solution 0.75 % + low-dose pilocarpine 0.4%	Miotic	Phase III trials are ongoing

twice-daily administration for up to eight hours of activation. The prescribing information states that it can be administered a second time three to four hours after the original dose. If a patient normally wears contact lenses, they should remove them before administering Qlosi. After 10 minutes, the patient can reinsert their lenses. Qlosi is scheduled to hit the market sometime this year.

Presbyopia Drop Pipeline

Currently, Vuity and Qlosi are the only two FDA approved miotic solutions for the treatment of presbyopia, but there are several others in development in the pipeline.

• ***LNZ100, LNZ101 (Lenz Therapeutics)***. In April of this year, Lenz announced positive topline results from its Phase III CLARITY trials for LNZ100 and LNZ101. These topical drugs both use 1.75% aceclidine as the mechanism of action, but LNZ101 incorporates 0.08% brimonidine with the hope of improving the performance of aceclidine on the pupil. After assessing the trial results, Lenz decided to move forward with LNZ100 as a commercial candidate and dropped LNZ101, since it showed similar results to the standard aceclidine solution without improving its performance. They made plans to submit a New Drug Application to the FDA in mid-2024.

The CLARITY 1 and 2 studies examined a total of 698 subjects randomized into a 1:1:1 ration between LNZ100, LNZ101 and a control (CLARITY 1 = 0.08% brimonidine, CLARITY 2 = vehicle). CLARITY 1 had a larger patient population, with a total of 469 accepted subjects. For the studies' primary endpoint, a significant percentage of subjects would need to achieve a ≥3-line improvement to their near vision assessed over a 10-hour time period. Secondary endpoints recorded were the percentage of subjects achieving at least a two-line improvement to near vision, the mean impact to distance vision when exposed to normal light over time, and the percentage of subjects achieving the primary endpoint on days one, 15 and 28, at 30 minutes, three hours and 10 hours post-dose. Adverse events were also reported.

According to the results, 71 percent of LNZ100 subjects from CLARITY studies achieved the primary endpoint 30 minutes into the trial compared to 12 percent of subjects on the control group. After 10 hours, the longest duration of action, 40 percent of LNZ100 subjects maintained the primary endpoint, while 5 percent of subjects in the control group achieved this goal.

Subjects in the LNZ100 group continued to meet their endpoints throughout the CLARITY studies. One hour after administration, 95 percent of LNZ100 subjects achieved two or more lines of improvement in their near vision and 69 percent of these subjects maintained this throughout the 10-hour time period. LNZ100 subjects' vision improved by two to four letters of distance vision in normal light without any negative impact. Furthermore, after 28 days, 82 percent of LNZ100 subjects achieved the originally set primary endpoint at 30 minutes, 78 percent of subjects achieved this at three hours and 35 percent of patients achieved this at 10 hours post-dose.

"Aceclidine was used in the glaucoma field and the strength of it, as I look at it, is that it has a longer duration of action," says Dr. Lindstrom. "So, if you want a drop that lasts longer, then it will last longer with a single drop, and at the concentration Lenz is using makes for an even smaller pupil. In bright light, it's going to have better near vision."

The most common adverse events reported across the CLARITY studies were instillation pain (20.1 percent), visual impairment defined as mild dimness (13.2 percent), hyperemia (9 percent) and headache (11.5 percent).

• ***Brimochol (Visus Therapeutics)***. In 2023, Visus Therapeutics announced positive topline results from their Phase III BRIO-I trial for Brimochol, a combination of carbachol and brimonidine miotic agents. This is the first drop to show a statistically significant "combination-of-elements" in presbyopia, which is an FDA requirement for fixed-dosed combination products.

According to the BRIO-I study, subjects receiving Brimochol had to achieve at least a 15-letter gain in near visual acuity without a loss of five or more letters at distance. If this was maintained and observed at various time points over a six-hour period, then the primary endpoint would be met. Although a statistical analysis has yet to be published, a total of 182 subjects were administered Brimochol in which 49.4 percent of them achieved the primary endpoint through the 45-day trial.

Brimochol was successful in achieving its secondary endpoints during the BRIO-1 study. There was a statistically significant number of subjects who

achieved a 10-letter gain when testing at near, and there was a statistically significant number of subjects whose near visual acuity achieved at least 20/40 Snellen. Additionally, Brimochol subjects gained two letters of distance vision after eight hours post-dose and was statistically significant compared to the results from subjects in the control group.

Some minor adverse events were reported during the study. Eye irritation (14.04 percent) and headache (8.99 percent) were among the most common events. A second Phase III trial, BRIO-II, is underway with more safety and efficacy results possibly coming out this year. This study will observe subjects over a 12-month period and will focus on the long-term effects of Brimochol.

• ***Nyxol (Ocuphire Pharmaceuticals)***. Phentolamine Ophthalmic Solution 0.75% is a preservative-free eye drop from Ocuphire Pharmaceuticals. It was FDA approved in 2023 for the treatment of mydriasis under the name Ryzumvi. The company is pushing for the approval of their ophthalmic solution for the treatment of presbyopia, currently titled Nyxol. They've completed gathering topline data from their VEGA-2 Phase III trial but haven't published any results.

The results from the VEGA-1 Phase II trial showed positive results for improving near visual acuity. During the study, a total of 74 subjects were administered a single drop of Nyxol and 73 subjects were administered a placebo. After 12 hours, the subjects' distance corrected near visual acuity was assessed. The percentage of Nyxol subjects who gained ≥15 letters in DCNVA was 30 percent compared to 14 percent of placebo subjects. More subjects were able to achieve a ≥10-letter gain in DCNVA, with 53 percent of Nyxol subjects achieving this endpoint compared to 28 percent of placebo subjects.

Nyxol subjects experience mild adverse events such as hyperemia, but no headaches or brow aches were reported. Ocuphire has an alternative solution for presbyopes which includes a low dose of pilocarpine along with phentolamine to improve visual acuity further. The addition of pilocarpine didn't promote any adverse events.

• ***Microline (Eyenovia)***. In 2022, Eyenovia announced positive results from their VISION-2 Phase III study of Microline. Since then, not much news has come out about Eyenovia's decision to move forward with the 2% pilocarpine solution, but some data had been released before then.

Subjects from the VISION-2 trial were able to achieve at least 15 letters of DCNVA improvement without losing five or more letters of distance vision. Additionally, less than 3 percent of subjects reported some adverse event, which were all mild and/or transient.

Microline is administered using Eyenovia's Optejet technology, a device that dispenses approximately 8 µL of solution into the eye without the need to tilt the head. This is much smaller compared to the amount of solution dispensed using a traditional eye dropper. This allows the patient to gain the full effect of the solution without wasting any product.

"[Presbyopia eye drops are] new and we're learning, and we've got a lot more to learn, but it's going to be a positive for the eye-care professional," says Dr. Lindstrom. "And I would say that means both for the MD and the OD or the physician's assistant and nurse practitioners who're seeing these patients." Currently, 128 million Americans are affected by presbyopia.[4] This is nearly 90 percent of the U.S. adult population over the age of 45. The need for presbyopic treatments is growing, which means the need for new treatment options is critical. Having presbyopia eye drops in physicians' armamentariums will give them the opportunity to satisfy the ever-growing patient population.

"We've got another useful tool in our toolbox and we're going to have more than one option in that toolbox as well with different concentrations and different active pharmaceutical ingredients," says Dr. Lindstrom. "Over the next five years, we're going to learn how to help patients benefit from that new modality." ◀

Eyenovia

To ensure presbyopes receive the necessary dosage of Microline, the Optejet is fitted with 109 laser-drilled ports within the spray nozzle which allows for more control over the direction of the spray.

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Managing IOP After Keratoplasty

Tips for how to avoid and reduce high pressures and glaucomatous damage after corneal transplant procedures.

JOANN GIACONI, MD
LOS ANGELES

Glaucoma and elevated IOP are common but challenging complications to wrangle following corneal transplantation. They may arise from various factors such as synechiae, inflammation and steroid use, impacting keratoplasty outcomes. Here, I'll explore strategies to control high pressures and minimize damage to the optic nerve, and discuss the importance of coordinated care between cornea and glaucoma specialists.

Risk Factors and Mechanisms

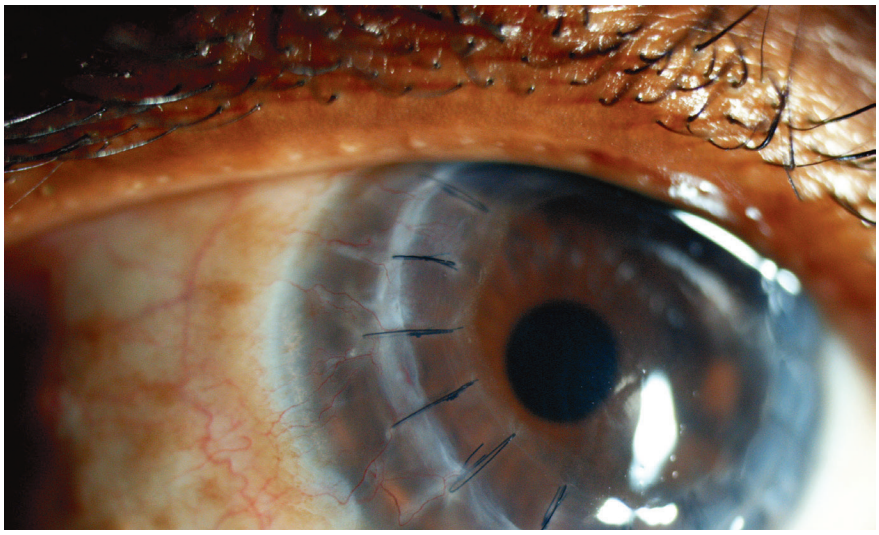
The incidence of glaucoma after penetrating keratoplasty is reported to range from 9 to 31 percent in the early postoperative period and from 18 to 35 percent in the late postoperative period, with incidence variation owing to differing definitions of glaucoma.[1] Causes of high IOP and glaucoma after PK include angle distortion and collapse of the trabecular meshwork due to tight, long, superficial sutures; large-diameter trephine use; same-sized or undersized grafts; retained viscoelastic; inflammation; steroid response; PAS formation; and exacerbation of pre-existing glaucoma. The last two of these are among the leading causes of increased intraocular pressure or glaucoma following a PKP procedure.

Steroid response and pre-existing glaucoma are the leading causes of high IOP and glaucoma after endothelial keratoplasty. Other causes include higher preoperative IOP, air bubble-induced angle closure, retained viscoelastic, PAS formation and inflammation. Additionally, certain EK indications, such as bullous keratopathy, are also associated with an increased risk of glaucoma and glaucomatous progression than other conditions.[2] IOP elevation after lamellar keratoplasty has been reported to occur at a lower incidence than following PK, potentially a result of less surgically induced angle and trabecular meshwork damage and a reduced need for postoperative steroids.[3] A study of 1,657 eyes reported the 10-year probability of glaucoma-related vision loss to be 1 percent after EK, 2.1 percent after ALK and 3.6 percent after PK (p=0.036).[3]

Avoiding Complications

Corneal surgeons must pay extra attention to those patients who go into surgery with established glaucoma. These are the patients who are most likely to have problems with pressure and progressive glaucoma after surgery. Gonioscopy is a must preoperatively to establish if the risk factor of PAS is present, and it should be performed periodically after the corneal transplantation, especially if IOP rises.

When performing PK, using over-



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For penetrating keratoplasty, using a slightly oversized full-thickness graft and placing sutures evenly may have some IOP-related benefits. For EK procedures, be sure to place an iridotomy inferiorly.

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sized donor tissue may confer some IOP-related benefits. Additionally, ensure sutures are evenly placed and avoid compressing the angle. In EK procedures, acute angle closure can occur because of the air or gas bubble, so it's important to make an iridotomy. Place it inferiorly to avoid occlusion by the bubble when the patient is upright.

Medical Management

Management of keratoplasty-induced glaucoma or high IOP requires careful monitoring in the immediate postoperative period. Perform frequent pressure checks to catch acute IOP increases and treat with topical medications. For chronic pressure increases due to steroids, taper off the steroids as quickly as is safely possible while balancing the risk of a graft rejection. Initiate topical drops as necessary. If the view of the angle is good, laser trabeculoplasty can be performed.

Managing topical glaucoma therapy requires careful consideration to both the glaucoma and corneal health. High pressures need to be managed, but many topical glaucoma medications have some degree of corneal toxicity. This toxicity may irritate the cornea while a PK graft re-epithelializes in the immediate postoperative period. Pilocarpine 4% and brimonidine 0.1% and 0.15% were reported to induce 60-percent epithelial cell death at four hours; pilocarpine 2% and latanoprost 0.005% resulted in nearly 100-percent toxicity after 16 hours; and timolol 0.5% and pilocarpine 1% induced 40-percent cell death at 24 hours.[4]

Switching to or initiating preservative-free topical medications can help avoid punctate epitheliopathy or other ocular surface irritation. Some BAK-preserved alternatives include preservative-free timolol, brimonidine preserved with Purite and travoprost preserved with Sofzia. Lamellar keratoplasty usually leaves the epithelium intact and glaucoma drops can be continued.

Reports of carbonic anhydrase inhibitors contributing to graft or corneal failure are rare, but if a graft has been in place for a long time and has significant endothelial cell loss, maintain suspicion of the CAI if the graft develops thickening or edema in the absence of rejection. Stop the CAI and observe whether the edema reverses. A recent patient of mine who didn't have a corneal transplant experienced vision loss and her cornea was noted to be very thick with mild Descemet's folds. After stopping the CAI and substituting with another medication, her cornea returned to normal, and her vision improved. She was happy that the solution involved switching medications rather than a step up in therapy.

> **Glaucoma specialists should be aware of and be prepared to check for signs of corneal graft rejection and communicate with the cornea specialist.**

Surgical Management

If the patient's pressure can't be controlled medically, surgery should be done to protect the optic nerve. Nerve damage can occur rapidly if pressures are high, so it's important to examine the nerve periodically.

Tube shunts are commonly performed in PK patients, often because the conjunctiva is scarred already in these eyes, perhaps due to past trauma or past surgery. If the conjunctiva is healthy, trabeculectomy is a suitable approach, especially given tube shunts' association with higher rates of endothelial loss, which puts the graft at risk for failure.

When implanting a tube shunt in a patient who's had a corneal transplant, ensure the tube enters below Schwalbe's line. Tube entry anterior to Schwalbe's line is a risk factor for endothelial cell loss. If the patient is pseudophakic, sulcus placement is recommended to keep the tube far from the corneal endothelium.

Co-managed Care

It's important to stay in contact with the patient's co-managing specialist. Glaucoma specialists should be aware of and be prepared to check for signs of corneal graft rejection and communicate these occurrences with the cornea specialist.

Also be sure to counsel patients about the need for two specialists. Many patients may be confused why they have to see two different doctors. They may have questions about the number of visits needed or it may be burdensome to attend so many appointments.

Discuss care with the co-managing specialist. Will they completely cede the follow-up of the optic nerve and visual fields to the glaucoma specialist, or will the cornea specialist also check for those things? When there are two clinicians managing a patient who doesn't want to have to come for all those visits, it's easy to assume the other clinician will do the dilating, for example. There needs to be a clear understanding of who's going to do what for the patient. ◀

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Best Practices for Managing RAO

When time is of the essence in a case of RAO, here's how to best respond with the proper treatment.

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First described by Albrecht von Graefe in 1859,[1] retinal artery occlusions are a well-known cause of significant visual morbidity. As suggested by Graefe's initial work, patients with the condition may harbor serious underlying pathology, which may be life-threatening. Over the past 150 years, the etiologies, pathophysiology, clinical features, and natural history of RAOs have been extensively investigated.

More recently, to help RAO patients mitigate vision loss, prevent secondary cerebral stroke, and improve their quality of life, there has been a paradigm shift in the way health-care teams think about acute painless vision loss. When it comes to retinal artery occlusions, "time is retina," much like "time is brain" for ischemic stroke.

In this article, we discuss the most recent guidelines regarding the workup and evaluation of patients with suspected RAOs and review the current evidence for proposed therapeutic interventions.

Pathogenesis

RAOs occur due to partial or complete cessation of blood flow through the central or branch retinal arteries. Once the initial vascular event has occurred, the compromised blood supply to the inner retinal layers leads to near immediate ischemia. Cytotoxic edema develops with resultant retinal whitening on fundoscopic examination *(Figure 1A)*. Subsequently, a period of inflammation occurs in response to the damage. Thereafter, retinal atrophy and thinning develop around six weeks from the initial occlusion.

In clinical practice, a major question arises as to when irreversible damage occurs. In the rhesus monkey, irreversible damage to the retina begins around 105 minutes[2] after the inciting vaso-occlusive event, with massive irreversible retinal damage by 240 minutes.[3] Of note, this experimental model involved placing a microclamp on the central retinal artery; the fidelity of this complete clamping model to the pathophysiology of real-world CRAs is unknown. More recent work proposes that complete occlusion of the CRA may result in retinal infarction in 12 to 15 minutes;[4] however, cautious interpretation of this timeline is warranted as the claim is extrapolated indirectly from the brain-ischemia literature.[5,6] Moreover, the real-world frequency of complete vessel occlusion as compared to partial vessel occlusion is

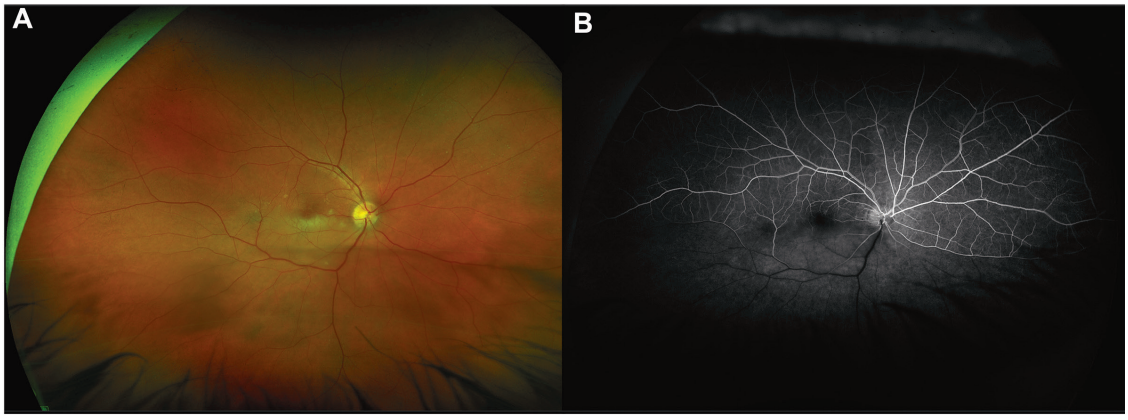

Figure 1. Multimodal imaging of an acute branched retinal artery occlusion. A) Color fundus photograph of a patient with decreased vision that started 24 hours prior to presentation who was found to have inferior retinal whitening along the macula with associated emboli that was consistent with a branched retinal artery occlusion. B) Fluorescein angiogram at 30 seconds of the same patient highlights delayed perfusion of the inferior retina.

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unknown. Persistent retinal arterial perfusion beyond occlusions on fluorescein angiography and retinal vessel boxcarring further suggests partial vessel occlusion in at least some RAOs.

Etiology

Retinal artery occlusions may occur due to a diverse array of etiologies. The most common causes of RAOs are summarized in Table 1. The vast majority of RAOs are embolic in nature (95 percent), with only 5 percent representing an arteritic etiology. Embolic RAOs may be differentiated based on exam features. Cholesterol emboli are the most common type and appear yellow, whereas platelet fibrin emboli appear gray, and calcium emboli appear white. One study found that among RAO emboli, 74 percent were cholesterol, 15 percent were platelet-fibrin and 11 percent were calcific.[9]

Less common types of emboli include tumor (e.g., atrial myxoma),[10,11] leuko-embolus (e.g., pancreatitis),[12] fat,[13] air[14] and septic[15] emboli. In one prospective study of cardiovascular risk factors for CRAOs, 20 percent of patients with CRAO were found to have atrial fibrillation.[16] Emboli causing CRAO may occur spontaneously or may be provoked in the setting of a recent intravascular procedure, such as cardiac catheterization.[17] Injected cosmetic facial filler may embolize causing CRAO.[18–20]

There are also multiple non-embolic etiologies of RAOs. Atherosclerosis of the central retinal artery may result in a RAO. Ocular trauma can lead to CRAO,[21] with proposed mechanisms of insult including endothelial damage[22] as well as direct vessel compression from optic nerve edema.[23] Coagulopathic conditions, such as antiphospholipid syndrome,[24] homocystinuria,[25] protein S deficiency[26] and nephrotic syndrome,[27] may cause CRAO. Patients presenting with central retinal vein occlusion may infrequently have a concomitant RAO *(Figure 2)*.[28]

A variety of inflammatory conditions have been linked to RAOs. These include giant cell arteritis (GCA),[29] systemic lupus erythematosus,[30] polyarteritis nodosa,[31,32] granulomatosis with polyangiitis[33,34] eosinophilic granulomatosis with polyangiitis,[35,36] Behçet disease,[37,38] Takayasu arteritis[39] and fibromuscular dysplasia.[40,41] Susac syndrome is another inflammatory condition that may cause RAO.[42] The condition is characterized by multiple infarctions of the retina, cochlea and central nervous system; as such, patients may present with a triad of vision loss, sensorineural hearing loss and encephalopathy. Recurrent RAOs in the same patient should raise suspicion for the condition.[43,44]

Rarely, infectious conditions have been implicated in RAOs such as SARS-COV-2 (COVID-19),[45–49] *Plasmodium falciparum* (malaria),[50] *Rhizopus oryzae* (mucormycosis)[51] and *Mycobacterium* tuberculosis,[52] among others.

RAO have also been reported after a number of ocular procedures and surgeries including retrobulbar anesthesia,[53,54] intravitreal anti-vascular endothelial growth factor injection,[55] cataract surgery with anterior vitrectomy,[56] cataract surgery with sub-Tenon's anesthesia[57] and Descemet's membrane detachment repair with pneumatic descematopexy,[58] among others. Intraoperative factors that may increase risk for procedure-related RAO include IOP fluctuation as well as the use of adrenaline-containing anesthetic agents.[59] Non-ophthalmic surgeries with face-down positioning may precipitate RAOs via prolonged extrinsic compression on the eye, as has been reported in association with spinal surgery.[60–62]

Malignancy has also been associated with RAOs; neoplastic infiltration of the optic nerve with CRAO has been described in patients with leukemia[63–65] and lymphoma.[66] CRAO has also been described in patients with solid malignancy, such as one patient with metastatic breast cancer involving the eye leading to combined CRAO and CRVO.[67]

TABLE 1. ETIOLOGIES OF RETINAL ARTERY OCCLUSION

Group	Condition
Embolus	cholesterol platelet-fibrin calcium tumor leuko-embolus fat air septic cosmetic filler
Inflammatory	giant cell arteritis systemic lupus erythematosus polyarteritis nodosa granulomatosis with polyangiitis eosinophilic granulomatosis with polyangiitis Behçet disease Takayasu arteritis fibromuscular dysplasia Susac syndrome
Coagulopathy	antiphospholipid syndrome homocystinuria protein S deficiency nephrotic syndrome
Infectious	SARS-COV-2 (COVID-19) *Plasmodium falciparum* (malaria) *Rhizopus oryzae* (mucormycosis) *Mycobacterium* tuberculosis
Malignancy	leukemia lymphoma metastatic solid tumor (e.g., breast)
Trauma	direct ocular insult carotid artery dissection chiropractic manipulation strangulation
Procedural	cardiac catheterization face down positioning (e.g., spine surgery) retrobulbar anesthesia intravitreal anti-VEGF injection cataract surgery with anterior vitrectomy cataract surgery with sub-Tenon's anesthesia Descemet's membrane detachment repair with pneumatic descematopexy
Other	atherosclerosis of central retinal artery ophthalmic artery aneurysm Moyamoya disease

Symptoms

Patients with RAOs may report symptoms of monocular vision loss that is sudden (seconds) and painless. Vision loss may include a total visual field defect or a hemifield defect in the case of a branch occlusions. There may have been transient episodes of vision loss (amaurosis fugax) that preceded

the permanent vision loss.[68–70] The duration of vision loss should be reported and patients should be queried regarding recent events such as trauma, surgery/procedure or recent illness.

In patients over the age of 50, symptoms of GCA should be assessed and documented (malaise, fatigue, myalgia, fever, temporal and scalp tenderness, jaw claudication, headache and diplopia). Preceding trauma with neck or facial pain should raise suspicion for carotid artery dissection[71,72] and prompt further investigation.

Patient Evaluation

In all cases of suspected RAO, a thorough medical history should be conducted. Clinicians should review the patient's medications as well as medical, ocular and surgical histories. Particular care should be given to systemic cardiovascular disease, hematologic conditions, malignancy and rheumatologic issues.

The degree of vision loss in RAO is often related to the location of the occlusion in the vascular tree. Among patients with BRAO, 74 percent of patients had an initial visual acuity of 20/40 or better; whereas in those diagnosed with a CRAO, 74 percent had an initial visual acuity of count fingers or worse.[73] In contrast, patients with occlusion of the ophthalmic artery often have a presenting visual acuity of light perception only or worse. An isolated cilioretinal artery occlusion should prompt consideration for GCA workup.[74]

Fundoscopic evaluation of RAO will reveal a cascade of pathologic changes to the retina. As the retinal nerve fiber layer becomes edematous due to ischemia, retinal whitening will occur in the distribution of affected perfusion. In cases of CRAO, a cherry-red spot appears in the fovea due to the histologic absence of the retinal nerve fiber layer in this region *(Figure 3)*. The degree of retinal edema may serve as a proxy for the degree of retinal ischemia.[75,76] In four to six weeks following the occlusion, the retinal whitening dissipates. During this period, the retinal vessels become attenuated; other late stage retinal findings include macular retinal pigment epithelial changes and cilioretinal collaterals.[77]

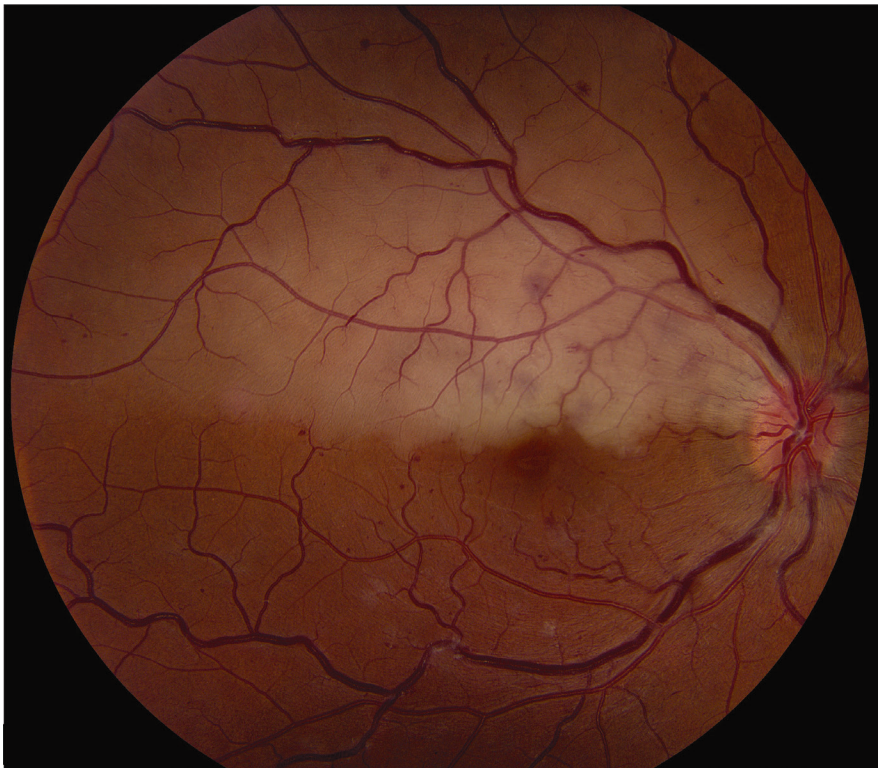

Figure 2. Color fundus photograph of a patient presenting with a combined retinal artery occlusion and central retinal vein occlusion. Fundus examination demonstrates increased vascular tortuosity, scattered intraretinal hemorrhages and retinal whitening along the superior macula.

In most cases of RAO, the optic disc initially appears normal or unaffected by the condition. However, optic disc edema with RAO may signal involvement of the posterior ciliary arteries or an occlusion of the ophthalmic artery. In this scenario, a vasculitis involving the posterior ciliary arteries should be considered, including GCA. In one prospective study of patients with biopsy-proven GCA, 14 percent of patients had concurrent RAO and 81 percent had anterior ischemic optic neuropathy.[29] In the late stages of RAOs, the optic nerves may develop pallor.[77]

Imaging

Multimodal ocular imaging may assist in confirmation of an RAO diagnosis but may not be required as the diagnosis can be made clinically. Importantly, ancillary imaging testing shouldn't delay transfer to a stroke center, as suspicion for RAO is a medical emergency requiring stroke evaluation.[78]

Optical coherence tomography is often the quickest modality to confirm the diagnosis. In the acute period after occlusion, the inner retina has increased thickness and appears hyperreflective from the ischemic process, whereas the outer retina appears hyporeflective *(Figure 4A)*. OCT features may disclose prognostic information to the clinician as well: Increased central macular thickness on OCT at baseline may be related to worse final vision and suggested an increased degree of ischemia in one study.[79] Within four to six weeks from the initial event, the inner retina appears thin and atrophic, while the outer retina laminations and RPE/choriocapillaris remain unchanged *(Figure 4B)*.[80]

Fluorescein angiography may serve

as a useful diagnostic tool when the etiology of the RAO is unclear *(Figure 1B)*. Choroidal perfusion is typically normal in FA of RAO; however, perfusion abnormalities of the choroid in suspected RAO suggests involvement of the posterior ciliary arteries (such as in GCA) or a more proximal lesion such as an ophthalmic artery occlusion. Choroidal perfusion defects on FA in the absence of emboli on examination should warrant a GCA evaluation as part of the stroke workup.

Systemic Evaluation

Upon initial diagnosis of a retinal artery occlusion, transfer to a stroke center for evaluation is a crucial step, as risk of strokes is significantly increased, especially within the first one to four weeks.[81,82] In one study, 23 percent of patients with CRAO showed acute brain infarcts on MRI within an average of 24 hours from symptom onset. Among those patients with acute brain infarcts, 89 percent reported no additional neurologic symptoms.[83] Another study found that 71 percent of non-arteritic CRAO had internal carotid plaques and that 52 percent of non-arteritic CRAO had abnormal echocardiogram with a suspected embolic source.[84] With regard to mortality risk, a population-based study in South Korea found that patients with RAO had a 7.33 higher risk (standardized mortality ratio) of all-cause mortality as compared to that of age-matched controls in the general population.[85]

A stroke workup often involves a neurology consultation with a prompt systemic evaluation for carotid occlusive and thromboembolic disease. Urgent imaging is often acquired including MRI brain, echocardiography, electrocardiogram and/or carotid artery dopplers. Systemic laboratory evaluation may include fasting blood sugar, hemoglobin A1C, complete blood count with differential and lipid profiles. In younger patients (under 50 years old), a workup for vasculitis or hypercoagulability may be indicated. In patients over 50, one must additionally suspect GCA; urgent corticosteroid therapy should be considered when GCA is diagnosed or is very likely to preserve vision in the affected eye and contralateral eye.

Despite the potential for systemic comorbidities upon initial RAO diagnosis, studies have indicated that urgent transfer to a stroke center upon RAO diagnosis may be limited by practice patterns, health-care system resources and patient medical literacy, among other factors.[86,87] Part of these discrepancies may arise when patients present with symptomatic vs asymptomatic RAOs. Acute, symptomatic RAOs should prompt an immediate referral to the nearest stroke referral center for prompt assessment for consideration of an acute intervention. The precise timing of evaluation for patients with an asymptomatic but newly diagnosed RAO is unclear, though these patients still warrant a timely referral. In our practice, all patients with asymptomatic BRAOs or CRAOs are routinely referred for an expedited stroke workup.

To minimize delays in care, treating ophthalmologists are encouraged to establish relationships with local stroke centers in their respective areas of practice. Resources should be directed towards alerting community practitioners in neurology, primary care and emergency medicine that acute, painless monocular visual loss can be a stroke analogue that needs to be assessed at a stroke center. Education regarding the potential impact that this diagnosis may have on their patients' future risks of stroke, myocardial infarction and death is also essential.

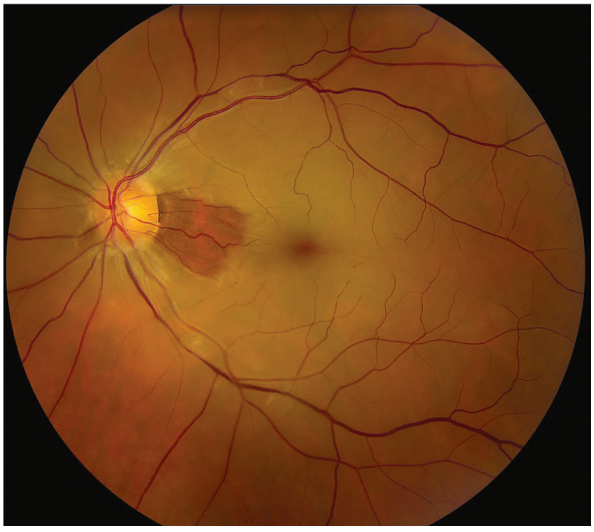

Figure 3. Color fundus photograph of a patient with a central retinal artery occlusion with cilioretinal sparing. There's a cherry red spot with associated retinal whitening involving the entire macula except for the area of the cilioretinal retinal artery along the nasal macula.

Treatment

Despite the significant interest, a safe and effective treatment remains elusive for RAOs. The sensitivity of retinal tissue to ischemia makes the therapeutic window for intervention in RAO small, likely between 90 to 240 minutes.[2,3] If an effective treatment were to become available, this narrow window would likely require significant public health education and health-care resource allocation to translate to a real-world reduction in visual morbidity. Current treatment guidelines focus on harm reduction for further sequelae of the underlying etiology of the RAO.

Several interventions have been trialed, though most have yielded ineffective or mixed results; moreover, some of these interventions confer considerable risk for serious side effects. A reduction in intraocular pressure to decrease resistance of retinal arterioles has been proposed as one treatment mechanism. Such a mechanism can be achieved via IV acetazolamide or mannitol, topical intraocular pressure drops, or anterior chamber paracentesis. Digital ocular massage leads to fluctuation in intraocular pressure to theoretically propagate the clot distally. Other proposed mechanisms of treatment include vasodilation to increase blood oxygen content using

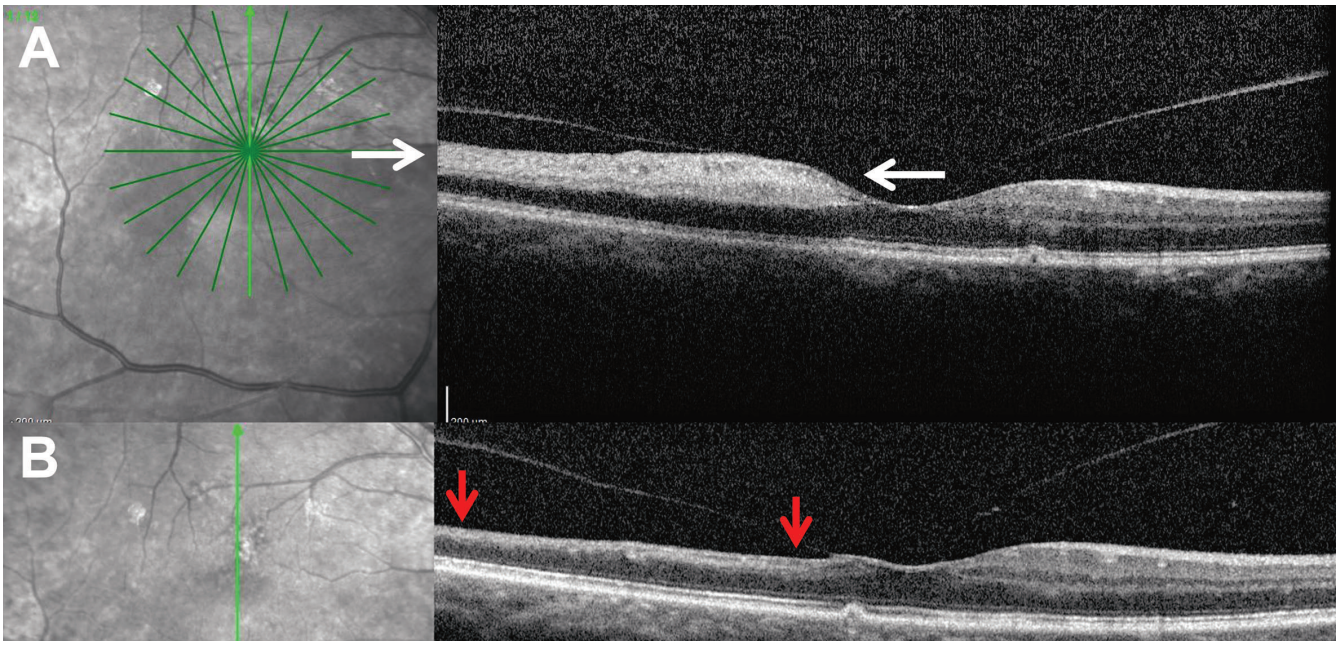

Figure 4. Optical coherence tomography of a branched retinal artery occlusion in the acute and chronic phase. A) OCT of a branched retinal artery occlusion within 24 hours of symptom onset. The OCT demonstrates increased thickness and appears hyperreflective (white arrows) while the corresponding areas of the outer retina appear relatively hyporeflective. B) Three months after initial presentation, OCT of the same patient shows signs of inner retinal atrophy in the areas that were previously hyperreflective (red arrows).

pentoxifylline, inhalation of carbogen, or sublingual isosorbide dinitrate.[88] Hyperbaric oxygen therapy increases blood oxygen tension, which has been proposed as a treatment option.[89]

Despite these potential mechanisms, there is no level I evidence to support any of these wide array of therapies. Furthermore, in one meta-analysis, conservative treatment measures (ocular massage, anterior chamber paracentesis and/or hemodilution) had a worse visual recovery rate than that of the natural history group; the number needed to harm in the conservative treatment group was 10.[90]

Both intra-arterial and intravenous thrombolytics have been investigated in RAO management; however, there is strong controversy regarding their use. For intra-arterial thrombolytics, this procedure is performed by a neuro-radiologist, complicating the logistics of care and prolonging the time between symptom onset and intervention. Via superselective microcatheterization, tPA is introduced into the ostium of the ophthalmic artery. Microvascular access mitigates systemic complications, but increases risk of catheter-induced spasm, arterial dissection and plaque dislodgement.[91]

The EAGLE trial (European Assessment Group for Lysis in the Eye) comparing intra-arterial lysis to conservative treatment was terminated prematurely due to a profound safety signal: 37.1 percent vs 3.4 percent risk of adverse events, respectively. Moreover, visual outcomes were similar between the two groups.[92] Intravenous thrombolytics also risk adverse events such as intracranial hemorrhage or death with no or minimal visual acuity gains reported.[93,94]

For non-arteritic RAO, there is no current treatment that is proven to yield superior outcomes when compared to that of the natural disease course. As has been highlighted before,[70] fibrinolysis doesn't significantly dissolve calcific or cholesterol emboli; as such the therapy only has a plausible mechanism of action for a minority of cases (platelet-fibrin emboli).

After the initial disease course, patients should still be regularly followed by an ophthalmologist to evaluate for ocular neovascularization. When anterior segment neovascularization develops, panretinal photocoagulation as well as off-label use of intravitreal anti-VEGF agents may be warranted to minimize the risk of neovascular glaucoma.

In conclusion, retinal artery occlusions are an ophthalmic emergency requiring detailed systemic workup. Although the visual prognosis in patients with RAO may be guarded, a prompt systemic workup is crucial as RAOs may be a harbinger of other systemic disease. Given the limited treatment armamentarium, investigation into novel therapeutic interventions for RAOs may confer significant benefit to future patients. Much work is left to be done for patients with this high-morbidity condition. ◀

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ADVERTISER INDEX

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Melatonin May Protect Against AMD

Since melatonin has been shown to oppose several processes known to mediate age-related macular degeneration, investigators looked at the association between melatonin supplementation and the risk of the development or progression of age-related macular degeneration.

The retrospective cohort study accessed data from TriNetX, a national database of deidentified electronic medical records from inpatient and outpatient health-care organizations across the United States, between December 4, 2023, and March 19, 2024. Patients ages 50 years or older, 60 years or older, and 70 years or older with no history of AMD and with a history of nonexudative AMD were queried for instances of melatonin medication codes between November 14, 2008, and November 14, 2023. Patients were then classified into a melatonin or a control group based on the presence of medication codes for melatonin. Propensity score matching (PSM) was performed to match the cohorts based on demographic variables, comorbidities and nonmelatonin hypnotic medication use.

Exposure included the presence of at least four instances of melatonin records occurring at least three months apart. After PSM, the melatonin and the control cohorts were compared to evaluate risk ratios (RRs) and the 95 percent CIs of having an outcome. For the AMD-naive group, the outcome was defined as a new diagnosis of any AMD, and for the nonexudative AMD group, the outcome was progression to exudative AMD.

Here are some of the findings:

• Among 121,523 patients in the melatonin-naive group ages 50 years or older (4,848 in the melatonin cohort [4,580 after PSM; mean (SD) age, 68.24 (11.47) years; 2,588 female (56.5 percent)] and 116,675 in the control cohort [4,580 after PSM; mean (SD) age, 68.17 (10.63) years; 2,681 female (58.5 percent)]), melatonin use was associated with a reduced risk of developing AMD (RR, 0.42; CI, 0.28 to 0.62).

• Among 66,253 patients ages 50 years or older in the nonexudative AMD group (4,350 in the melatonin cohort [4,064 after PSM; mean (SD) age, 80.21 (8.78) years; 2,482 female (61.1 percent)] and 61,903 in the control cohort [4,064 patients after PSM; mean (SD) age, 80.31 (8.03) years; 2,531 female (62.3 percent)]), melatonin was associated with a reduced risk of AMD progression to exudative AMD (RR, 0.44; CI, 0.34 to 0.56).

• The results were consistent among subsets of individuals ages 60 years or older:

– AMD-naive cohort: RR, 0.36; CI, 0.25 to 0.54; and

– nonexudative AMD cohort: RR, 0.38; CI, 0.30 to 0.49.

• The results were consistent among subsets of individuals ages 70 years or older:

– AMD-naive cohort: RR, 0.35; CI, 0.23 to 0.53; and

– nonexudative AMD cohort: RR, 0.40; CI, 0.31 to 0.51.

Melatonin use was associated with a decreased risk of development and progression of age-related macular degeneration. Investigators wrote that, although lifestyle factors may have influenced this association, these findings provide a rationale for further research on the efficacy of using melatonin as a preventive therapy against age-related macular degeneration.

JAMA Ophthalmol 2024; Jun 6. [Epub ahead of print].
Jeong H, Shaia JK, Markle JC, et al.

CME after Cataract Surgery in Uveitis Patients

Scientists evaluated the incidence, remission and relapse of post-surgical cystoid macular edema (PCME) following cataract surgery in inflammatory eye disease.

A total of 1,859 eyes that had no visually significant macular edema prior to cataract surgery while under tertiary uveitis management were included. Standardized retrospective chart review was used to gather clinical data. Univariable and multivariable logistic regression models with adjustment for inter-eye correlations were performed.

Here are some of the findings:

• PCME causing VA 20/50 or worse was reported in 286 eyes (15 percent) within six months of surgery;

• The following was associated with development of PCME within six months of cataract surgery:

– adults ages 18 to 64 years vs. children: adjusted OR [aOR]: 2.42, for ages 18 to 44 vs. aOR: 1.93 for ages 45 to 64; overall p=0.02);

– concurrent use of systemic immunosuppression (conventional aOR: 1.53; biologics aOR: 2.68; overall p=0.0095);

– preoperative VA 20/50 or worse (overall p<0.0001);

– cataract surgery performed before 2000 (overall p=0.03); and

– PCME in fellow eye (aOR 3.04; p=0.0004).

• PCME resolution was seen in 81

percent of eyes at 12 months and 91 percent of eyes at 24 months.

• CME relapse was seen in 12 percent eyes at 12 months and 19 percent eyes at 24 months.

Scientists concluded that post-surgical cystoid macular edema occurred frequently in uveitic eyes undergoing cataract surgery although most cases resolved within a year. They added that surgical cystoid macular edema recurrences likely were due to the underlying disease process and not relapses of post-surgical cystoid macular edema.

Am J Ophthalmol 2024; Jun 14 [Epub ahead of print].
Gangaputra S, Newcomb C, Ying GS, et al; Systemic Immunosuppressive Therapy for Eye Diseases (SITE) Cohort Study Research Group.

Decreased Perfusion In Dry AMD

Investigators looked at the relationships between contrast sensitivity, choriocapillaris perfusion and other structural OCT biomarkers in dry age-related macular degeneration, as part of a cross-sectional, observational study.

One hundred AMD eyes (22 early, 52 intermediate and 26 late) from 74 patients and 45 control eyes from 37 age-similar subjects were included.

All participants had a visual acuity assessment, quantitative contrast sensitivity function (qCSF) testing, macular OCT and 6 x 6 mm swept-source OCT angiography scans on the same day. OCT volumes were analyzed for subretinal drusenoid deposits and hyporeflective drusen cores, and to measure thickness of the outer nuclear layer (ONL). OCTA scans were used to calculate drusen volume, inner choroid flow deficit percentage (IC-FD percent) and to measure the area of choroidal hypertransmission defects (HTD). IC-FD percent was measured from a 16 μm-thick choriocapillaris slab after compensation and binarization with Phansalkar's method. Generalized linear mixed-effects models were used to evaluate the associations between functional and structural variables.

Main outcome measures included associations between qCSF-measured CS, ICFD percent and various AMD imaging biomarkers.

Here are some of the findings:

• AMD exhibited significantly reduced qCSF metrics eyes across all stages compared to controls.

• Univariate analysis revealed significant associations between various imaging biomarkers, reduced qCSF metrics and VA in both groups.

• Multivariate analysis confirmed that higher IC-FD percent in the central 5 mm was significantly associated with decreases in all qCSF metrics in AMD eyes (β=-0.74 to -0.25, all $p<0.05$), but not in VA ($p>0.05$).

• ONL thickness in the central 3 mm correlated with both VA (β=2.85; $p<0.001$) and several qCSF metrics (β=0.01-0.90, all $p<0.05$), especially in AMD eyes.

• Further, larger HTD areas were associated with decreased VA (β=-0.89, $p<0.001$) and reduced CS at low-intermediate frequencies across AMD stages (β=-0.30 to -0.29; $p<0.001$).

Researchers wrote that the significant association between inner choroid flow deficit percentage in the central 5 mm and quantitative function-measured contrast sensitivity reinforced the hypothesis that decreased macular choriocapillaris perfusion contributes to vision changes in dry AMD, which are more pronounced in contrast sensitivity than in visual acuity.

Ophthalmol Retina 2024; Jun 13. [Epub ahead of print].
Romano F, Vingopoulos F, Yuan M, et al.

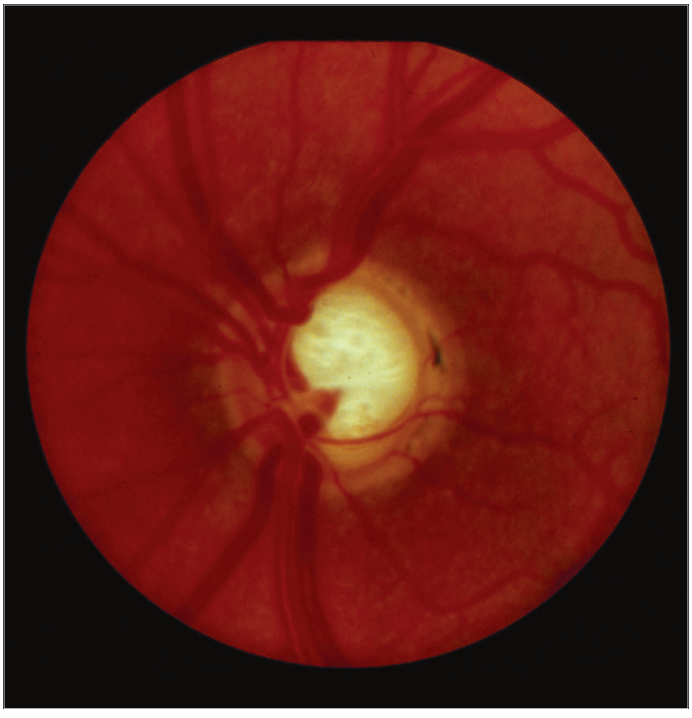
Practice Patterns for Managing Open-angle Glaucoma

Researchers aimed to characterize primary treatment preferences (topical medication vs. laser trabeculoplasty or intracameral sustained release implants) in primary open-angle glaucoma patients and determine factors related to primary intervention selection.

A 33-question survey was distributed to an American Society of Cataract and Refractive Surgery database on treatment choices made by ophthalmologists for POAG. Data collected included country of practice, years of practice, completion of glaucoma fellowship training, type of practice and preference for first line of treatment of POAG. Multiple logistic regression was used to compare the effect of covariates on physicians' choice of either topical medication or laser trabeculoplasty for POAG.

Here are some of the findings:

• A total of 252/19,246



Researchers analyzed preferences for drugs vs. laser in OAG.

(1.3 percent) of surveys were returned. Almost three-quarters of respondents used topical medication as the first line of treatment for POAG (73.6 percent) while 26.4 percent preferred to start with laser.

• Significant variables associated with the selection of laser (vs. drops) were:

– practicing in the United States (OR: 2.85; CI, 1.33 to 6.10);

– more recent completion of ophthalmology residency (OR: 1.95; CI, 1.00 to 3.77);

– greater volume of minimally invasive glaucoma surgeries (MIGS)(OR: 1.68, CI, 1.18 to 2.40); and

– a glaucoma patient base greater than 25 percent (OR: 2.21; CI, 1.09 to 4.48).

Researchers wrote that, for the first-line treatment of POAG, laser trabeculoplasty was more likely to be preferred over topical drops by U.S. physicians who were relatively new in practice, who had a larger glaucoma patient base and who performed more minimally invasive glaucoma surgery.

J Glaucoma 2024; Jun 17. [Epub ahead of print].
Rhee DJ, Sancheti H, Rothman AL, et al.

Correlation Between Pupil Size and Depth of Focus After EDOF IOL Implantation

Scientists evaluated whether depth of focus after the implantation of extended depth of focus intraocular lenses correlated with pupillary size.

This retrospective case series study evaluated eyes undergoing cataract surgery with implantation of EDOF IOLs. At least one month postoperatively, the depth of focus (DoF) was measured to determine the correlation with pupillary size, age, anterior chamber depth (ACD), axial length (AXL) and corneal spherical aberrations (SA).

The study evaluated 64 eyes of 49 patients. Here are some of the findings:

• The mean depth of focus was 2.67 D.

• The mean preoperative photopic pupil size was 3.36 mm.

• A significant negative association was found between preoperative photopic pupil size and depth of focus (r=0.30, Pearson's correlation coefficient), and between preoperative mesopic pupil size and depth of focus (r=0.274, Pearson's correlation coefficient).

Scientists found smaller pupil size had a strong association with good postoperative depth of focus, with extended depth of focus intraocular lenses. No significant correlation was observed between age, anterior chamber depth, axial length, corneal spherical aberrations, and depth of focus in extended depth of focus intraocular lenses. ◀

J Cataract Refract Surg 2024; May 09. [Epub ahead of print].
Yalamanchili SP, Cleary SM, Sell SS, et al.

(Continued from page 33)

improve vision over time." Genentech recently announced Susvimo will be re-introduced at some point this summer.

• Switch the drug class. "Switching to stronger drugs or switching the class of drug is very important," Dr. Chhablani says. "However, don't expect faricimab to work as well if you switch the patient after three or four years. Switching earlier produces a better response. Switching the drug class or combining it with steroids or other anti-VEGF can also help."

• Remain vigilant and diagnose early. "Be aware of any new signs and symptoms," Dr. Starr says. "Getting patients into the retina clinic sooner can lead to better patient outcomes and better treatment outcomes."

Dr. Chhablani adds that it's important to diagnose resistance as soon as possible. "Doing regular scans helps," he says. "Do the invasive angiography tests. They help us understand the disease profile and the network status, which may reveal things that were hiding such as PCV."

• Confirm the diagnosis. "If you have a patient who you think should be responding better, go back to the drawing board and investigate whether there's another diagnosis you're missing," Dr. Starr says.

The Future

New approaches on the horizon include gene therapy, sustained-release drug delivery and therapies that address multiple disease pathways. Dr. Almeida and Dr. Chhablani are involved in RegenXbio's RGX-314 viral vector gene therapy research. They say the results so far are interesting. "This gene therapy is a subretinal therapy which will limit its use to only vitreoretinal surgeons, but I believe the company is exploring suprachoroidal gene therapy as well, and other companies are looking to intravitreal gene therapy," Dr Chhablani says.

"There's a lot of interest in tyrosine kinase inhibitors," Dr. Garg says. "There are nearly half a dozen companies looking at different TKIs, which have an anti-VEGF effect but may also help reduce inflammation in some of these eyes. They have the potential of lasting longer than our current treatments, so that's exciting, though these treatments are still in Phase I and II."

"We were all really excited for the port delivery system, it'll be interesting to see now that it is coming back into the market how it will be used by retina physicians," Dr. Starr says.

"We're hopeful that some of the changes with the device design will make [the port delivery system] more consistently good for our patients," Dr. Garg adds.

Dr. Chhablani says he's also looking forward to home OCT. "I think that home OCT will help us pick up recurrences much sooner," he says. "It'll definitely factor into our treatment plan in the future." ◀

PRODUCT NEWS

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

GLAUCOMA TREATMENT

FDA OK's KDB for POAG

New World Medical announced a 510(k) indication expansion from FDA for its Kahook Dual Blade Glide that allows it to be used for the reduction of IOP in adult patients with primary open-angle glaucoma during cataract surgery or as a standalone procedure.

New World Medical says the FDA's decision was "based on extensive data that supports the device's safety and efficacy in reducing IOP in patients with POAG." Over the course of more than 100 published studies, including Level-I randomized controlled trial data and five-year published data, the KDB Glide has been shown to reduce IOP by at least 20 percent on average, the company says.

For information, visit newworldmedical.com.

DRY-EYE THERAPY

Wipe Away Lid Problems

For patients with dry eye, styes or blepharitis, TearRestore recently launched NeutraWipe Eco, a new eyelid cleanser that uses manuka honey and antibacterial hydrolyzed soy protein infused on an ultra-soft, biodegradable bamboo material.

The company says that NeutraWipe Eco is specifically designed to be an effective eyelid cleansing solution for even the most sensitive eyes. TearRestore adds that the addition of sustainably sourced manuka honey provides soothing and moisturizing benefits, promotes healthy eyelids, reduces inflammation, and soothes red, puffy, irritated eyes.

NeutraWipe Eco has only three ingredients: natural manuka honey; antibacterial hydrolyzed soy protein; and purified New Zealand water. Because of this, the company says that NeutraWipe Eco offers a hypoallergenic, oil-free, and salt-free formula suited for use in sensitive eyes.

For information, visit tearrestore.com.

IMAGING AND DIAGNOSTICS

A New Dimension in Slit Lamp Imaging

Haag-Streit has launched the Imaging Module 910 3D for slit lamp applications to give physicians a deeper view of pathology.

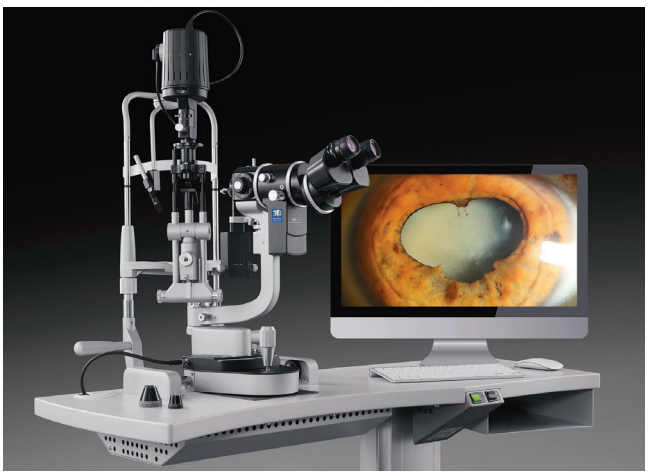
The company notes that, to-date, ophthalmologists have only been able to document slit lamp images in 2-D. The images presented in two dimensions lack depth, Haag-Streit argues, which "limits the comprehensive visualization of the observed content."

By enhancing the Haag-Streit Imaging Module 910 (IM 910) through the addition of a second 4K camera, ophthalmologists can now experience images with "immersive depth," which the company says unveils more detail and provides a richer viewing experience. The device's maker says that, through the recording of videos and images in 3-D, clinicians enjoy a more detailed and authentic representation of the slit lamp exam, making the perception of anatomical relationships easier to identify, thereby enhancing the overall clarity and interpretability of the eye.

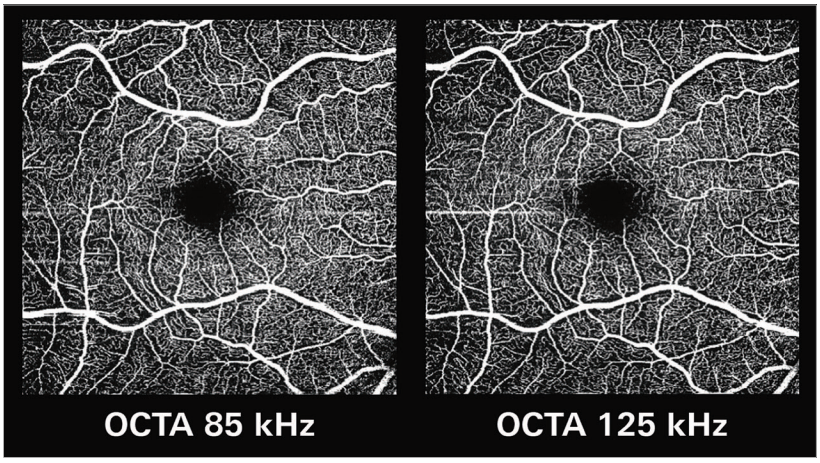
Haag-Streit says the new module will help with teaching, as well, noting that, with traditional methods such as co-observer tubes, trainees have to hunch over the eyepieces, which can be uncomfortable. By sharing an enhanced 3-D digital view between the monitor and the oculars, ophthalmology instructors can be sure that residents are seeing the relevant details. This, plus the ability to stream quality digital videos and images in 3-D to multiple residents around the world, creates a modern, comfortable, and collaborative teaching environment, the company says.

Moreover, Haag-Streit believes the ability to transmit this immersive 3-D experience remotely between teleconsultant and examining clinicians supports new possibilities in health care.

For more information, visit haag-streit.com.



Haag-Streit's new imaging model allows 3-D imaging.



Heidelberg's Shift technology makes OCTA exams twice as fast.

Tono on the Go

Reichert Technologies has released its portable Tono-Vera Tonometer with ActiView Positioning System.

The company says that Tono-Vera provides quick, automated, and reliable intraocular pressure measurements using rebound tonometer technology, which eliminates the need for topical anesthetic.

The device features the company's patented ActiView Positioning System, which Reichert says quickly guides the user to the apex of the cornea, providing confidence in the obtained IOP readings. The company says the ActiView Positioning System is highlighted by a full-color view of the eye, combined with an "intuitive and interactive" user interface, ensuring an optimum position for measuring IOP. When the user achieves the correct alignment, Tono-Vera automatically measures the pressure, providing results in as few as three measurements taken in under a second. The device also features a Flexi-Soft forehead rest that's designed for easy distance control and patient comfort.

Tono-Vera has two model options to choose from: Rechargeable and AA battery-powered. Both models are portable and allow for a quick and easy battery change with no tools required, the company says. The instrument's base stores and dispenses single-use Ocu-Dot tonometer probes, as well as charges the Tono-Vera Rechargeable Model. The Tono-Vera is also equipped with Bluetooth connectivity for ease of transferring data.

To learn more about Reichert Tono-Vera Tonometer, visit reichert.com.

OCTA Shifts into High Gear

Heidelberg Engineering recently announced the FDA clearance of its Spectralis OCTA Module with Shift technology, which the company says reduces acquisition time by half compared to the previous model. Heidelberg says the preset OCTA speed of 125 kHz is designed to help streamline workflow, enhance clinical efficiencies, and maintain image quality.

The company says that, combined with a more powerful OCT engine, updated graphics processing technology, and software optimization, Shift technology delivers increased speed, maintains data integrity, and improves performance. The technology is available exclusively on third-generation Spectralis devices.

Both the 85-kHz preset for structural OCT and the 125-kHz preset for OCTA allow physicians to complete their patient exams more efficiently, the company says. In addition, the 125 kHz OCTA image acquisition rate allows for visualization of flow, even in miniscule vessels, while minimizing artifacts, resulting in sharp and detailed images of the capillary network, according to Heidelberg.

For more information about Spectralis OCTA with Shift Technology, visit heidelbergengineering.com.

Be Sensitive to Patients' Needs

Virtual Vision has rolled out a Color Sensitivity update to its Virtual Eye Device.

With the Color Sensitivity update, technicians can now update answers or even complete the test plates on behalf of the patient. The company says this means patients no longer need to input anything into the device; they can simply respond verbally while the technician manages the inputs.

For tele-health purposes, the test can be fully automated, allowing patients to complete the exam remotely. Alternatively, the test can be conducted manually with the assistance of a technician using the guided interactive color testing system, ensuring patients receive the support they need throughout the process, Virtual Vision says.

For information, visit virtualvision.health. ◀

The Reichert Tono-Vera uses ActiView Positioning to find the corneal apex.

A 34-year-old female presents to an outside emergency room with left eye vision going "in and out" for 20 to 30 seconds.

SUNIDHI RAMESH, MD, AND SARAH THORNTON, MD
PHILADELPHIA

Presentation

A 34-year-old female presents to an outside emergency room with left-eye vision going "in and out" for 20 to 30 seconds.

History

At presentation, she didn't report any past ocular history. Past medical history included asthma, obstructive sleep apnea, anxiety, depression, obesity and recent upper respiratory infections; past surgical history was non-contributory. Medications included an albuterol inhaler every six hours as needed, trazadone nightly, venlafaxine once daily, and a medroxyprogesterone injection (depot) once every three months.

Family history included Huntington's disease in her maternal grandfather, aunt, and uncle; the patient herself had declined testing for the condition. She was a former 10-pack-year smoker with daily nicotine vape use at the time of presentation; she was also a former methamphetamine, MDMA and marijuana user, in remission for about nine months. She worked as a waitress and had three children. Allergies included ciprofloxacin (hives) and vancomycin (hives). Review of systems was negative for pain, dizziness, nausea, vomiting, weakness or numbness.

Initial Examination Work-Up

On initial presentation to the outside ER, visual acuity without correction was 20/20 in both eyes. Intraocular pressure was 13 in the right eye and 14 in the left eye. Pupils were equal, round and reactive with a 2+ relative afferent pupillary defect in the left eye. Motility and confrontation visual fields were normal in each eye. Color perception was normal in the right eye with 50 percent red desaturation in the left eye. External examination was unremarkable; anterior exam was normal. Posterior exam showed circumferential disc elevation with obscuration of major vessels and surrounding Paton's lines in the left eye; in the right eye, the disc was flat and sharp with a cup-to-disc ratio of 0.1.

In the ER, she underwent MRI of the brain and MRA of the head; both were unremarkable. Subsequent MRI orbits with gadolinium contrast showed "enhancement of the intraorbital and intracanalicular segments of the left optic

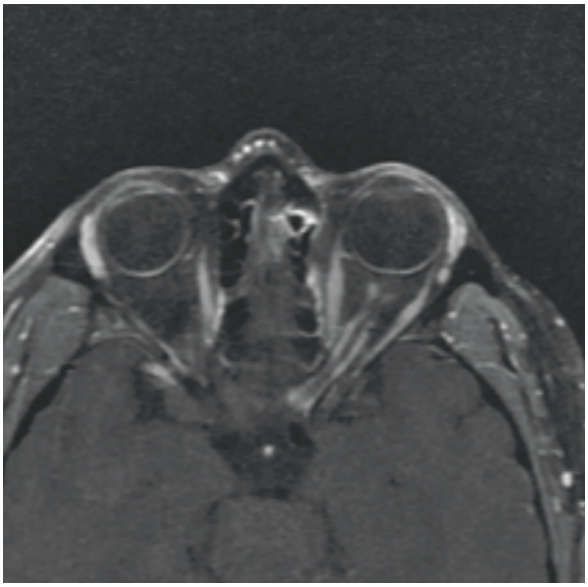


Figure 1. T1-weighted post-gadolinium axial MRI showing left optic nerve sheath enhancement with a "tram track" appearance.

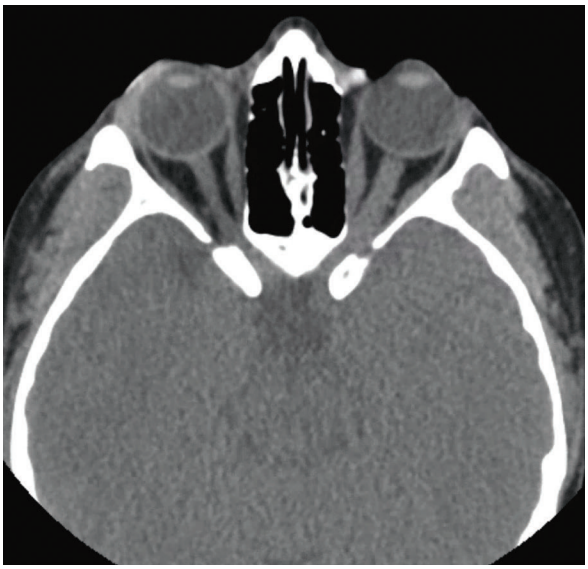


Figure 2. CT scan of the orbits showing some enlargement of the left optic nerve with no evidence of optic nerve sheath calcification.

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

nerve." MRI of the C-spine and T-spine with gadolinium contrast did not show other lesions. Chest X-ray, ACE, NMO, MOG, ANA, ESR, CRP, Lyme, IgG4/IgG, Bartonella and FTA-Abs were normal. She was diagnosed with left optic neuritis and admitted for five days of intravenous methylprednisolone with some improvement in her visual symptoms; she was later discharged on an oral prednisone taper.

One month after initial presentation, an exam with an outside ophthalmologist re-demonstrated disc edema in the left eye. Repeat MRI orbits with contrast several weeks later showed "persistent thickening of the left optic nerve sheath with enhancement." She continued on her oral steroids during this time.

Ten weeks after initial presentation, she re-presented to the outside emergency room with two weeks of intermittent blurred, "washed-out" vision in the left eye and numbness/tingling in the right upper extremity. MRI brain was again unremarkable. A lumbar puncture showed a normal opening pressure (20 mmHg) in the left lateral decubitus position, elevated oligoclonal bands (7 in the cerebrospinal fluid without correlating bands in the serum), normal protein (62), normal glucose (103), and an elevated white blood cell count (23, with 13-percent neutrophils) with zero red blood cells. MOG CSF antibody was negative. Given her new visual complaints, she was again admitted for three days of intravenous methylprednisolone and discharged on an oral prednisone taper; she reportedly had mild improvement in her vision at this time. Two weeks after discharge, she was seen by an outside neurologist and started on Rituximab for presumed "multiple sclerosis with recurrent optic neuritis."

Eight months after the initial presentation, she awoke with complete loss of peripheral vision in the left eye with a preserved "slit" of blurred central vision. MRI brain and orbits with and without contrast showed "persistent thickening and enhancement of the left ON sheath; possible left thalamic T2 hyperintensity." CT chest/abdomen/pelvis was negative for inflammatory process or malignancy. She was again admitted for four days of intravenous methylprednisolone and discharged on an oral prednisone taper. At this time, due to her worsening vision and overall atypical course, she was sent to the Wills ER for further evaluation and work-up.

In the Wills ER, visual acuity without correction was 20/25 in the right eye and 20/300 in the left eye. Intraocular pressure was 16 mmHg OD and 18 mmHg OS. Pupils were equal, round and reactive with a 3+ relative afferent pupillary defect in the left eye. Motility was full in each eye; confrontation visual fields were normal in the right eye with diffusely constricted fields in the left eye. Color plates were full in the right eye, and she was only able to identify the control plate in the left eye. External examination was unremarkable; anterior exam was normal. Posterior exam showed circumferential disc elevation with obscuration of major vessels and surrounding Paton's lines in the left eye; in the right eye the disc was flat and sharp with a cup-to-disc ratio of 0.1. Rare anterior vitreous cells and focal RPE changes inferotemporal to the disc were seen in the left eye. MRI brain and orbits with contrast showed "tram track enhancement of the left optic nerve sheath extending from intraorbital through the canalicular segment"; given persistence of this abnormality, differential considerations included optic nerve sheath meningioma *(Figure 1)*. A CT scan of the orbits was performed to look for calcification along the left optic nerve sheath to suggest optic nerve sheath meningioma, but this wasn't identified *(Figure 2)*. The patient was discharged with urgent neuro-ophthalmology follow-up.

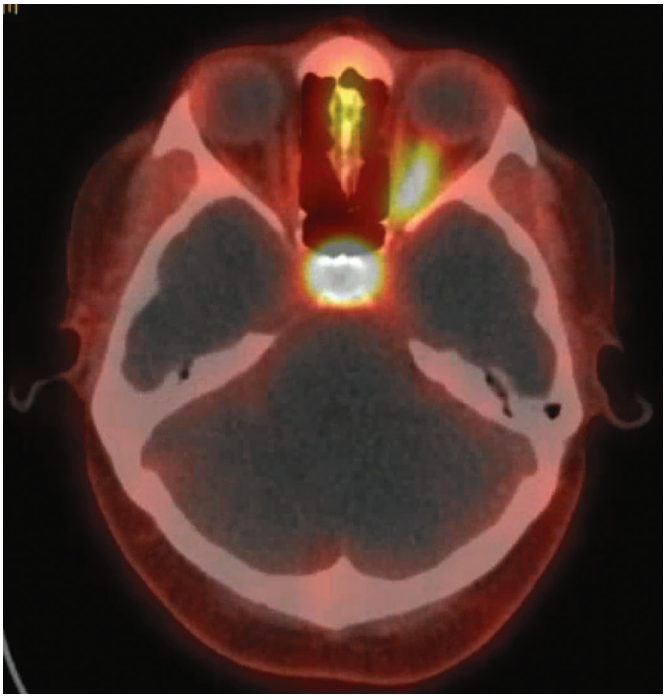


Figure 3. Ga-68 PET scan showing intense radioactive uptake along the left optic nerve.

Diagnosis and Treatment

Although the patient was suspected to have optic nerve sheath meningioma based on neuroimaging findings, her rapid progression over eight months and the presence of oligoclonal bands in the CSF would be atypical for this diagnosis. Therefore, a PET DOTATATE Ga-68 scan was ordered in attempt to clarify her diagnosis. These positron emission tomography scans use radiolabeled somatostatin receptors (SSTR) ligands (which are overexpressed in

meningiomas) to better visualize meningiomas.[1] Her scan showed "intense uptake along the left optic nerve [which] would support the pattern of enhancement of the left optic nerve on the recent MRI imaging to most likely be a meningioma… although sarcoid remains on the differential as it also expresses SSTR 2 receptors" *(Figure 3)*. Because inflammatory optic neuropathy secondary to sarcoidosis typically responds to steroid treatment (and this patient had poor visual recovery despite multiple rounds of steroids), her diagnosis was presumed to be optic nerve sheath meningioma; radiation therapy was thus recommended.

However, during her follow-up visit, the patient stated she "would rather lose vision in [her] left eye completely from an [optic nerve sheath] biopsy" than to not have a definitive answer. She was referred to Oculoplastics where she was counseled extensively on the risks of severe, permanent vision loss if she were to proceed with an optic nerve sheath biopsy; after several visits, the patient persisted in seeking a pathologic diagnosis and ultimately underwent an optic nerve sheath biopsy via transorbital approach.

The pathological specimen showed neoplastic cells with minimally pleomorphic nuclei as well as eosinophilic cytoplasm in a whorled and nested syncytial arrangement *(Figure 4)*; and lamellated extracellular calcifications ("psammoma bodies") without appreciable nuclear atypia, mitotic figures or necrosis *(Figure 5)*. There was diffuse and strong nuclear expression of progesterone receptors (PR) in the neoplastic nuclei *(Figure 6)* as well as strong, diffuse cytoplasmic and membranous immunoreactivity for somatostatin receptor 2 (SSTR2) *(Figure 7)*. The pathological diagnosis was meningothelial meningioma, WHO Grade 1.

Several days after the biopsy, the patient returned for a follow-up visit at Wills Eye Hospital. Visual acuity without correction was 20/20 in the right eye and hand motions in the left eye. IOP was 20 mmHg OD and 23 mmHg OS. She had mild, <5 prism diopters of left exotropia with 90-percent abduction in the left eye; the exam was otherwise unchanged. She was referred for radiation therapy.

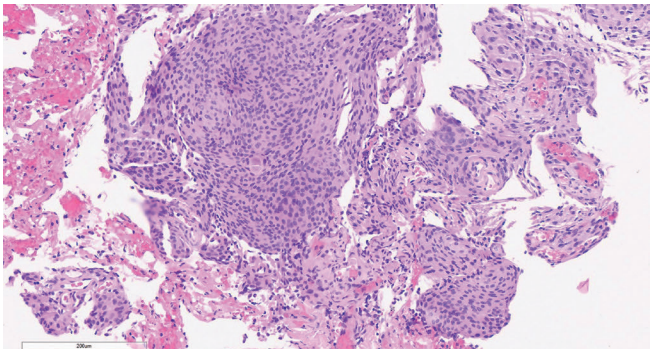


Figure 4. Optic nerve sheath pathology specimen showing neoplastic cells with minimally pleomorphic nuclei and eosinophilic cytoplasm in a whorled and nested syncytial arrangement.

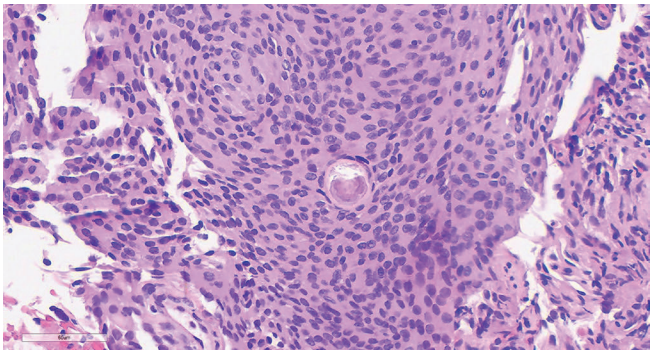


Figure 5. Optic nerve sheath pathology specimen showing lamellated extracellular calcifications ("psammoma bodies") without appreciable nuclear atypia, mitotic figures, or necrosis.

Discussion

Optic nerve sheath meningiomas comprise a third of all primary optic nerve tumors and originate from the meningothelial cells of arachnoid villi surrounding the optic nerve. Although ONSM are considered benign tumors, patients may experience progressive and permanent vision loss secondary to compression of the optic nerve and its blood supply.[2] The tumors have a female predominance (female-to-male ratio is about 3:1) and typically manifest in the 4th or 5th decade of life.[3] Generally considered a rare entity, ONSM encompass only about 1 to 2 percent of all meningiomas.[2] Of note, there's an association between ONSM and neurofibromatosis type 2.

Per Dr. Neil Miller in his 2006 paper[4] regarding evaluation of ONSM, "the diagnosis of [optic nerve sheath meningioma] can be suspected in most cases from clinical findings and supported by the results of neuroimaging, obviating tissue biopsy in the majority of cases." Overall, MRI is the preferred imaging modality for ONSM over CT; Ga-68 PET, however, may be helpful in uncertain cases.[5] In fact, one 2012 study[6] showed an "overall detection rate of 92 percent [by MRI] of the meningioma lesions that were found by PET/CT." Primary findings on imaging include three distinct morphological patterns: tubular ("tram-track" pattern); fusiform; and globular. Calcifications on CT scan can increase the diagnostic probability of ONSM, although lack of calcifications doesn't definitively rule out meningioma.

For cases of progressive optic neuropathy of uncertain etiology, optic nerve sheath biopsy is considered a last resort, as even subtotal optic nerve sheath biopsies limit the potential for visual recovery.[7] Therefore optic nerve sheath biopsies may be more readily indicated for patients who already have severe vision loss. Other risks of optic nerve sheath biopsies include diplopia, abnormal eye move-

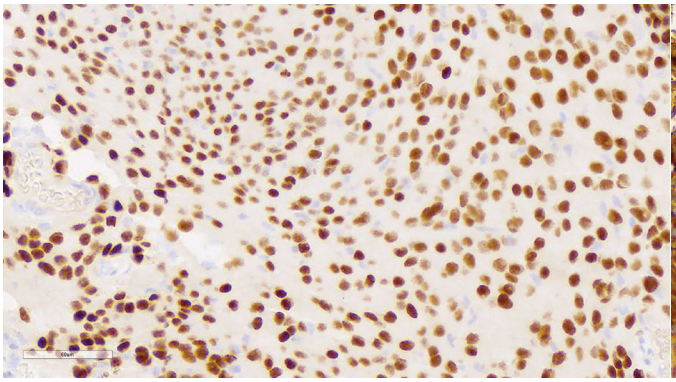


Figure 6. Optic nerve sheath pathology specimen showing diffuse and strong nuclear expression of progesterone receptors (PR) in the neoplastic nuclei.

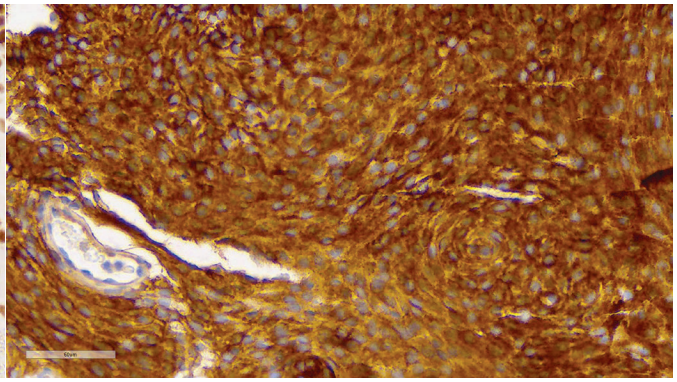


Figure 7. Optic nerve sheath pathology specimen showing strong, diffuse cytoplasmic and membranous immunoreactivity for somatostatin receptor 2.

ments, ptosis, numbness, eyelid/orbital deformity, infection, bleeding, inadequate specimen for diagnosis, CSF leakage and scarring. Given the inherent risks involved, all optic nerve sheath biopsies require careful counseling and shared decision-making between the patient and the physician.

Pathological findings of ONSM are similar to those of cerebral and spinal cord meningiomas although several variant forms exist including angiomatous, fibroblastic, meningothelial, transitional and psammomatous.[8] Meningothelial meningiomas are the most common and may include findings of syncytial cells with indistinct cell membranes and eosinophilic cytoplasm; scant psammoma bodies; somatostatin receptor (SSTR) positivity; and diffuse, strong nuclear progesterone receptor (PR) positivity (particularly in low-grade meningiomas).[8] Meningiomas are typically graded in accordance to the World Health Organization classification; grade 1 variants are benign while grade 2 and 3 variants are aggressive with malignant or metastatic potential.[9]

Treatment options for meningioma traditionally include observation, surgical excision or radiation therapy.[10,11] Asymptomatic cases are observed, while surgical excision is reserved for blind eyes with severe proptosis, cosmetic concern or threat of intracranial spread.[12] Radiation therapy is otherwise the standard of care for symptomatic ONSM.[13] One retrospective case series by Rutgers' University's Roger Turbin, MD, and colleagues[14] examining 64 patients with ONSM with at least 50 months of follow-up showed patients with radiation alone (compared to surgery alone, observation alone and surgery with radiation) demonstrated the best overall vision outcome during the study period. Other studies have similarly demonstrated the efficacy of radiation in vision preservation.[15-17]

Optic nerve sheath meningioma is a rare entity that presents with painless, progressive optic neuropathy. Patients are typically diagnosed based on clinical suspicion and imaging findings on CT, MRI and Ga-68 PET scans. Biopsy is reserved for ambiguous cases with severe vision loss. Treatment options include observation, surgery and radiation although the latter has been shown to have the best visual outcomes. In our case, the patient had an unusual, rapid progression of vision loss and ultimately underwent an optic nerve sheath biopsy showing low-grade meningothelial meningioma. ◀

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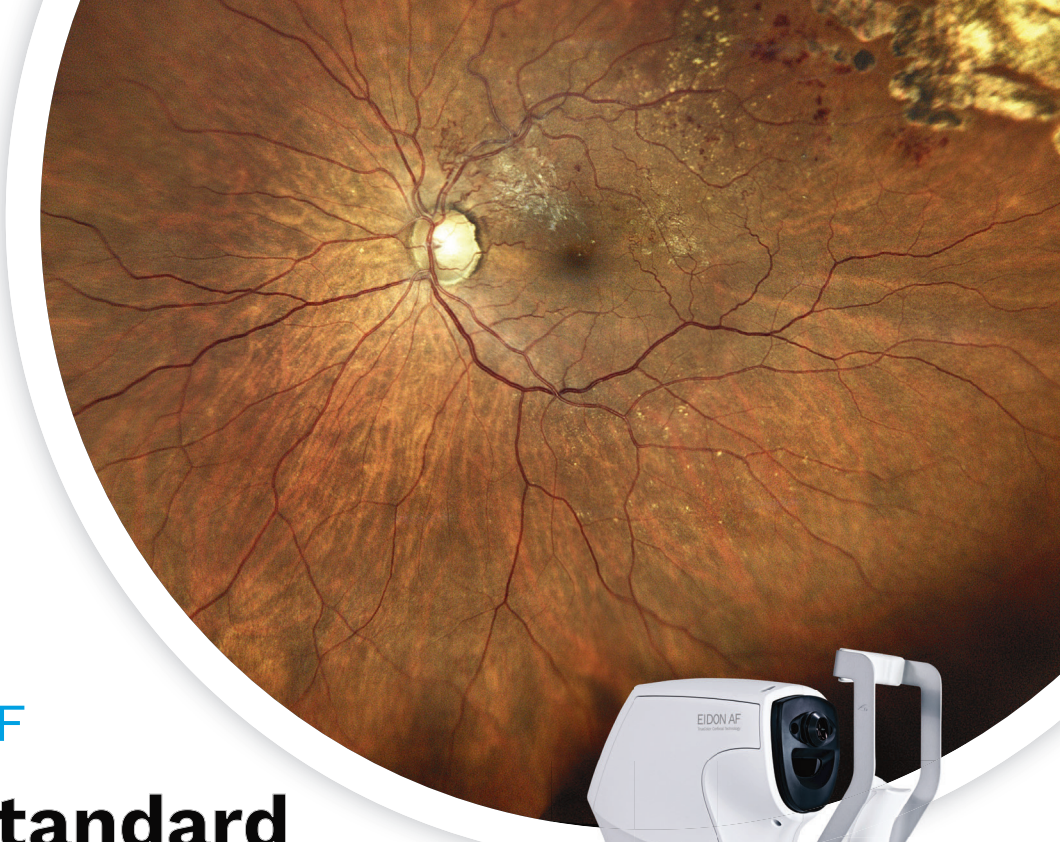

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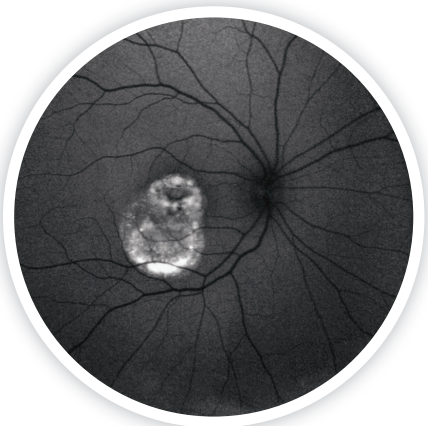

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