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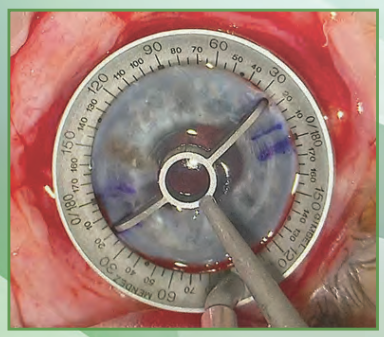
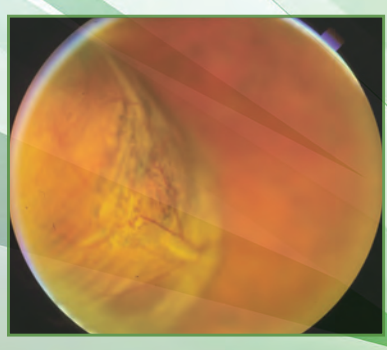
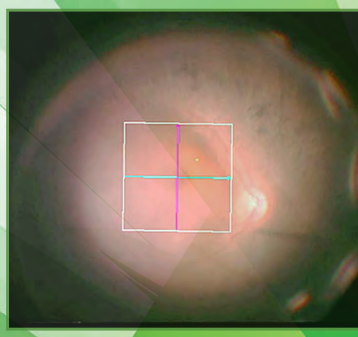
RT Retina Today

JANUARY/FEBRUARY 2026 VOL. 21, NO. 1
RETINATODAY.COM

20TH ANNIVERSARY

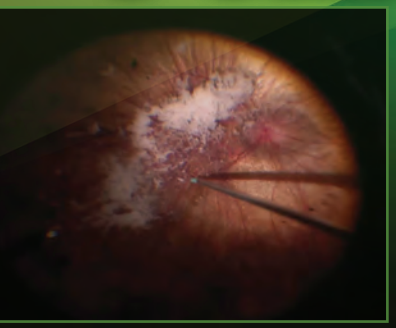


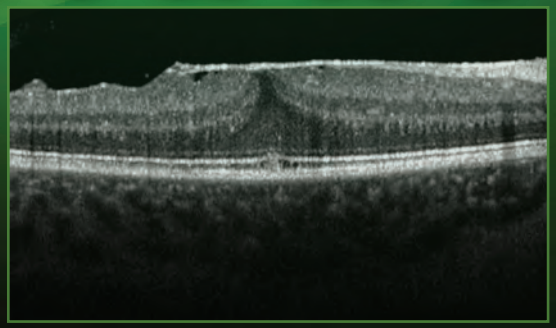




THE CUTTING-EDGE RETINA OR

Exploring the new tools and techniques improving surgical care.





eyetube

THE NEW RETINA OR: THE LATEST VITRECTOMY TOOLS

TIPS FOR FIXATING TORIC IOLS

MTM: SURGICAL TIMING AND TECHNIQUES

SUBSCRIBE FOR FREE

Ken is a real patient with GA, and Dr. Arshad Khanani is his retina specialist who treats his GA with IZERVAY.

Moments like this deserve your protection.

Ken loves to golf—Dr. Khanani loves to keep him golfing for longer.

Dr. Arshad Khanani is a compensated physician.

INDICATION

IZERVAY™ (avacincaptad pegol intravitreal solution) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD)

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

IZERVAY is contraindicated in patients with ocular or periocular infections and in patients with active intraocular inflammation.

WARNINGS AND PRECAUTIONS

Endophthalmitis and Retinal Detachments

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

References: 1. Holz FG, Strauss EC, Schmitz-Valckenberg S, van Lookeren Campagne M. Geographic atrophy: clinical features and potential therapeutic approaches. *Ophthalmology*. 2014;121(5):1079-1091. **2.** Izervay. Package insert. Northbrook, IL: Astellas Pharma US, Inc.; 2025. **3.** Syfovre. Package insert. Waltham, MA: Apellis Pharmaceuticals, Inc.; 2025. **4.** Astellas Pharma US, Inc. Izervay. Data on File.

Protect healthy retinal cells for longer with IZERVAY[1,2]

Only IZERVAY showed efficacy at one year in two Phase 3 trials[2,3]

In 2 clinical trials of 624 people, IZERVAY was proven to reduce the annualized rate of GA lesion growth by 18%-35% in one year compared to those who were not treated.[2]

Demonstrated safety through 2 years in the GATHER trials[2]

Consistent real-world safety across more than 400k vials distributed.[2,4*]

izervay™ (avacincaptad pegol intravitreal solution) 2 mg

Treat GA to help preserve vision for longer[1,2]

Scan to explore IZERVAY:
The #1 prescribed FDA-approved treatment for new GA patients[4†]

*As of 08/25. Based on samples and commercially distributed vials.
†Based on Symphony data from 3/24-7/25. May not represent entire population.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Neovascular AMD

- In clinical trials, use of IZERVAY was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (7% when administered monthly and 4% in the sham group) by Month 12. Over 24 months, the rate of neovascular (wet) AMD or choroidal neovascularization in the GATHER2 trial was 12% in the IZERVAY group and 9% in the sham group. Patients receiving IZERVAY should be monitored for signs of neovascular AMD.

Increase in Intraocular Pressure

- Transient increases in intraocular pressure (IOP) may occur after any intravitreal injection, including with IZERVAY. Perfusion of the optic nerve head should be monitored following the injection and managed appropriately.

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥5%) reported in patients receiving IZERVAY were conjunctival hemorrhage, increased IOP, blurred vision, and neovascular age-related macular degeneration.

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

MAT-US-IZE-2025-00719 11/25

astellas

IZERVAY™ (avacincaptad pegol intravitreal solution)
Rx only
Brief Summary: This information is not comprehensive. Visit IZERVAYecp.com to obtain the FDA-approved product labeling or call 800-707-4479.

1 INDICATIONS AND USAGE
IZERVAY is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

2 DOSAGE AND ADMINISTRATION
2.1 General Dosing Information
IZERVAY must be administered by a qualified physician.
2.2 Recommended Dosage
The recommended dose for IZERVAY is 2 mg (0.1 mL of 20 mg/mL solution) administered by intravitreal injection to each affected eye once monthly (approximately every 28 ± 7 days).

4 CONTRAINDICATIONS
4.1 Ocular or Periocular Infections
IZERVAY is contraindicated in patients with ocular or periocular infections.
4.2 Active Intraocular Inflammation
IZERVAY is contraindicated in patients with active intraocular inflammation.

5 WARNINGS AND PRECAUTIONS
5.1 Endophthalmitis and Retinal Detachments
Intravitreal injections may be associated with endophthalmitis and retinal detachments. Proper aseptic injection techniques must always be used when administering IZERVAY in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay, to permit prompt and appropriate management.
5.2 Neovascular AMD
In the GATHER1 and GATHER2 clinical trials, use of IZERVAY was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (7% when administered monthly and 4% in the sham group) by Month 12. Over 24 months, the rate of neovascular (wet) AMD or choroidal neovascularization in the GATHER2 trial was 12% in the IZERVAY group and 9% in the sham group. Patients receiving IZERVAY should be monitored for signs of neovascular AMD.
5.3 Increase in Intraocular Pressure
Transient increases in intraocular pressure (IOP) have been observed after an intravitreal injection, including with IZERVAY. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

6 ADVERSE REACTIONS
The following potentially serious adverse reactions are described elsewhere in the labeling:

- Ocular and periocular infections
- Active intraocular inflammation
- Endophthalmitis and retinal detachments
- Neovascular AMD
- Increase in intraocular pressure

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.
The safety of avacincaptad pegol was evaluated in 733 patients with AMD in two sham-controlled studies (GATHER1 and GATHER2). Of these patients, 292 were treated with intravitreal IZERVAY 2 mg (0.1 mL of 20 mg/mL solution). Three hundred thirty-two (332) patients were assigned to sham.
Adverse reactions reported in ≥2% of patients who received treatment with IZERVAY pooled across GATHER1 and GATHER2, are listed below in Table 1.

Table 1: Common Ocular Adverse Reactions (≥2%) and greater than Sham in Study Eye

Adverse Drug Reactions	IZERVAY N=292	Sham N=332
Conjunctival hemorrhage	13%	9%
Increased IOP	9%	1%
Blurred Vision*	8%	5%
Choroidal neovascularization	7%	4%
Eye pain	4%	3%
Vitreous floaters	2%	<1%
Blepharitis	2%	<1%

* Blurred vision includes visual impairment, vision blurred, visual acuity reduced, visual acuity reduced transiently.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy Risk Summary
There are no adequate and well-controlled studies of IZERVAY administration in pregnant women. The use of IZERVAY may be considered following an assessment of the risks and benefits.
Administration of avacincaptad pegol to pregnant rats and rabbits throughout the period of organogenesis resulted in no evidence of adverse effects to the fetus or pregnant female at intravenous (IV) doses 5.5 times and 3.4 times the human exposure, respectively, based on Area Under the Curve (AUC), following a single 2 mg intravitreal (IVT) dose (see Data).
In the U.S. general population, the estimated background risks of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15%-20%, respectively.
Animal Data
An embryo fetal developmental toxicity study was conducted with pregnant rats. Pregnant rats received daily IV injections of avacincaptad pegol from day 6 to day 17 of gestation at 0.1, 0.4, 1.2 mg/kg/day. No maternal or embryofetal adverse effects were observed at any dose evaluated. An increase in the incidence of a non-adverse skeletal variation, described as short thoracolumbar (ossification site without distal cartilage) supernumerary ribs, was observed at all doses evaluated. The clinical relevance of this finding is unknown. Plasma exposures at the high dose were 5.5 times the human AUC of 999 ng•day/mL (23976 ng•hr/mL) following a single 2 mg IVT dose.
An embryo fetal developmental toxicity study was conducted with pregnant rabbits. Pregnant rabbits received daily IV injections of avacincaptad pegol from day 7 to day 19 of gestation at 0.12, 0.4, 1.2 mg/kg/day. No maternal or embryofetal adverse effects were observed at any dose evaluated. Plasma exposure in pregnant rabbits at the highest dose of 1.2 mg/kg/day was 3.4 times the human AUC of 999 ng•day/mL (23976 ng•hr/mL) following a single 2 mg IVT dose.
8.2 Lactation
There is no information regarding the presence of avacincaptad pegol in human milk, or the effects of the drug on the breastfed infant or on milk production. Many drugs are transferred in human milk with the potential for absorption and adverse reactions in the breastfed child. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for IZERVAY and any potential adverse effects on the breastfed infant from IZERVAY.
8.4 Pediatric Use
Safety and effectiveness of IZERVAY in pediatric patients have not been established.
8.5 Geriatric Use
Of the total number of patients who received IZERVAY in the two clinical trials, 90% (263/292) were ≥65 years and 61% (178/292) were ≥75 years of age. No significant differences in efficacy or safety of avacincaptad pegol were seen with increasing age in these studies. No dose adjustment is required in patients 65 years and above.

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Northbrook, IL 60062

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A BIG YEAR FOR RETINA (TODAY)


This year marks *Retina Today*'s 20th anniversary! It's hard to believe we've been collaborating with and educating our peers for 2 decades—and it's been an incredible ride. The publication launched in 2006, at the dawn of anti-VEGF therapy and just as OCT was becoming a go-to imaging tool in the clinic. Now, we have second-generation anti-VEGF therapies for major retinal conditions such as diabetic retinopathy and AMD; surgically delivered gene therapy for *RPE65*-associated retinal dystrophy (Luxturna, Spark Therapeutics); treatments to slow the growth of intermediate AMD (Valeda, Alcon) and geographic atrophy (Izervay [Astellas] and Syfovre [Apellis]); surgically implanted genetically programmed cell therapy for macular telangiectasia type 2 (Encelto, Neurotech); sustained-release therapeutics such as the port delivery system (Susvimo, Genentech/Roche); and more. In our clinics and ORs, we have OCT angiography, intraoperative OCT, 3D heads-up displays, 27-gauge instruments, and retinal robotic surgery in clinical trials. Suffice to say, our practices look very different today than they did 20 years ago, and innovation seems to be progressing as fast as ever.

To celebrate these advances and milestones, we are asking our earliest contributors to reflect on the changes that have taken place since they first wrote for us. In the first installment of our *Retina: Then and Now* series, Donald J. D'Amico, MD, revisits his 2006 article on surgical approaches to retinal detachment repair. He was an early adopter of vitrectomy for primary detachments, but he notes some interesting differences in his practice patterns over the years.

We look forward to a year of reflection (on our part) and growth in the field. Who knows…perhaps some of the later *Then and Now* articles will tout new therapies fresh out of the pipeline. After all, we have a lot to look forward to in 2026, with up to nine phase 3 readouts on investigational tyrosine kinase inhibitors, a topical dexamethasone option, and gene therapies (for more on the pipeline, check out the November/December 2025 issue at retinatoday.com). We may also see an FDA response to Nanoscope Therapeutics' rolling Biologics Licensing Application for its optogenetics therapy, which would be an exciting development for our field to say the least—it could mean having an option to actually restore vision for our patients with photoreceptor degeneration. We can also look forward to some big changes in our surgical tools with the introduction of the Unity Vitreoretinal Cataract system (Alcon), Virtuoso Duel (BVI), and Oertli's OS 4 Up surgical system. This issue includes a fantastic roundup article detailing the hardware and software upgrades you can expect with these systems.

Also in this issue, experts discuss more novel tools and techniques reshaping our ORs, including scleral-fixating toric IOLs, the use of methotrexate to address proliferative vitreoretinopathy, subretinal gene therapy delivery, surgical techniques for myopic traction maculopathy, and a look at shifting treatment approaches for epiretinal membranes.

Our profession is constantly evolving, and that's one of our favorite things about it. Please join us throughout the year as we celebrate the collaboration that takes place within each issue, reminisce a little about "the good ol' days," and dream about what the next 20 years will bring to our patients. ■

ALLEN C. HO, MD
CHIEF MEDICAL EDITOR

ROBERT L. AVERY, MD
ASSOCIATE MEDICAL EDITOR

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JANUARY/FEBRUARY 2026

VOL. 21, NO. 1 | RETINATODAY.COM

IRD-ASSOCIATED GENETIC VARIANTS MAY ONLY PARTIALLY PREDICT RETINAL DISEASE

A study recently published in *The American Journal of Human Genetics* revealed that the percentage of individuals who carry a genetic variant linked to an inherited retina disease (IRD) and subsequently develop clinical retinal degeneration is smaller than has traditionally been thought.[1] These findings are challenging widely held notions regarding both the prevalence and penetrance of IRD-associated genetic variants.

Using data from large population biobanks, including the National Institutes of Health's All of Us Research Program and the United Kingdom Biobank, the researchers screened nearly 318,000 participants for variants in 33 different genes previously associated with IRDs. Of those who carried genetic variants, approximately 28% showed clinical signs of retinal degeneration when broad criteria for disease were applied; with stricter criteria, the penetrance dropped to only 9.4%.[1] While IRDs have widely been considered Mendelian in nature (ie, caused by mutations in single genes that lead to disease in almost all cases), this study suggests carrying IRD-associated genetic variants does not fully predict vision loss. Rather, additional genetic modifiers and/or environmental factors may also contribute to determining whether a person with a pathogenic IRD gene will develop retinal disease.[1]

Based on these findings, the researchers suggest it may be prudent for genetic testing and patient counseling to shift toward models that account for polygenic and environmental modifiers. In addition, future therapeutic strategies may include protective measures to help prevent disease in carriers who are unaffected.[1]

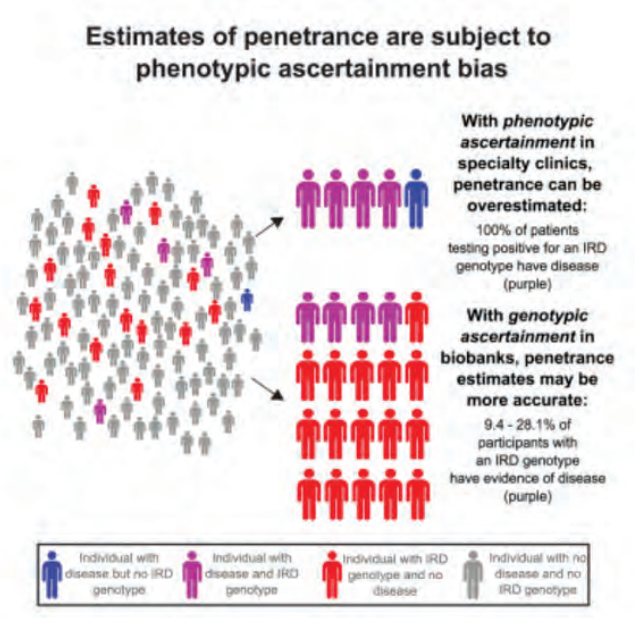

Image reprinted with permission via Creative Commons CC-BY-NC-ND.[1]

1. Zaslavsky K, Chen L, Park C, et al. Low population penetrance of variants associated with inherited retinal degenerations [published online ahead of print December 22, 2025]. *Am J Hum Genet*.

ROP TRENDS ANALYSIS REVEALS SHIFT IN DISEASE BURDEN

A recent study suggests patients with retinopathy of prematurity (ROP) continue to experience worse clinical outcomes in countries with a lower social demographic index (SDI).[1] In addition, the prevalence of ROP-associated visual impairment is on the rise in high-middle SDI countries.

This cross-sectional study included 8.79 million patients and used the Global Burden of Disease 2021 dataset to identify ROP-related visual outcomes across 204 countries between 1990 and 2021. The analysis showed countries with a low SDI and low-middle SDI accounted for most ROP-related vision-loss cases in 2021, and despite a sharp decline since the 2000s, prevalence of ROP-related blindness remains disproportionately high in these countries.[1] In addition, the prevalence pattern shows high-middle SDI countries are experiencing an increasing prevalence rate in all-grade vision loss related to ROP.[1]

Moreover, projections out to 2050 indicate the burden of ROP-related visual impairment may continue to escalate, particularly in middle and high-middle SDI countries, unless targeted action is taken.[1]

1. Wong ES, Choy RW, Zhang Y, Chan HY, Chen LJ, Pang CP, Tham CC, Yam JC. Global and regional trends in retinopathy of prematurity [published online ahead of print December 26, 2025]. *JAMA Ophthalmol*.

STUDY FINDS ELEVATED RISK OF NAION WITH COMMON DIABETES DRUGS

A large study suggests an increased risk of certain optic nerve disorders, including nonarteritic anterior ischemic optic neuropathy (NAION), with use of semaglutide and tirzepatide, glucagon-like peptide-1 receptor agonists widely used in the treatment of adults with diabetes.[1]

This study compared treatment with either semaglutide or tirzepatide versus treatment with other antidiabetic medications among patients with type 2 diabetes without prior diagnoses of ocular conditions using a database of US patient electronic health records from December 2017 to January 2023. After propensity score matching, 79,699 patients were included in the semaglutide or tirzepatide group and 79,699 in the comparison group. During a 2-year follow-up period, 35 patients in the semaglutide or tirzepatide group were diagnosed with NAION versus 19 patients in the matched comparison group (hazard ratio = 1.76). In addition, 93 patients in the semaglutide or tirzepatide group developed other optic nerve disorders versus 54 patients in the matched comparison group (hazard ratio = 1.65).[1]

The researchers concluded that there seems to be an increased risk of NAION associated with semaglutide or tirzepatide use, although the overall risk was still low.[1] Close monitoring of patients using these drugs is warranted.

1. Wang L, Volkow ND, Kaelber DC, Xu R. Semaglutide or tirzepatide and optic nerve and visual pathway disorders in type 2 diabetes. *JAMA Netw Open*. 2025;8(8):e2526327.

Eyewire+ Pharma Update

- **Aviceda Therapeutics** announced that treatment with AVD-104 demonstrated clinically meaningful reductions in geographic atrophy lesion growth rates compared with historical sham and natural history data, sustained visual acuity gains, and a favorable safety profile in its phase 2b SIGLEC trial.
- **Formycon** received FDA approval for ranibizumab-leyk (Nufymco), a biosimilar interchangeable with ranibizumab (Lucentis, Genentech/Roche), for the treatment of wet AMD, diabetic macular edema, diabetic retinopathy, macular edema following retinal vein occlusion, and myopic choroidal neovascularization.
- **Ocular Therapeutix** announced that it plans to submit a new drug application for its lead investigational therapy OTX-TKI (Axpaxli) for wet AMD shortly after receiving 1-year data from its ongoing SOL-1 phase 3 trial, which is expected in the first quarter of 2026.
- **Outlook Therapeutics** received a third complete response letter from the FDA regarding its biologics license application resubmission for bevacizumab-vikg (ONS-5010/Lytenava) for the treatment of wet AMD; the letter recommends the company submit confirmatory evidence of efficacy.
- **Samsung Bioepis** began direct commercialization of ranibizumab-nuna (Byooviz), a biosimilar to ranibizumab, across multiple European countries. The pre-filled syringe formulation is expected to become available in European markets starting in the second quarter of 2026.

Want more retina news from ***Eyewire+***?

RESEARCHERS USE DEEP LEARNING TO ENHANCE RETINAL IMAGING

A research team has developed a novel deep-learning AI framework that enables adaptive optics OCT (AO-OCT) systems to produce high-quality images using significantly fewer data than traditionally required.[1]

With high-resolution retinal imaging, dense pixel sampling is used to yield detailed imagery; however, this comes at several costs, including slow acquisition speeds, large data burdens, and motion artifacts. To circumvent the need for dense pixel sampling, researchers implemented a residual in residual transformer generative adversarial network (RRTGAN) that worked alongside traditional AO-OCT to enhance the resolution of sparsely sampled images, effectively "filling in" missing information with high fidelity. According to the researchers, the RRTGAN restored dense image quality using only 25% of the data typically required for high resolution.[1] Importantly, they also found that the RRTGAN was able to preserve structural details, such as cone cell spacing and contrast, in the enhanced images.[1] ■

1. Das V, Bower AJ, Aguilera N, Li J, Tam J. Artificial intelligence-assisted retinal imaging enables dense pixel sampling from sparse measurements. *NPJ Artif Intell*. 2025;1(1):48.

RETINA: THEN AND NOW

As part of our 20th anniversary, *Retina Today* is digging into the archives to reflect on how much the profession has changed.

JANUARY/FEBRUARY SPOTLIGHT: RETINAL DETACHMENT (RD) REPAIR

In *Retina Today*'s (*RT*) inaugural issue, which published in March 2006, Donald J. D'Amico, MD, penned an article on the *Changing Surgical Approaches for Retinal Detachment*. The primary surgical options he focused on were pneumatic retinopexy, scleral buckling, and vitrectomy. Rarely used (but still mentioned) approaches included observation, laser delimitation, and the Lincoff balloon.

At the time, Dr. D'Amico noted that a substantial percentage of primary detachments in the United States were managed with pneumatic retinopexy. Is that still the case today? *RT* sat down with Dr. D'Amico to discuss the evolution in RD repair surgery over the past 20 years. Here's what he had to say.

RT: WHAT WAS YOUR GO-TO APPROACH TO RD REPAIR IN 2006?

Dr. D'Amico: By 2006, I was already in the group (certainly still a minority at the time) that had shifted to vitrectomy as the go-to approach for most primary RDs. That would include virtually all pseudophakic cases and the majority of phakic cases. The few buckles I did back then included phakic cases with inferior breaks and very young patients without a posterior vitreous detachment (Figure).

RT: HOW HAS YOUR TREATMENT APPROACH CHANGED?

Dr. D'Amico: I have continued to expand my use of vitrectomy for primary RD, and now I do less than a handful of buckles every year; I am frequently teased for being a "buckle basher" by my colleagues. Once, while speaking at a conference, I mentioned that my first case after the meeting was a straight buckle; several friends stood up in the audience and offered to be available for a phone call from the OR if I had forgotten how to perform it!

RT: WHAT TOOLS HAVE HELPED RESHAPE YOUR APPROACH TO RD REPAIR?

Dr. D'Amico: Several breakthrough technologies have revolutionized vitreoretinal surgery. Small-gauge/transconjunctival approaches have greatly reduced operative trauma and inflammation while also offering new approaches to vitreous and membrane removal. Wide-angle intraoperative viewing, now coupled with 3D digital imaging, has given us more control of the operative field while offering a range of digital tricks to improve our view.

Vitreous cutters have become more capable with faster cutting speeds, more stable fluidics with valved cannulas, and better port placement on the probe. Even the newest stains and colorants for membranes and internal limiting membranes now allow for more complete relief of traction in complicated cases. There is even a "retro" tool; I use cryotherapy for treating breaks during vitrectomy in phakic patients because I feel it is safer for the lens.

RT: WHAT CLINICAL/SURGICAL ADVANCES ARE ON THE HORIZON?

Dr. D'Amico: First, I hope we can bring some of the power of pharmacology, such as we brought with anti-VEGF agents, to RD. Currently, all we can do is reattach a detached retina and hope for the best, but there is the possibility that adjuvant drugs, such as neurotrophic growth factors, might improve retinal recovery.

Second, in a complementary approach, we need to work on transplantation of critical cells—retinal pigment epithelium, photoreceptors, even whole blocks of retina. Researchers have done this in goldfish for a long time, and we shouldn't just throw up our hands and say it can't ever be done in humans. ■

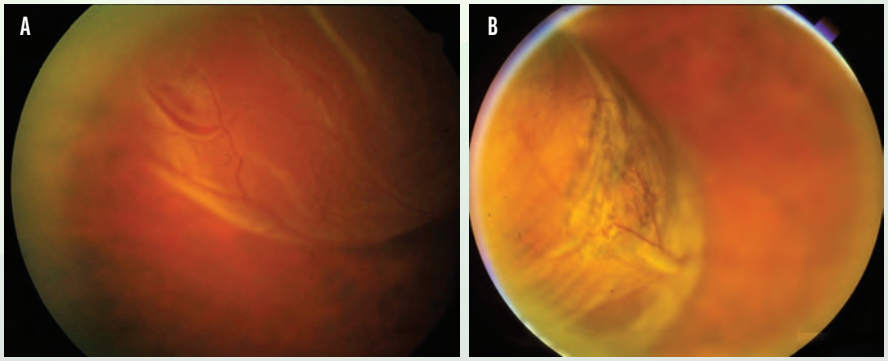

Figure. In 2006, this 43-year-old phakic patient with a bullous detachment and a single superotemporal horseshoe tear (A) was successfully treated with a scleral buckle (B). Although still a good option, Dr. D'Amico's choice in 2026 would be a vitrectomy, cryotherapy to the break, and air or short-acting gas.

DONALD J. D'AMICO, MD
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- Ophthalmologist-in-Chief, New York-Presbyterian Hospital, New York
- djd2003@med.cornell.edu
- Financial disclosure: None

FURTHER READING
Changing Surgical Approaches for Retinal Detachment
March 2006
By Donald J. D'Amico, MD

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Developed in cooperation with
Martin Charles, MD, FASRS, Argentina

3316 GentleJect™ Cannula 25g

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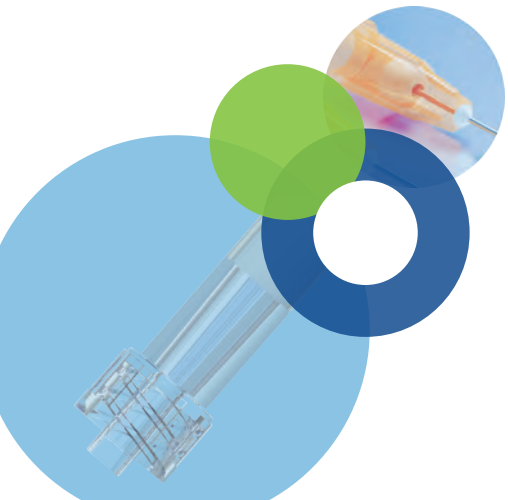

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HIGHLIGHTS FROM THE ADVANCES IN PEDIATRIC RETINA COURSE


Here's what happens when experts from around the world convene to share all things pediatric.

BY ANGELA LI, MD, AND YUXI ZHENG, MD

The 2025 Advances in Pediatric Retina (APR) Course, held September 18 – 20 at Duke University, brought together global leaders in pediatric ophthalmology and retina to share the latest research, clinical insights, and surgical innovations. The event was led by Course Director Lejla Vajzovic, MD, FASRS, and Co-Directors Cynthia A. Toth, MD, and Mary Elizabeth Hartnett, MD. With an agenda spanning retinopathy of prematurity (ROP), imaging technologies, surgical approaches, gene therapy, myopia, ocular tumors, and Coats disease, the meeting provided an unparalleled forum for advancing care for children with blinding retinal diseases.

DAY 1: ROP AND MORE

The course opened with sessions dedicated to ROP, reflecting its central role in pediatric retina worldwide. Early talks explored translational science such as novel OCT angiography models (by Pete Campbell, MD, MPH), metabolomics-derived biomarkers (by Carina Slidsborg, MD, PhD), and hypoxia-inducible factor stabilization for disease prevention (by Jonathan E. Sears, MD). Clinical updates from Baker Hubbard, MD, and Dr. Hartnett included data from the ROP4 trial on low-dose bevacizumab and strategies to extend peripheral vascularization, respectively.

Rapid-fire presentations highlighted the complex interplay between systemic factors (eg, maternal diabetes, neonatal hyperglycemia) and ROP outcomes, while also addressing screening algorithms and diagnostic variability. In a keynote lecture, Maria B. Grant, MD, emphasized the value of nutritional interventions, specifically the potential of dipeptides to modify disease pathways (Figure 1).

The afternoon transitioned to clinical ROP care, with speakers tackling controversies in preoperative anti-VEGF use, the International Classification of ROP's new P-score integration, and challenges of stage 5 disease. Decades-long surgical perspectives were shared, while discussions on atypical presentations and global screening initiatives underlined the importance of collaboration.

Figure 1. (From left to right) Drs. Vajzovic, Grant, Hartnett, and Toth gather to celebrate the first keynote lecture of the 2025 APR Course.

Sessions later in the day expanded into imaging and systemic disease, connecting OCT findings in sickle cell retinopathy and hypoxic-ischemic encephalopathy to broader pediatric health. Faculty presented advances in handheld OCT, ultra-widefield imaging, and AI-based screening. Our presentations illustrated how handheld OCT could guide surgical decision making in advanced ROP, underscoring the clinical utility of imaging innovation.

The day concluded with pediatric myopia and syndromic disorders, including Stickler and Marfan syndrome, alongside technical strategies for managing complex detachments such as those that can occur in Coats disease.

DAY 2: SURGICAL INNOVATION AND GENETICS

The second day began with sessions on pediatric retina surgery, during which experts presented novel techniques in complex detachments, persistent fetal vasculature, trauma, and Stickler-type detachments. Presentations explored how patient size, comorbidities, and genetic backgrounds shaped surgical planning, emphasizing the nuanced approach required in pediatric care.

Figure 2. (From left to right) Drs. Hartnett, Vajzovic, Berrocal, and Toth celebrate a successful day 2 keynote lecture.

Figure 3. (From left to right) Drs. Hartnett, Jalali, Toth, and Vajzovic honor the final keynote lecturer of the meeting.

In her keynote session, Audina M. Berrocal, MD, reflected on her journey toward becoming a world-renowned pediatric retina surgeon, including being the first person to use an anti-VEGF agent in an infant with ROP and leading the pediatric retina service at Bascom Palmer (Figure 2). She left the audience with inspiring pearls about the importance of mentorship, collaboration, and innovation.

The afternoon turned to genetic eye diseases and gene therapy. Talks covered subretinal injections in children (by Fanny D. Nerinckx, MD), real-world voretigene neparvovecrzyl (Luxturna, Spark Therapeutics) outcomes (by Aaron Nagiel, MD, PhD), antisense oligonucleotide therapy in retinitis pigmentosa (by Marc Mathias, MD), and interventional strategies for rare conditions such as Norrie disease and incontinentia pigmenti (by Kimberly A. Drenser, MD, PhD, and Şengül Özdek, MD, respectively). Experts shared how genetics increasingly shape both prognosis and intervention, moving the field closer to personalized pediatric retina care.

A set of rapid-fire presentations, moderated by George Caputo, MD, showcased research on Stickler syndrome, Stargardt disease, and familial exudative vitreoretinopathy, emphasizing genotype-phenotype correlations and preventive treatment strategies. This session demonstrated the power of genetics to predict outcomes and guide interventions that could prevent lifelong blindness.

Wet Lab and Challenge Stations

One of the hallmarks of the APR Course is the wet lab and challenge stations, which bridged the gap between theory and practice. After 2 days of intense didactic and case-based learning, participants spent Friday afternoon rotating through state-of-the-art surgical training stations supported by leading industry partners.

At these stations, attendees gained hands-on exposure to the latest surgical tools, imaging platforms, and visualization systems. Faculty guided small groups through techniques such as vitrectomy in premature infants, advanced visualization for ROP surgery, and innovative imaging with ultra-widefield handheld OCT. This format enhanced technical proficiency and fostered direct mentorship and dialogue between trainees, seasoned surgeons, and device innovators.

Complementing the wet lab were the challenge stations, where complex cases were presented in real time by expert faculty. Participants tested their decision-making skills, proposed strategies, and learned from diverse approaches across international practices. The interactive format encouraged collaboration and critical thinking while highlighting the variability of surgical and clinical approaches.

DAY 3: TUMORS, COATS DISEASE, AND CLOSING PERSPECTIVES

The final day started off with pediatric retinal tumors and Coats disease. Talks ranged from survival-to-vision paradigms in retinoblastoma (by Aparna Ramasubramanian, MD) to innovative biopsy techniques (by Scott Oliver, MD) and systemic cancer therapies with ocular implications (by Prithvi Mruthyunjaya, MD, MHS). Discussions also addressed the balance between globe salvage and visual function, a critical tension in pediatric oncology.

Keynote speaker Subhadra Jalali, MS Ophthalmology, discussed her decades-long experience screening and treating ROP patients in India (Figure 3). She shared the triumphs and challenges she faced along the way, including her experience being one of the only female retina specialists at the time. She has treated more than 20,000 babies during her career and continues to feel inspired to care for these most vulnerable patients.

The course concluded with a session on Coats disease, supported by the Jack McGovern Foundation, highlighting advances in our understanding of macular exudation, surgical approaches, and international collaborative outcomes.

A GLOBAL HUB FOR PEDIATRIC RETINA

Across the 3 days, the APR Course emphasized cross-disciplinary collaboration, from basic science to surgical practice and from imaging to genetics. Poster sessions, industry symposia, and networking opportunities strengthened ties among clinicians, researchers, and industry partners, all with the shared goal of improving outcomes for children with retinal diseases.

By uniting cutting-edge research with clinical expertise, the 2025 APR Course has set the stage for the next generation of therapies, innovative surgical and imaging technologies, and international partnerships in pediatric retina. ■

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ONE TO WATCH

RT Retina Today

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Nita Valikodath, MD, MS

Dr. Valikodath's advice: Don't be afraid of change or setbacks. When one path comes to an end, another inevitably appears—and it may lead to the opportunity of a lifetime. Embrace the uncertainty, trust in your growth, and enjoy the journey.

WHERE IT ALL BEGAN

I was born and raised in Michigan, and from an early age, I was drawn to science and fashion—an early appreciation for detail and beauty now reflected in my love for retina. I attended the University of Michigan Medical School and went on to complete my residency at the University of Illinois and fellowship at Duke Eye Center.

MY PATH TO RETINA

I was originally deciding between pediatric cardiology and ophthalmology. That changed during my first vitrectomy; I saw the retina through the operating microscope and was captivated. During residency, I tried to keep an open mind, but I kept coming back to retina (pediatrics specifically). I love how retina is both challenging and deeply rewarding. Being entrusted with a patient's vision is an incredible privilege I approach with the utmost care, and it continues to inspire me every day.

SUPPORT ALONG THE WAY

I've been fortunate to have many people shape my career. First and foremost is my family, especially my husband, Matthew, who has been my greatest supporter. I would not be where I am without him and our three wonderful children. In medical school, Maria Woodward, MD, MS, sparked my joy for research and set me on a clinician-scientist path. R. V. Paul Chan, MD, MSc, MBA, FACS, helped me become involved in the pediatric retina community. He invited me to sit in on the International Classification of Retinopathy of Prematurity, Third Edition, meeting, and I was honored to be in a room with leaders in the field, watching history unfold. I am grateful to all the retina faculty at Duke, especially Cynthia Toth, MD, who inspired my dedication to pediatric retina and caring for patients and their families. In addition, my interest in how technological innovation can transform patient care stems directly from her influence. That inspiration continues to drive my current work in robotic OCT. Sharon Fekrat, MD, also supported me early in my career and continues to provide guidance in my professional growth and development.

At the University of Michigan, Cagri Giray Besirli, MD, PhD, has been my primary mentor in pediatric retina and research, supporting all my academic endeavors. I am deeply grateful to all my colleagues at Michigan for their unwavering support of my career and family.

AN EXPERIENCE TO REMEMBER

I will never forget caring for an infant with persistent fetal vasculature (PFV). The family was incredibly loving but understandably anxious about the implications for their child's vision. In the OR, I encountered a thick PFV stalk inserting in a trigonal pattern across the macula and optic nerve. I proceeded with a lens-sparing vitrectomy, and although the surgery was complex, the traction was successfully relieved. With the retina more relaxed, the fovea was spared. Guiding this family through the preoperative, surgical, and postoperative stages—and watching their baby grow and do well visually at each follow-up—has been profoundly rewarding. It reminds me why I chose this field: the privilege of pairing technical skill with compassionate, lifelong care. ■

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FELLOWS' FOCUS

FELLOWSHIP: LOOKING BACK TO SEE AHEAD

Advice for the end of fellowship from those who have completed their own.

BY LUIS ACABÁ-BERROCAL, MD; JORDAN D. DEANER, MD; SAMIR N. PATEL, MD; AND JOSHUA H. UHR, MD

As rising second-year fellows, we often wonder how best to take advantage of this final year of training to prepare for life as an attending. These are some of our last opportunities to hone our skills under the guidance of mentors, and we want to absorb every last morsel of advice to make the transition to independent practice as smooth and stress-free as possible.

To answer some of these pressing questions, I asked several vitreoretinal surgeons at Wills Eye Hospital what advice they would give their younger selves as they transitioned from fellows to attendings.

LUIS ACABÁ-BERROCAL, MD: WHAT DO YOU WISH YOU KNEW SOONER AS A NEW ATTENDING RETINA SURGEON?

Jordan D. Deaner, MD: Being a vitreoretinal surgeon can be difficult, and that's okay. We didn't choose this path because it's easy; we chose it because it's challenging and demands the best of our skill, judgment, and resilience. Tough cases are inevitable, and how you prepare for and respond to them makes all the difference. Preparation begins well before you enter the OR. In about 90% of cases, I can predict exactly what I'll do and what I'll need preoperatively. Mentally rehearsing the case helps the procedure run smoothly. Anticipate what could go wrong, especially in complex surgeries, and plan how you'll respond. This foresight can be the difference between staying calm under pressure or being caught off guard.

When things go awry—and they will—act swiftly to stabilize the situation. Once you have things under control, take a moment to center yourself, assess the situation, and plan a new path forward. Following a tough case, don't carry the weight alone.

I encourage all my fellows to have a trusted peer confidant, someone they can call to talk through difficult cases in confidence. Sometimes, complications occur not because of any error, but because of the complexity of the disease itself. Having someone who understands this is invaluable. We must ensure our minds and our emotions are just as well tuned and taken care of as our hands to be the very best vitreoretinal surgeons.

Samir N. Patel, MD: As a new attending retina surgeon, you've been trained to intervene and fix problems. However, one of the most powerful skills you'll develop is knowing when to not intervene but observe instead. This might seem counterintuitive after years of focused surgical training, but it's a cornerstone of excellent patient care and long-term success.

Joshua H. Uhr, MD: I did not fully appreciate how much I still had to learn. I felt stressed early on that I did not know everything. I worried that, without an attending sitting next to me at the microscope, I might not be prepared to manage an intraoperative complication. To prepare, I read extensively and watched tons of surgical videos before my OR days, and I ran many cases by colleagues and mentors. I went over every conceivable "what if" scenario and challenged myself to hypothetically manage them. I realized that 2 years of retina fellowship, while sufficient to learn and master the fundamentals, is not enough to see every clinical

scenario or encounter every complication. In the few years I've been in practice since completing fellowship, I feel like I've completed another fellowship.

DR. ACABÁ-BERROCAL: WHAT ADVICE WOULD YOU GIVE SOMEONE AS THEY FINISH FELLOWSHIP?

Dr. Deaner: Always rely on the fundamentals of vitreoretinal surgery. No matter how complex or overwhelming a case may seem, every surgery can be broken down into basic principles and approached one step at a time. This mindset has helped me navigate many cases that initially felt impossible. When you're faced with a challenging scenario, pause for a moment. Assess the situation. Remember the goals of surgery and then move forward using the core foundation skills that you learned during your training.

Dr. Patel: It is important to predict and account for all requirements of the surgery. The OR in which you operate as an attending may be very different from that of your training institution. I would recommend getting into the OR ahead of time to get used to things so that you don't have the weight of new adjustments added to your first case on your own. I would also recommend reaching out to local surgical reps to help ease the transition. Observing a colleague prior to your first case also gives you perspective on how things run. On your first day operating, schedule lightly. This will allow you plenty of time and eliminate at least one pressure for the day.

Dr. Uhr: Being a new attending is a big adjustment. For the first time, the full weight of responsibility for a patient's care and outcome rests squarely on your shoulders. To add to the stress, you'll see cases for which you don't know the diagnosis or are unsure of the best management approach. You'll encounter situations in surgery that you haven't seen before. If you're like me, you'll second guess yourself. My advice to manage this is simple: Always ask for help. Having a good support system is immensely helpful as a new attending to learn more not only about your cases, but also about others'.

DR. ACABÁ-BERROCAL: IF YOU COULD GO BACK TO FELLOWSHIP, WHAT WOULD YOU FOCUS MORE ON OR TAKE ADVANTAGE OF?

Dr. Deaner: This is a bit of a double-edged sword. In fellowship, you want to operate as much as possible to gain technical skill and experience. However, some of my most valuable experiences as a fellow were at the end of my training. Observing how experienced attendings approach surgery—both technically and strategically—offered insights I couldn't have appreciated earlier. Even when you're not the one holding the instruments, stay engaged. There's a tremendous amount to learn by watching experienced surgeons operate.

Dr. Patel: Most retina fellowships provide the highest levels of medical and surgical training. However, whether you join a university-based practice or a private practice, there is a steep learning curve in understanding the business and administrative side of medicine. Try to spend some dedicated time with your fellowship mentors to understand the nuances of CPT and ICD-10 codes, modifiers, payer-specific policies, and the documentation required to support them.

Dr. Uhr: During fellowship, I wish I focused less on absolute surgical numbers and more on getting as broad of a surgical experience as possible. I was fortunate to train at an institution with many attendings trained through diverse fellowship programs and brought a wide range of surgical techniques, preferences, and tips and tricks to the table. Take advantage of the breadth and diversity of your attendings' skillsets. Try to use as many instruments, techniques, and surgical platforms as you can. If there's a particular area that you want to work on, don't be afraid to tell your attendings. The broader of an experience you have, the more prepared you'll be after fellowship. ■

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NEONATAL VITREOUS HEMORRHAGE DIFFERENTIALS



ROP isn't the only condition that can present with complications in infants.

BY PREEYA MEHTA, MD; ZACHARY ELKIN, MD; AND VAIDEHI DEDANIA, MD

The incidence of retinal and optic nerve hemorrhages in neonates is around 20%,[1] yet the incidence of neonatal vitreous hemorrhage (VH) is unknown. While retinopathy of prematurity (ROP) is a well-recognized cause of VH in premature neonates,[2] clinicians must be knowledgeable of other conditions that can present with VH, are associated with serious systemic manifestations, or may lead to blindness. In particular, the risk of amblyopia is a critical point of consideration, as are structural changes that may affect vision. Here, we discuss various etiologies of neonatal VH and briefly outline diagnostic considerations.

VASCULAR ABNORMALITIES

Familial exudative vitreoretinopathy (FEVR) is a bilateral hereditary disorder that typically presents in full-term infants. This feature distinguishes it from ROP, which develops in pre-term infants.[3] Mutations in *FZD4*, *LRP5*, *TSPAN12*, and *NDP* lead to impaired vascularity and arrested retinal angiogenesis during the last trimester of pregnancy.[3,4]

Clinical examination demonstrates peripheral retinal avascularity with minimal vitreous condensation. This avascularity creates a hypoxic drive that can lead to secondary neovascularization and VH. Routine monitoring with widefield imaging and fluorescein angiography (FA) is necessary to assess disease activity and progression.[3]

ROP and FEVR (ROPER) is a subset of FEVR that presents in premature infants. As it can be challenging to distinguish ROPER from ROP, FA can help differentiate the two. In ROP, FA demonstrates a homogenous front/border; in ROPER, there are irregular sprouts as well as vessel pruning, segmental vascular leakage, and vascular loops beyond the edge of vascularization. Because the clinical course in ROPER is unpredictable with stages of inactivation and re-activation, patients require regular, life-long evaluation.[4]

Incontinentia pigmenti is a rare, inherited condition caused by a mutation in the *NEMO* gene, which regulates NF-kB activity and is vital for cell survival.[3,5] Systemic manifestations include skin blisters that eventually resolve into streaks of hypopigmented macules, dental abnormalities, and neurologic impairment.[5] The majority of cases are female, as the mutation is lethal in males.[3]

Ocular involvement occurs secondary to vaso-occlusion and ischemia.[6] In contrast to ROP and FEVR, retinal ischemia does not follow a developmental vascular pattern.[3] Thus, while peripheral ischemia leads to classic neovascularization and subsequent tractional retinal detachment (RD), central ischemia can lead to foveal hypoplasia.[3,6]

FA can identify areas of avascular retina requiring laser photocoagulation, while OCT and OCT angiography can aid in the identification of macular abnormalities.[3,7] These patients should be followed monthly with dilated fundus examination and, preferably, FA from birth to 4 months of age and then every 3 months until 1 year of age.[3]

Persistent fetal vasculature (PFV) is a sporadic condition caused by failed involution of the embryonic hyaloid vasculature.[8] It is typically unilateral but may be bilateral in systemic conditions.[9,10]

Clinically, PFV is characterized into anterior and posterior ocular involvement, although patients can present with both forms simultaneously.[10,11] Posterior involvement is characterized by the presence of a retrolental stalk or persistent fibrovascular tissue extending from the optic nerve.[9,10] This tissue causes traction on the retina, resulting in retinal folds and distortion of the optic nerve and macula, which can progress to RD.[10] VH is secondary to hyaloid artery fragility and can be precipitated by ocular trauma.[12]

Norrie disease is a severe, rare X-linked disorder caused by a mutation in the *NDP* gene.[3,13] This genetic defect primarily affects retinal development.[13,14] Systemic manifestations commonly include progressive hearing loss and various neurologic abnormalities.[13,15] As it is an X-linked condition, the vast majority of affected patients are male.[16]

Patients typically present with bilateral leukocoria at or within a few weeks of birth.[15] The fundus examination reveals a dysplastic retinal mass located behind the lens, which is often termed a *pseudoglioma* because it resembles the tumor

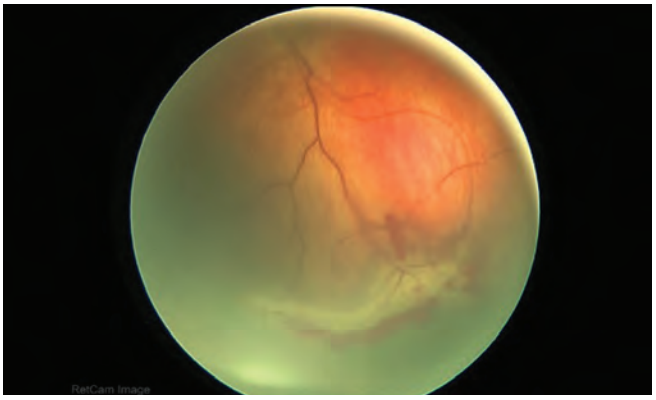

Figure 1. Fundus photography of CMTC demonstrates severe peripheral nonperfusion and subsequent hemorrhage and traction.

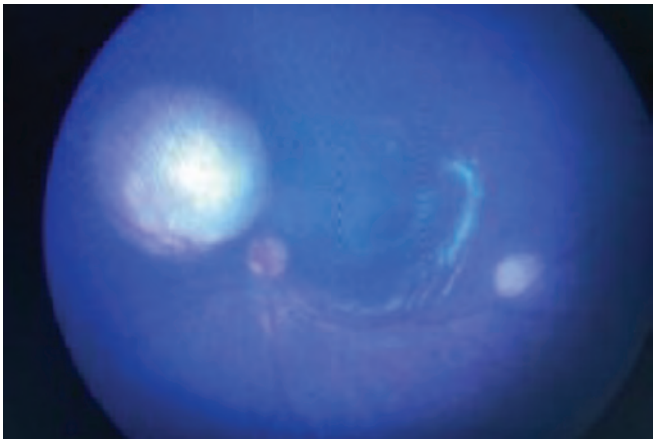

Figure 2. Fundus photography shows an RB.

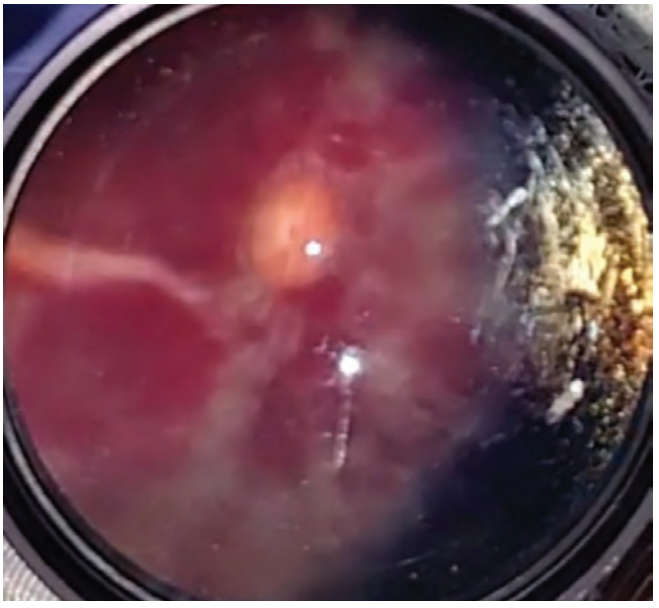

Figure 3. Retinal hemorrhages can be seen in AHT.

retinoblastoma (RB).[3] The retina immediately beyond this mass is often avascular.[3] This widespread avascularity leads to severe retinal traction,[3] resulting in VH and progressive RD. Persistent stalk tissue connecting the lens to the dysplastic retina significantly contributes to retinal traction.[3,14]

Cutis marmorata telangiectatica congenita (CMTC) is a spontaneous, cutaneous vascular disorder characterized by three main features of the skin: a mottled, net-like pattern, telangiectasias, and a potential for skin ulcerations and other vascular lesions, including port wine stains.[17,18] The associated ocular abnormalities are varied and include glaucoma,[19] peripheral retinal vasculopathy, nonperfusion, and RD.[17]

The spectrum of retinal pathology in CMTC is wide, ranging from subtle findings such as mild vessel straightening to severe complications, including widespread nonperfusion, fibrovascular proliferation, and subsequent RD (Figure 1).[17] Severe nonperfusion is hypothesized to occur secondary to vascular occlusion within the retina.[20] The potential for rapid deterioration is significant, as demonstrated in one case series where the avascular retina progressed to retinal hemorrhage or VH within a week, underscoring the critical importance of close and timely ophthalmic follow-up for these patients.[17]

Patients diagnosed with CMTC must receive a comprehensive ophthalmic examination immediately after birth.[17] Given the risk of rapid progression, these patients require frequent follow-up examinations and FA throughout the first few months of life.[17] As this condition is rare, no established guidelines exist. However, the more severe the initial findings, the more frequently patients must be seen.

NEOPLASMS

Retinal cavernous hemangioma (RCH) is a benign vascular tumor defined by unique grape-like clusters of thin-walled intraretinal angiomatous lesions.[21,22]

These lesions often have a distinctive cap of glial tissue on their surface. Although typically stable and asymptomatic, RCH lesions have been known to occasionally present with VH. This hemorrhage is often secondary to the inherent fragility of the thin vascular walls of the hemangioma, although some neonatal cases have been hypothesized to be secondary to birth trauma.[22,23]

Due to the occasional association between VH and birth trauma, RCH should be included in the differential diagnosis when evaluating infants presenting with VH of unknown cause.[22,23] If RCH is confirmed, a systemic evaluation for associated lesions is mandatory, particularly for cavernous hemangiomas of the brain and skin.

RB is the most common primary intraocular malignancy in children and is a critical diagnosis to exclude in any young patient presenting with a suspicious intraocular mass.[24] RB is well described to cause VH in older infants and children when the tumor necrosis or bleeding vessels disrupt the inner retinal boundary (Figure 2).[25] Therefore, RB must be kept high on the differential diagnosis for any child with unexplained VH.

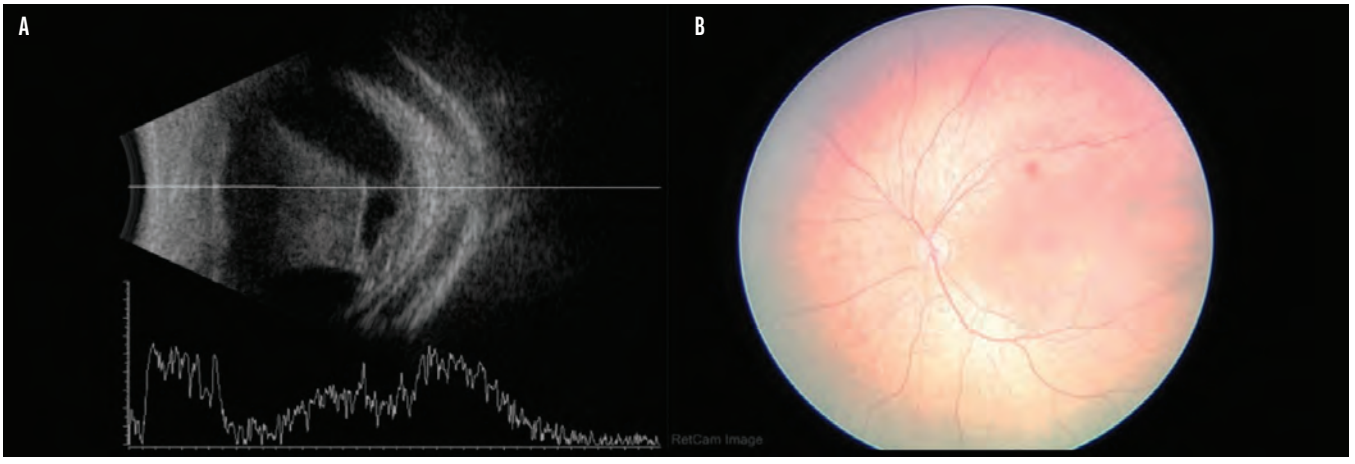

Figure 4. B-scan ultrasound of the right eye shows VH in association with Terson syndrome that required vitrectomy (A). Fundus photography of the left eye shows intraretinal hemorrhage (B).

Neonatal RB, while rare, commonly presents in association with familial RB. In these high-risk familial cases, specialized screening for tumors can be performed as early as the third trimester of pregnancy or immediately at birth.[26,27] Thus, unexplained VH in a newborn should prompt additional questioning on any history of familial RB and warrants a low threshold for obtaining further imaging.

TRAUMA

Abusive head trauma (AHT) frequently presents with hemorrhages in all three retinal layers (preretinal/subhyaloid, intraretinal, and subretinal) and is often accompanied by VH (Figure 3).[28] The presumed mechanisms include a rapid shearing motion generated during shaking or a sudden, dramatic rise in intracranial pressure that is rapidly transmitted to the eye.[29]

In neonates with AHT, the presence of VH is a marker for a poor neurological and ocular prognosis.[28] This is likely secondary to concurrent visual pathway dysfunction and other concomitant retinal pathology.[28]

Birth trauma typically presents with retinal hemorrhages, but it has also been documented to present with VH, although less commonly.[1,30,31] When a significant birth-related VH does not clear spontaneously, vitrectomy may be performed to remove the blood and prevent amblyopia.[32]

RARE VH DIFFERENTIALS

Terson syndrome is defined as the presence of intraocular hemorrhage concurrent with an acute intracranial hemorrhage (Figure 4).[33] Terson syndrome is rare in the neonate and pediatric population compared with the adult population.[34] This rarity is likely due to physiologic protective factors in children, including better autoregulation of cerebral vasculature and potentially more restrictive communication between the optic nerve sheath and intracranial space, limiting the transmission of pressure.[35]

Terson syndrome, when reported in children, is associated with several underlying causes, including accidental trauma, birth trauma, and leukemia.[34,36,37] If there is minimal improvement in VH, a low threshold for vitrectomy should be maintained to prevent amblyopia.[34]

Toxoplasmosis, other agents such as syphilis/parvovirus, rubella, cytomegalovirus, and herpes simplex virus (TORCH) have been shown to cause intraocular inflammation and VH in premature and systemically ill neonates. The challenge in diagnosis is highlighted by a case report where the initial working diagnosis was aggressive ROP. Subsequent definitive diagnosis during vitrectomy revealed findings consistent with bilateral retinal necrosis.[38]

Hematologic abnormalities can lead to neonatal VH due to underlying coagulopathy. Case reports have described neonatal VH from severe vitamin K deficiency or untreated galactosemia, with associated liver dysfunction likely causing widespread coagulopathy.[39,40]

KEEP AN OPEN MIND

When faced with VH in a neonate, clinicians must consider a robust list of differentials beyond ROP to ensure proper diagnosis and treatment. In the management of VH, clinicians must account for the significant risk of amblyopia—an outcome equally as important as the structural ocular changes seen with these conditions. Optimal care for these patients requires the unified expertise of pediatric ophthalmology and vitreoretinal surgeons. ■

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Severe vision loss defined as three or more lines of visual acuity loss [≥15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters] has occurred following ENCELTO implantation. Monitor patients for signs and symptoms of vision loss and manage as clinically indicated.

Infectious Endophthalmitis

Infectious endophthalmitis may occur following ENCELTO implantation. Signs and symptoms of infectious endophthalmitis include progressively worsening eye pain, vision loss, or scleral and conjunctival injection. To mitigate the risk of endophthalmitis, use proper aseptic surgical technique for ENCELTO implantation. Monitor patients for signs or symptoms of infectious endophthalmitis. Remove ENCELTO implant if infectious endophthalmitis occurs and manage symptoms according to clinical practice.

Retinal Tear and Detachment

Retinal tears and retinal detachment may occur following ENCELTO implantation. Signs and symptoms of retinal tears include acute onset of flashing lights, floaters, and/or loss of visual acuity. Signs and symptoms of retinal detachment may include progressive visual field loss and/or loss of visual acuity. Use standard vitreoretinal surgical techniques during ENCELTO implantation to minimize the risk of retinal tears and retinal detachment. Monitor for any signs or symptoms of retinal tear and/or retinal detachment. Treat rhegmatogenous retinal detachment and retinal tears promptly. Remove ENCELTO implant, if vitrectomy with a complete gas fill or silicone oil fill is required.

Vitreous Hemorrhage

Vitreous hemorrhage, which may result in temporary vision loss, has occurred following ENCELTO implantation. Patients receiving antithrombotic medication (e.g., oral anticoagulants, aspirin, nonsteroidal anti-inflammatory drugs) may be at increased risk of vitreous hemorrhage. To reduce the risk of vitreous hemorrhage, interrupt antithrombotic medications prior to the ENCELTO implantation. Vitrectomy surgery may be necessary to clear severe, recurrent, or non-clearing vitreous hemorrhage. If the patient has a late onset vitreous hemorrhage (greater than one year following ENCELTO implantation surgery), examine the ENCELTO implantation site for possible implant extrusion. If implant extrusion has occurred, surgically reposition ENCELTO.

Implant Extrusion

Implant extrusion through the initial scleral wound has occurred following ENCELTO implantation. Signs and symptoms of implant extrusion include recurrent uveitis, vitreous hemorrhage, eye pain more than one year after implantation, or visibility of titanium fixation loop under the conjunctiva. To reduce the risk of implant extrusion, carefully follow the specific surgical steps for ENCELTO implantation.

Evaluate patients after 6 months to confirm proper positioning of ENCELTO and then annually. If ENCELTO begins to extrude, surgically reposition ENCELTO to a proper scleral wound depth either in the same site or in the opposing inferior quadrant of the vitreous cavity.

Cataract Formation

Cataract formation, including cataract cortical, cataract nuclear, cataract subcapsular, cataract traumatic, and lenticular opacities, has occurred following ENCELTO implantation. To reduce the risk of ENCELTO-related cataract formation or progression, carefully follow the specific surgical steps for ENCELTO implantation.

Suture Related Complications

Suture related complications, including conjunctival erosions due to suture tips and suture knots, have occurred following ENCELTO implantation.

To mitigate the risk of suture related complications, carefully follow the specific surgical steps for ENCELTO implantation and manage suture-related complications as clinically indicated.

Delayed Dark Adaptation

Delayed Dark Adaptation, a delay in the ability to adjust vision from a bright lighting condition to a dim lighting, has occurred following ENCELTO administration which remained unchanged for the duration of study follow up. Advise patients to take caution while driving and navigating in the dark.

ADVERSE REACTIONS

The most common adverse reactions (≥2%) reported with ENCELTO were conjunctival hemorrhage, delayed dark adaptation, foreign body sensation, eye pain, suture related complications, miosis, conjunctival hyperemia, eye pruritus, ocular discomfort, vitreous hemorrhage, blurred vision, headache, dry eye, eye irritation, cataract progression or formation, vitreous floaters, severe vision loss, eye discharge, anterior chamber cell, iridocyclitis.

Please see Brief Summary of full Prescribing Information on following pages.

Reference: ENCELTO [prescribing information]. Cumberland, RI. Neurotech Pharmaceuticals, Inc.

neurotech

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all of the information needed to use ENCELTO™ safely and effectively.

See full Prescribing Information for ENCELTO.

ENCELTO (revakinagene taroretcel-lwey) implant, for intravitreal use

Initial U.S. Approval: 2025

INDICATIONS AND USAGE

ENCELTO is indicated for the treatment of adults with idiopathic macular telangiectasia type 2 (MacTel).

DOSAGE AND ADMINISTRATION

Recommended Dose

For intravitreal implantation only

- ENCELTO is administered by a single surgical intravitreal procedure performed by a qualified ophthalmologist.
- The recommended dose is one ENCELTO implant per affected eye. Each ENCELTO implant contains 200,000 to 440,000 allogeneic retinal pigment epithelial cells expressing recombinant human ciliary neurotrophic factor (rhCNTF) (NTC-201-6A cell line), a neurotrophic factor.

CONTRAINDICATIONS

ENCELTO is contraindicated in patients with:

- Active or suspected ocular or periocular infections.
- Known hypersensitivity to Endothelial Serum Free Media (Endo-SFM)

WARNINGS AND PRECAUTIONS

Severe Vision Loss

Severe vision loss defined as three or more lines of visual acuity loss [≥15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters] has occurred following ENCELTO implantation. Monitor patients for signs and symptoms of vision loss and manage as clinically indicated.

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ADVERSE REACTIONS

Clinical Trials Experience

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

ADVERSE REACTIONS (cont'd)

Clinical Trials Experience (cont'd)

The safety data described in this section reflects exposure to ENCELTO in two clinical trials, Study 1 (NTMT-03-A) and Study 2 (NTMT-03-B) and are pooled for analysis. A total of 117 patients received ENCELTO, and 111 patients underwent a sham procedure and were followed for a duration of 24 months.

Serious adverse reactions occurred in six patients (5%) including suture related complications (n=5) and implant extrusion (n=1).

Table 1 lists the most common adverse reactions that occurred in ≥2% patients and with higher frequency in ENCELTO group compared to Sham group in Study 1 and Study 2.

Table 1. Adverse Reactions occurring in ≥2% of Patients and with higher frequency in ENCELTO group compared to Sham group in ENCELTO studies*

Adverse Reactions	ENCELTO (N=117) n (%)	Sham (N=111) n (%)
Conjunctival hemorrhage	36 (31)	29 (26)
Delayed dark adaptation	27 (23.1)	1 (1)
Foreign body sensation in eyes	18 (15)	15 (13.5)
Eye pain	18 (15)	10 (9)
Suture related complication**	18 (15.4)	3 (2.7)
Miosis	18 (15.4)	0 (0.0)
Conjunctival hyperemia	13 (11)	9 (8)
Eye pruritus	10 (9)	4 (3.6)
Ocular discomfort	10 (9)	1 (1)
Vitreous hemorrhage	10 (8.5)	0 (0.0)
Vision blurred	8 (7)	4 (4)
Headache	8 (7)	1 (1)
Dry eye	7 (6)	2 (2)
Eye irritation	6 (5.1)	2 (2)
Cumulative cataract incidence	6 (5)	0 (0)
Vitreous floaters	6 (5)	0 (0.0)
Severe visual loss>15 letters***	4 (3)	0 (0)
Eye discharge	4 (3.4)	1 (0.9)
Anterior chamber cell	4 (3.4)	0 (0.0)
Iridocyclitis	3 (2.6)	0 (0)

*Pooled data from Study 1 and Study 2; Adverse reaction rates were comparable between the two studies

**Suture related complications include exposed suture, foreign body sensation, conjunctival wound dehiscence, painful sutures, suture irritation, suture granuloma, scleral wound opening, and itchy suture

***Includes one case of visual loss due to cataract formation which remained unresolved at the end of the study

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no data on the use of ENCELTO in pregnant women. Endogenous CNTF is naturally found in maternal plasma, placental cells, and umbilical cord blood. It is not known if the use of ENCELTO increases CNTF above naturally occurring levels in these tissues.

In animal reproduction studies, subcutaneous administration of rhCNTF to pregnant rats and rabbits demonstrated no evidence of teratogenic effects on the fetus. However, when administered to rabbits at a dose level of 10ug/kg/day, a decrease in implantations and live fetuses was observed. When administered to rats at a dose level of 100ug/kg/day a decrease in corpora lutea was observed.

The estimated background risk of major birth defects and miscarriage in the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. 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

See *Risk Summary* for details on data.

Lactation

Risk Summary

There is no data on the presence of ENCELTO in human milk, its effects on the breastfed infant, or its impact on milk production.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ENCELTO and any potential adverse effects on the breastfed infant from rhCNTF or from the underlying maternal condition.

Pediatric Use

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

Geriatric Use

There were 38 patients (32%) 65 years of age and older and two patients (1%) 75 years of age and older in Study 1 and Study 2 who received ENCELTO. Clinical studies of ENCELTO did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger patients.

Manufactured for:
Neurotech Pharmaceuticals, Inc.
Cumberland, RI 02864

ENCELTO™
(revakinagene taroretcel-lwey)
implant, for intravitreal use

neurotech

US-EO-PM-250200024 04/2025

IMPLANTING ENCAPSULATED CELL-BASED GENE THERAPY

Add MacTel therapy to your surgical armamentarium.

BY THOMAS M. AABERG JR, MD; CHARLES C. WYKOFF, MD, PHD, FASRS, FACS; AND LILIYA SUTHERLAND, DO

In March 2025, revakinagene taroretcel-lwey (Encelto, Neurotech Pharmaceuticals) was approved by the FDA for the treatment of adults with idiopathic macular telangiectasia type 2. This encapsulated cell-based gene therapy, designed to continuously release human ciliary neurotrophic factor into the vitreous cavity, is implanted using a surgical approach that falls within every retina surgeon's skillset.

To begin the implantation procedure, a 7 mm x 7 mm conjunctival limbal peritomy is performed in an inferior quadrant (although not required, a limbal traction suture is recommended to rotate the eye and improve access). Dissect Tenon capsule from the bare sclera and ensure meticulous hemostasis with wet-field cautery.

A 3-mm sclerotomy should be made 3.75 mm posterior and parallel to the limbus. This full-thickness incision can be achieved using a 20-gauge microvitreoretinal blade, followed by further enlargement with a 15° asymmetric blade. If required, apply cautery to ensure hemostasis within the scleral incision.

Prior to insertion, revakinagene taroretcel-lwey should be rinsed with at least 5 mL of sterile balanced salt solution to remove the cell medium, with continuous rinsing every 10 minutes to prevent dehydration of the implant.

A 9-0 polypropylene double-armed suture is passed through the titanium fixation loop located at the end of the implant. The sclerotomy incision is gently opened using toothed forceps, and the implant is inserted perpendicular to the globe, ensuring that the fixation loop remains exposed. Direct the implant toward the optic nerve, avoiding the lens. The implant is released into the sclerotomy by squeezing the gripper at the designated area (Figure 1).

Keeping both needles attached, an anchor knot (3-1-1) is used to secure the polypropylene suture to the fixation loop. The knot should be placed at the apex of the fixation loop, ensuring tight, locking throws. Each end of the suture is then passed through the sclera at 90% depth such that the fixation knot and apex of the titanium loop rest just inside the scleral incision (Figure 2). Tie the polypropylene suture down to the sclera with a 3-1-1 episcleral knot. Optimally, the knot is positioned away from the incision. Leave the needles attached to the polypropylene suture to be used for the final closure.

With the needles still attached, bury the polypropylene suture into the sclera by taking at least a 2.0-mm long bite of the sclera at 50% to 75% depth beyond the end of the

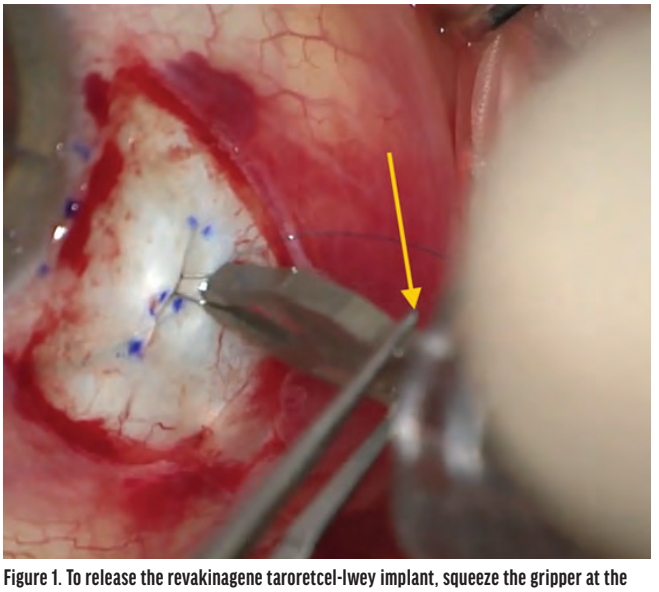

Image courtesy of Neurotech and Charles C. Wykoff, MD, PhD

Figure 1. To release the revakinagene taroretcel-lwey implant, squeeze the gripper at the designated area, as shown here.

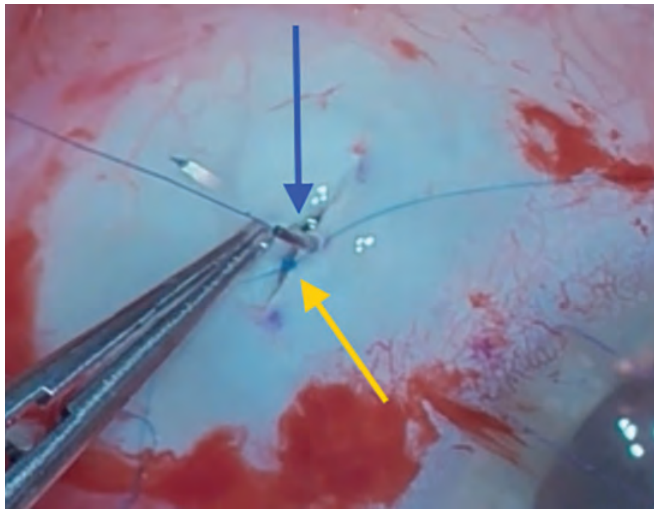

Image courtesy of Neurotech and Liliya Sutherland, DO

Figure 2. The polypropylene suture is passed at 90% scleral wound depth (blue arrow). The 3-1-1 polypropylene fixation knot sits at the apex of the titanium loop (yellow arrow).

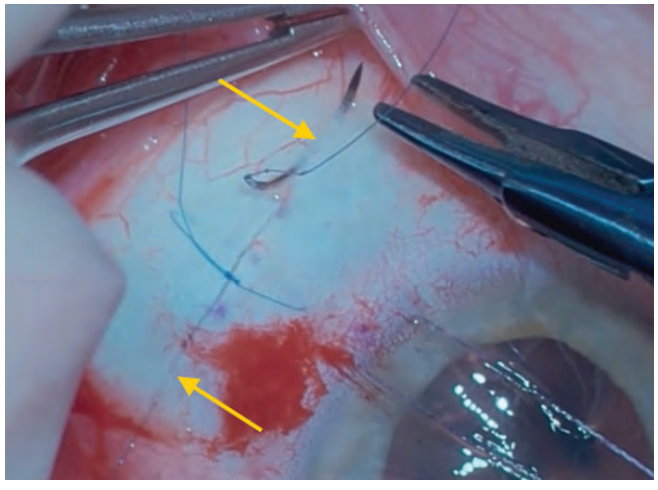

Image courtesy of Neurotech and Liliya Sutherland, DO

Figure 3. Bury the polypropylene suture tails into the sclera at 50% to 75% depth beginning just beyond the end of the scleral wound.

sclerotomy (Figure 3). This minimizes the risk of the polypropylene suture tails eroding through the conjunctiva. Keep the needles attached until the wound is fully closed.

The scleral incision should be closed using 9-0 nylon sutures, ensuring a watertight closure. To ensure there is no internal wound gape, each nylon suture should be passed at a depth of 75% to 80%, with the knots rotated into the sclera. If the knot cannot be buried in the sclera, replace the suture and use a 1-1-1 "Dangle" style knot. When closing the scleral wound, divide the wound into thirds, essentially ignoring the polypropylene suture. The nylon sutures should be closer to the polypropylene suture than to the end of the scleral wound. Once the wound is closed, the polypropylene suture is cut flush to the sclera.

Close the conjunctiva and Tenon capsule using 6-0 plain gut or chromic sutures, or 7-0 vicryl suture with a three-point fixation. Ensure the closure is secure to prevent conjunctival retraction and exposure of the scleral sutures.

WHAT-IF SCENARIOS

While rare, the polypropylene suture can break. If the suture breaks while tying the fixation knot to the apex of the titanium loop, the suture must be replaced. Pass a new double armed 9-0 polypropylene suture through the islet, then remove the broken suture and proceed as described above. If the suture breaks after the polypropylene suture has been passed through the edges of the scleral wound, complete the episcleral 3-1-1 knot, thereby securing the revakinagene taroretcel-lwey implant and keeping the broken suture tail long. Capture the tail with the closing nylon sutures and consider adding another nylon suture to keep the polypropylene suture tail flat on the sclera.

NEW CHALLENGES IN THE OR

A new surgical implant such as revakinagene taroretcel-lwey might not challenge your skillset, but you can be successful by paying attention to the details of the surgery and maintaining a focus on surgical best practices. ■

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- Financial disclosure: Consultant (Castle Laboratories, Regeneron); Employee (Neurotech Pharmaceuticals)

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LILIYA SUTHERLAND, DO

- Retina Specialist, Retina Specialists of Michigan, Grand Rapids, Michigan
- Financial disclosure: None

ONE TO WATCH

RT Retina Today

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Hasenin Al-khersan, MD

Dr. Al-khersan's advice: Find your passion—it's a cliché for a reason. Find the role that will motivate you for the next 10, 20, and 30 years. If that role doesn't yet exist, create it.

WHERE IT ALL BEGAN

My perspective on life is fundamentally informed by my background as an immigrant, born in Baghdad, Iraq. When I was 5 years of age, my family moved first to New Zealand to escape political turmoil and economic strife and then to Michigan, where we lived in a rural town for much of my childhood. While it was difficult adjusting to vastly different cultures, the help I received along the way fostered a desire to pay it forward and find a way to help others. For me, this meant a career in medicine and following in the footsteps of my father.

MY PATH TO RETINA

When I was a child, my uncle lost his vision due to a brain tumor. The effect this had on him and our family has stayed with me from an early age. Since then, I have had a deep respect for the importance of vision on quality of life. My interest in the visual sciences narrowed into a focus on retina during my undergraduate years at the University of Michigan, where I worked in a retinal physiology lab. I tended to my cultured retinal pigment epithelial cells, captivated by their complexity. Although I was deeply interested in the physiology of vision, I knew I also wanted to help patients on the front lines of clinical medicine. The opportunity to acutely preserve vision as a retina specialist remains the core motivator of my clinical pursuits.

SUPPORT ALONG THE WAY

I have had many great mentors in my training and early career. As a medical student at the University of Chicago, Seenu M. Hariprasad, MD, was the first retina specialist I shadowed, and he took me under his wing. During residency, fellowship, and chief residency at Bascom Palmer Eye Institute, I looked to Audina M. Berrocal, MD, and Harry W. Flynn Jr, MD, for advice. Dr. Flynn taught me to understand the full context of the patient—remembering that patients are people, not pathology. Dr. Berrocal modeled for me the art of the doctor-patient relationship. As a pediatric retina specialist, she mastered the intense technicality of pediatric retina surgery while also compassionately navigating the relationships with her young patients and their families.

Lastly, in my early career at the Retina Consultants of Texas, Charles C. Wykoff, MD, PhD, has been a selfless mentor, advocate, and friend. He has helped open doors for me to advance as a clinical trialist. I seek his advice on a near daily basis.

AN EXPERIENCE TO REMEMBER

Serving as chief resident at Bascom Palmer remains the most challenging and rewarding experience of my career. As a chief, I directed the ocular trauma service while also running a bustling retina service. Additionally, the opportunity to teach brilliant residents and fellows in the OR made the experience especially fulfilling. While the hours were long, I was lucky to serve in the role with a wonderful co-chief and lifelong friend, Thomas Lazzarini, MD. ■

Hasenin Al-khersan, MD, is a vitreoretinal specialist at the Retina Consultants of Texas in Houston. He is a consultant for Abbvie, Adverum, ANI, Annexon, Apellis, Eyepoint, Genentech/Roche, Ocular Therapeutix, and Regeneron. He can be reached at hakmd@retinaconsultantstexas.com.

THE NEW RETINA OR: THE LATEST VITRECTOMY TOOLS

New platforms and instruments can help improve surgical efficiency and patient outcomes.

By María H. Berrocal, MD; Luis Acabá-Berrocal, MD; Priya Vakharia, MD; David Steel, MBBS, FRCOphth, MD(Res); and MitroFanis Pavlidis, MD, PhD

Vitrectomy technology continues to advance rapidly with new platforms, hardware and software upgrades, and innovative new surgical instrumentation. Now, surgeons have myriad platforms to choose from, along with a robust lineup of integrated tools. Here, we share the latest advances to hit our retina ORs.

ALCON'S UNITY VITREORETINAL CATARACT SYSTEM


By María H. Berrocal, MD, and Luis Acabá-Berrocal, MD

The Unity Vitreoretinal Cataract System (VCS) integrates intelligent fluidics, IOP control, aspiration, and illumination—made possible through sensors that maintain constant flow and stable IOP during procedures (Figure 1). It is complemented by a redesigned 27-gauge instrument portfolio with stiffening sleeves, TetraSpot laser probes, enhanced entry and infusion systems, and a 4D phaco handpiece with thermal sentry and volumetric ultrasound technology.

The Unity VCS operates with flow-controlled rather than vacuum-controlled fluidics. Thus, the flow remains constant regardless of media viscosity. The advanced pressure and flow regulation and dual venturi-peristaltic pump technology provides exceptional efficiency and chamber stability. The intelligent IOP control dynamically compensates for leakage and pressure fluctuations, maintaining the target IOP within ± 2 mm Hg.[1] Intelligent aspiration enables high-vacuum capability for rapid posterior vitreous detachment induction.

The new 27-gauge vitrectomy probe and light pipe incorporate a dynamic stiffener for increased rigidity, a dual-blade cutter, beveled tip, and 30,000 cpm cutting capability. The continuously open port enhances vitreous removal efficiency while reducing tractional forces. The beveled 25-gauge tip allows 47% closer proximity to the retina compared with rounded tip probes, improving

AT A GLANCE

- Alcon's Unity Vitreoretinal Cataract System delivers high efficiency and performance across all steps of vitreoretinal and cataract surgery, integrating intelligent fluidics, IOP control, aspiration, and illumination.
- BVI's Virtuoso DUAL combined phacovitrectomy machine provides low-traction, high-speed vitrectomy, optimized energy delivery during phacoemulsification, and enhanced operational efficiency.
- DORC's Eva Nexus includes VTi pump fluidics, Smart IOP intelligence, and the TDC Veloce, which enhances flow, suction force, rigidity, and ergonomics.
- Bausch + Lomb's Stellaris Elite now includes the Adaptive Fluidics software, which monitors the vacuum and adjusts the infusion pressure to compensate for IOP changes during vitrectomy.

access to tissue planes and enabling many maneuvers to be completed with the vitrector alone.[1] The 25- and 27-gauge dual pneumatic cutter of the Unity VCS provides 50% faster cut speeds compared with the Constellation (Alcon) with significantly less traction on mobile retina.[1]

The Unity TetraSpot laser probe reduces laser application time by up to threefold compared with a single-spot laser. Its curved, illuminated design enhances efficiency and supports continuous delivery. The improved entry system of the Unity, compared with the Constellation, uses recessed cannulas, facilitating smoother soft-tip instrument entry and enabling nearly two-times faster silicone oil injection and extraction in all gauges.[1]

Figure 1. The Unity VCS incorporates intelligent IOP control and fluidics, aspiration, and illumination.

Compared with the Constellation, the Unity VCS offers 25% faster setup with single-step prime-and-test, fewer connections, and 42% faster tear-down.[2] The reduced-impact consumable packs lessen the carbon footprint.

The Unity VCS streamlines combined procedures, delivers intelligent globe stability, optimizes pressure and fluidics, and makes even the smallest 27-gauge surgeries highly efficient.

BAUSCH + LOMB'S STELLARIS ELITE

By Priya Vakharia, MD

The Stellaris Elite has been a staple in my OR for years, in part because it provides flexibility for ORs that support both cataract and vitreoretinal surgery (Figure 2). The platform comes with a versatile wireless pedal with separate pitch and yaw control and laser control, eliminating the need for a second laser pedal.[3] I find this particularly helpful in cases involving the fragmatome.

One recent update to the system is the Adaptive Fluidics software, which monitors the vacuum and automatically adjusts the infusion pressure to compensate for IOP changes during vitrectomy. Using Adaptive Fluidics can lead to a 62% reduction in the average infusion pressure compared with procedures that do not use Adaptive Fluidics.[4] When Adaptive Fluidics is used in conjunction with the company's Bi-Blade dual-port vitrectomy cutter, the drop in operating IOP is cut in half.[4]

The new Bi-Blade+ cutter now offers 25,000 cpm efficiency with twice the cutting rate compared with single-port cutters. It also provides 100% duty cycle for continuous aspiration and 25% increased flow compared with the legacy 25-gauge Bi-Blade.[4]

In addition, Bausch + Lomb has partnered with Heidelberg Engineering to distribute the SeeLuma digital visualization platform. The fully digital system allows surgeons to use the binoculars as they would with analog binoculars with all the benefits of a 3D system. SeeLuma also allows for integrated intraoperative OCT.[5]

These latest advances for the Stellaris Elite and accompanying tools offer meaningful improvements to the retina OR.

Figure 2. Updates to the Stellaris Elite platform include a wireless pedal with laser control, Adaptive Fluidics, and 25,000 cpm cutters.

BVI'S VIRTUOSO

By David Steel, MBBS, FRCOphth, MD(Res)

The Virtuoso phacoemulsification system and Virtuoso DUAL combined phacovitrectomy machine recently gained CE mark in Europe and is awaiting FDA approval (Figure 3).[6] The platforms include innovative features that provide low-traction, high-speed vitrectomy, optimized energy delivery during phacoemulsification, and enhanced operational efficiency.

Both machines feature an aspiration pump system that blends the performance of a vacuum-controlled pump with the precision of a flow-controlled system. The platforms can be set to vacuum-controlled, flow-controlled, or a hybrid that allows vacuum control with flow capping.[7]

Similarly, both systems use a fluidics approach that maintains consistent target IOP, matching aspirational flow to infusion flow. The Virtuoso DUAL extends this capability across all procedural steps and any surgical fluid, providing stability during complex combined anterior and posterior segment procedures.[7]

A standout feature of the Virtuoso DUAL is its machine-assisted fluid-air exchange capability, which helps surgeons maintain full IOP control during surgical fluid exchanges and viscous fluid injection. A high-flow and directional infusion cannula integrated with a valved trocar further supports stable fluidics during posterior segment procedures.[7]

The Virtuoso DUAL comes with a dual-action, 20,000 cpm, pneumatically driven vitrectomy probe with a beveled tip that allows the cutter to be positioned closer to target tissue than ever before. This, combined with increased probe stiffness, allows for impressive 27-gauge

Figure 3. The Virtuoso DUAL combined phacovitrectomy machine, which has CE mark in Europe, is awaiting FDA approval.

performance. These refinements enable more efficient vitreous removal and membrane dissection during complex posterior segment procedures.[7]

Recognizing that surgical efficiency extends beyond the procedure itself, the Virtuoso platform enables simultaneous preoperative setup of both phacoemulsification and irrigation/aspiration handpieces before a cataract case. This simple innovation eliminates sequential setup steps, reducing room turnover time and enhancing OR productivity.[7]

The platform also introduces an energy delivery system that senses lens load to maintain target energy levels regardless of lens hardness. This allows surgeons to set lower energy parameters while achieving efficient phacoemulsification across varying cataract densities. By automatically adjusting to lens characteristics, the system minimizes energy exposure to adjacent ocular tissues, potentially reducing postoperative inflammation and accelerating visual recovery.[7]

In conclusion, the Virtuoso and Virtuoso DUAL systems represent thoughtful engineering focused on the real challenges surgeons face: maintaining stable surgical conditions, delivering appropriate energy safely, and working efficiently. These platforms offer meaningful advances for both routine and complex anterior and posterior segment surgery.

NEW SYSTEM DEBUTS IN EUROPE

Oertli Instrumente introduced the OS 4 Up platform for both vitreoretinal and cataract surgery at the 2025 Euretina and ESCRS congresses. The platform includes the new Caliburn Trocar System and the Continuous Flow Cutter.[1]

The new system introduces several features, such as a dynamic infusion concept, which responds to intraoperative dynamics in real time, allowing surgeons to maintain lower IOP levels in both anterior and posterior procedures–closer to physiologic norms, according to the company.[1]

1. Oertli unveils OS 4 Up surgical platform at Euretina and ESCRS [press release]. Eyewire+. September 4, 2025. Accessed December 19, 2025. eyewire.news/news/oertli-unveils-os-4-up-surgical-platform-at-euretina-and-escrs

DORC'S EVA NEXUS

By MitroFanis Pavlidis, MD, PhD

The Eva Nexus platform fundamentally changed the way I approach vitrectomy after switching from the previous Eva system (Figure 4). What makes the decisive difference is the dual VacuFlow VTi pump, which enables a stable and highly controllable flow profile—high flow when surgical efficiency is needed and stable aspiration when operating near delicate, mobile tissues such as a detached retina, lens capsule, or a floppy iris. Not to mention the EVA Nexus is the only platform cleared by the FDA for subretinal injection.[8]

Another major innovation is the Smart IOP, which uses flow-based fluidics to balance irrigation and aspiration, continuously calculating the volume entering and leaving the eye to maintain stable intraoperative IOP. Unlike gravity or vacuum-compensation systems, Smart IOP regulates fluid displacement directly, minimizing surges and pressure drops. This results in unprecedented chamber stability, allowing consistency even in the most demanding cases.[8]

Figure 4. The Eva Nexus includes the dual VacuFlow VTi pump, Smart IOP, and the TDC Veloce.

An important advance to the system is the TDC Veloce cutter. In combination with the VTi pump, the TDC Veloce provides markedly higher flow, and both in vivo and in vitro evaluations confirm substantially increased flow rates and stiffness compared with the TDC. During surgery (especially 27-gauge) this translates into faster vitrectomy and improved efficiency across all aspiration-dependent steps: quicker fluid-air exchange, more effective dye removal, easier evacuation of silicone oil droplets and perfluorocarbon liquids, and smoother drainage of highly viscous subretinal fluid.[8]

Suction force is another key improvement. Due to the larger inner lumen, the TDC Veloce delivers a stronger and more reliable tip vacuum, facilitating posterior vitreous detachment induction (particularly in 27-guage) and engagement of diabetic fibrovascular membranes or vitreoschisis layers. The redesigned ergonomic grip, enlarged tip-orientation marker, and optional extension handle contribute to an instrument that feels natural and controllable.[8]

When all components converge—the VTi pump fluidics,

(Continued on page 33)

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February 4, 2022
2022-0005

CURRENT SUBRETINAL GENE THERAPY DELIVERY

This technique may become more mainstream as new therapies work through the pipeline.

By Nell (Ninel) Gregori, MD

Many gene therapy trials for inherited retinal disease (IRDs) and AMD are underway, exploring both gene-specific and gene-agnostic strategies. Rather than intravitreal or suprachoroidal delivery, many trials use transvitreal subretinal delivery. Although many surgeons are familiar with subretinal TPa administration, it's not a common surgical technique. Here, I describe the current standard surgical approach used in clinical trials and offer pearls to enhance the success and safety of subretinal injections.

THE SURGICAL STEPS

The principle of this procedure involves performing a 23- or 25-gauge three-port vitrectomy followed by the creation of a subretinal bleb—a localized detachment between the neurosensory retina and the retinal pigment epithelium (RPE)—where the viral vector is injected (Figure 1).

Inducing a Posterior Vitreous Detachment

The vitreous and hyaloid often behave unusually in IRD cases. The vitreous may be more stringy and less dense than usual, even in younger patients. The hyaloid is often wispy or membrane-like and very adherent, making the vitrector suboptimal for lifting the cortical vitreous over the posterior pole. To better visualize and remove residual vitreous, it is critical to use diluted triamcinolone acetonide (Triesence, Harrow) or kenalog (Bristol-Myers Squibb). If vitreous wisps remain over the posterior pole following removal of the vitreous bulk with the vitrector, surgeons can use a soft-tip silicone cannula, such as a backflush cannula, to safely and effectively gather, pull up, and detach the wispy hyaloid off the posterior pole (Video 1). However, if a membrane-like hyaloid remains over the macula, a retinal scraper such as the Finesse Flex Loop (Alcon) is safer and more effective (Video 2). Lifting the hyaloid off the posterior pole is essential for successful subretinal bleb formation because the 38- or 41-gauge subretinal cannula used for the procedure can be impeded by residual cortical vitreous.

Removing Peripheral Vitreous

The vitreous tends to adhere strongly to the peripheral retina in many IRD eyes. To avoid iatrogenic breaks, it is important to be gentle in lifting the peripheral hyaloid. When strong adhesion is encountered, surgeons should stop aspirating and trim the vitreous to the retina without attempting complete peripheral removal. Creating a break in a fragile, atrophic peripheral retina poses a high risk of retinal detachment, which is difficult to repair due to the thin

AT A GLANCE

- Rather than intravitreal or suprachoroidal delivery, many gene therapy trials for inherited retinal diseases use transvitreal subretinal delivery of the therapeutic.
- During the subretinal injection, real-time guidance with microscope-integrated intraoperative OCT can confirm subretinal placement, prevent suprachoroidal delivery, monitor foveal integrity, and map the bleb location.
- Post-injection, patients are closely monitored for intraocular inflammation, which may present as subretinal deposits, intraretinal cysts, or anterior/vitreous cells and flare.

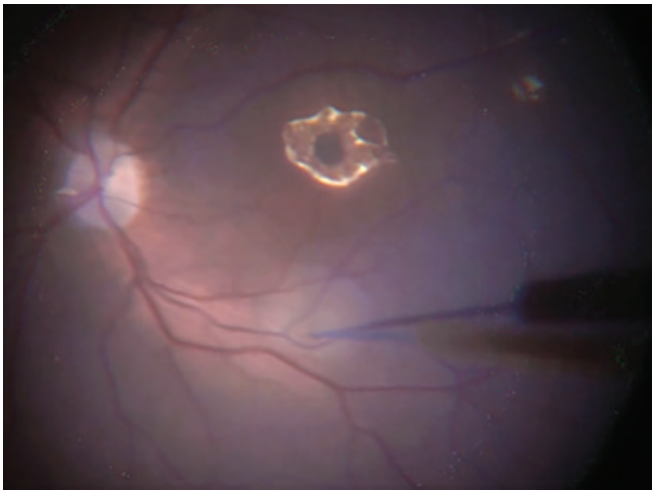


Figure 1. A subretinal cannula is used to begin a subretinal bleb via an injection along the superotemporal arcade (surgeon's view). Triamcinolone acetonide was used to stain the vitreous, and the remnant is seen over the fovea.

atrophic neurosensory retina and degenerated RPE. Even if the retinal detachment is small, the surgeon may have to forego gene therapy delivery.

Selecting a Retinotomy Site

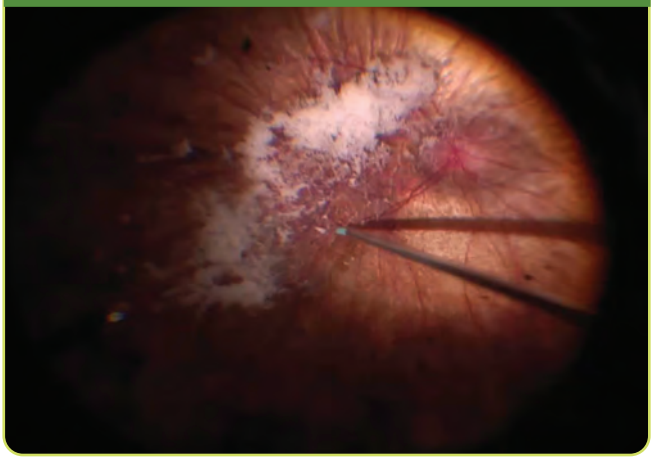
Once the hyaloid is cleared from the macula, surgeons must select the retinotomy site, typically near a recognizable vascular landmark. The gene therapy is injected under the retina to create a subretinal bleb in a one-step procedure. For patients with particularly adherent retinas (eg, those with choroideremia and some forms of retinitis pigmentosa), a two-step procedure may be useful, in which the surgeon instills a small pre-bleb of balanced salt solution (BSS) to facilitate entry into the subretinal space and reduce the risk of consuming the gene product while attempting to lift the retina. The retinotomy is usually placed at least two disc diameters from the fovea, near the superotemporal or inferotemporal arcades. Beginning closer to the fovea increases the risk of overstretching the fovea and creating a macular hole.[1] Depending on how the bleb spreads, even a small amount of subretinal fluid may reach and stretch the fovea.[2] In current clinical trials, the typical volume of viral vector injected into a bleb ranges from 50 µL to 300 µL.

To aid in the subretinal delivery, surgeons can lower the main infusion cannula pressure to 10 mm Hg to 20 mm Hg. During the injection, real-time guidance with microscope-integrated intraoperative OCT (iOCT) can confirm subretinal placement, prevent suprachoroidal delivery, monitor foveal integrity, and map the bleb location to ensure adequate coverage of the treatment target zone.[3]

Because the direction of bleb expansion is unpredictable, multiple blebs are often required to adequately cover the target area. Most trials permit one to three blebs (Figure 2). For example, a superior bleb may expand peripherally

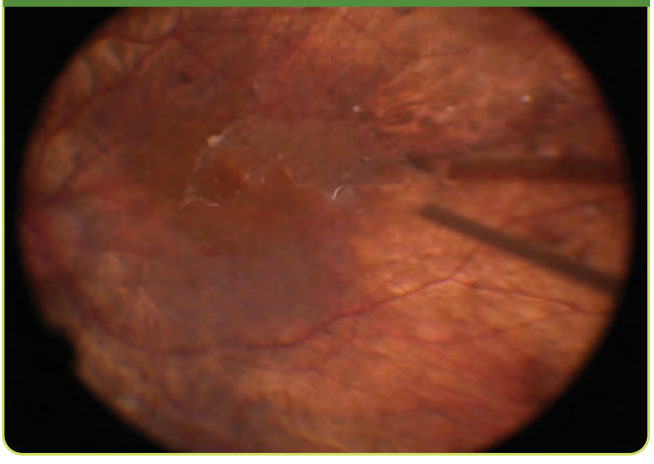
WATCH NOW

Video 1. Lifting the Hyaloid With a Soft-Tip Cannula.



WATCH NOW

Video 2. Lifting the Hyaloid With a Retinal Scraper.



without involving the fovea, while a second bleb near the inferotemporal arcade may cover the inferior macula and the fovea. In some trials (eg, for Stargardt disease), investigators seek to treat the macula without lifting the fovea or the central atrophic zone by initiating multiple blebs around the atrophy. iOCT is invaluable for tracking bleb formation and ensuring the targeted area is effectively covered.[4]

Following the gene therapy injection, a gentle BSS rinse or fluid-air exchange can remove any refluxed vector and minimize postoperative inflammation induced by the viral vector.[5] Sclerotomies are sutured to prevent postoperative hypotony and potential gene therapy reflux. A fluid-air exchange may push the bleb toward the fovea—a maneuver

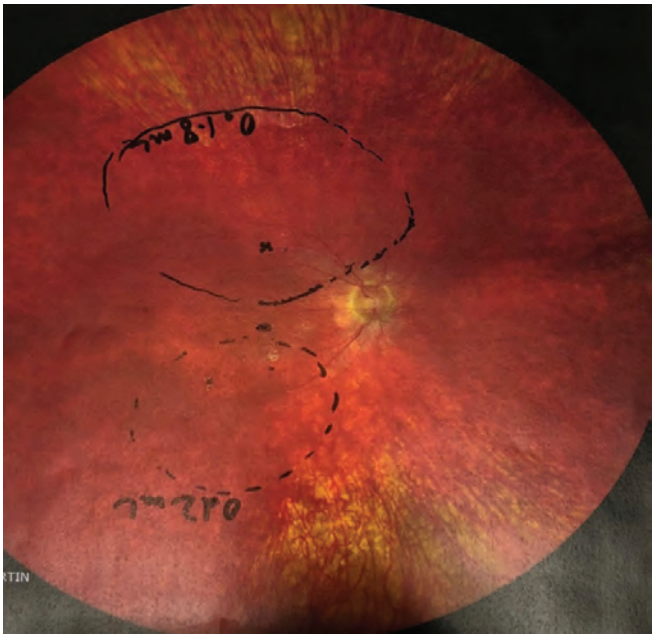


Figure 2. These drawings demarcate the blebs and injection sites near the vascular arcades to cover most of the macula and deliver a total of 300 µL of viral vector.

recommended in some trials but undesirable in others.

At the end of surgery, some trials also require sub-Tenon triamcinolone acetonide. The risk of postoperative intraocular hypertension must be balanced against potential postoperative inflammation. Patients are typically kept in a supine position for at least 1 hour to promote bleb absorption and avoid gravity-induced bleb displacement.

Postoperative care includes standard eye drops and trial-specific oral prednisone regimens with a taper.

RISKS OF TRANSVITREAL SUBRETINAL INJECTIONS

In addition to the usual risks of vitrectomy, this approach carries specific concerns, including the following:

- Inflammation due to the viral vector
- Vector reflux, reducing delivered dosage
- Postoperative macular hole
- Perifoveal chorioretinal and RPE atrophy
- Subretinal deposits
- Iatrogenic choroidal neovascularization

Patients are closely monitored for intraocular inflammation, which may present as subretinal deposits, intraretinal cysts, or anterior/vitreous cells and flare. These are generally managed with escalated oral/topical steroids or intraocular steroids, depending on the severity and the trial protocol.

IMPROVING SAFETY

Subsequent to the clinical trials for voretigene neparvovec-rzyl (Luxturna, Spark Therapeutics) for *RPE65*-associated retinal degeneration, innovations such as the MedOne microinjector have allowed surgeons to connect the syringe with gene therapy product to the viscous fluid

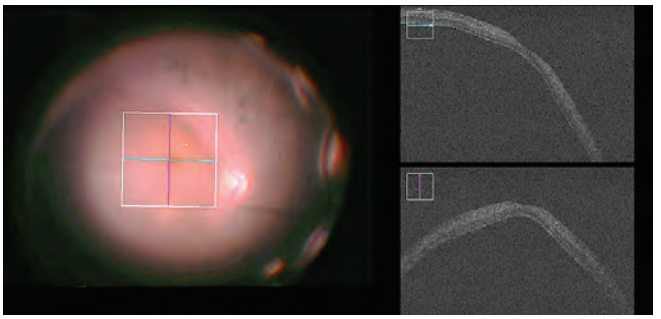


Figure 3. iOCT can help surgeons monitor the fovea during a subretinal injection.

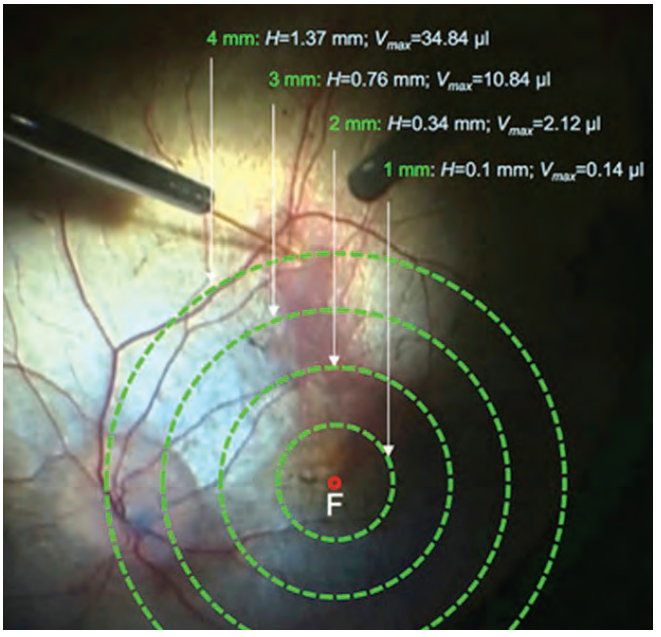


Figure 4. Retinal stretch as a function of distance from the fovea and volume.[1] Reproduced with permission through creativecommons.org/licenses/by/4.0.

control (VFC) function on the vitrectomy machine. The pedal control this provides offers excellent control over injection pressure and speed.

For example, a typical VFC injection pressure of 10 psi to 12 psi produces a steady drip and not a forceful jet from the tip of the subretinal cannula, minimizing mechanical trauma to the retina. The retina typically elevates with pressures around 10 psi to 14 psi, occasionally up to 18 psi.

Experimental animal models show that excessive pressure during subretinal injections is harmful. In monkey eyes, subretinal BSS injection at 20 psi caused temporary inner segment/outer segment disruption and RPE changes, persisting for 5 to 6 weeks.[6] Similarly, Olufsen et al reported significant damage to the outer retina and RPE at 32 psi versus 14 psi in pig eyes.[7]

OPTOMIZING BLEB FORMATION

In my clinical experience, the ease of bleb formation and required pressure vary widely among patients. Removal of the cortical vitreous at the injection site is crucial for

successful access using 38- or 41-gauge subretinal cannulas.

A common misconception among novice surgeons is that higher manual pressure of the cannula against the retina aids in bleb formation. In fact, excess pressure may occlude the cannula tip against the retina, visible as RPE compression on iOCT. Lifting the cannula slightly can restore flow and allow the fluid to penetrate the neurosensory retina. If I have trouble inducing a bleb, I typically trim the cannula tip at a 45° angle, which creates a sharp tip to nick the internal limiting membrane and allow fluid to penetrate and lift the neurosensory retina.

FOVEAL INCLUSION IN SUBRETINAL GENE THERAPY

When treatment requires foveal involvement, it is essential to monitor the fovea in real-time using iOCT. OCT-guided visualization allows precise monitoring of foveal elevation, stopping the injection if the foveal stretch is significant and minimizing trauma and macular hole formation—a serious complication that may lead to vector reflux, additional surgical procedures, and postoperative vision loss (Figure 3).[5]

Xue et al demonstrated that foveal stretch correlates with injection volume and retinotomy proximity. The study suggests placing the retinotomy at least 3 mm from the foveal center reduces mechanical stress (Figure 4).[1]

EASING THE STRAIN ON SURGEON'S HANDS

Manual subretinal injections are also affected by the surgeon's physiological tremor and fatigue during prolonged injections. While robotic systems are in development, current procedures rely on the surgeon's precision. A stable hand and adequate wrist support, including a reliable wrist rest and avoidance of caffeine prior to surgery, can enhance hand steadiness and delivery accuracy. ■

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(Continued from page 28)

the Smart IOP intelligence, and the enhanced flow, suction force, rigidity, and ergonomics of the TDC Veloce—27-gauge surgery becomes fundamentally different from what it was a decade ago. You gain the advantages of minimally invasive access while achieving performance previously associated with larger-gauge instruments. For routine and highly complex cases alike, this combination raises the standard of what is achievable in modern vitreoretinal surgery. ■

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TIPS AND TRICKS FOR SCLERAL-FIXATING TORIC IOLS

Small adjustments to your surgical technique can help you meet your patients' refractive goals.

By Barton L. Blackorby, MD

Cataract surgery remains the most performed surgical procedure in the United States,[1] restoring functional vision, driving ability, and quality of life for millions of patients. Since Sir Harold Ridley implanted the first IOL in 1949,[2] the available IOL portfolio has expanded substantially. Although most patients achieve excellent visual outcomes with monofocal lenses, many benefit from astigmatic correction with toric lenses or desire reduced glasses dependence through extended depth-of-focus and multifocal IOLs. Many of these patients are willing to invest significantly in premium IOL technologies to optimize visual performance for decades to come.

Despite modern designs and surgical consistency, IOL subluxation or dislocation may occur. When this complication arises, complex anterior segment or vitreoretinal surgeons are often required to reposition or replace the lens. Scleral fixation is among the most performed approaches in these scenarios. Many techniques have been described, including suturing the IOL to the iris, flanged haptic fixation (ie, the Yamane technique), and fixation of specialty IOLs incorporating eyelets, such as the EnVista (Bausch + Lomb) and Akreos (Alcon) lenses.[3-6] Improvements in reproducibility, stability, and refractive outcomes have encouraged some surgeons to consider secondary fixation of premium optics, rather than defaulting to monofocal designs.

This article highlights several surgical considerations for scleral fixation of a toric EnVista IOL, with an emphasis on case selection, intraoperative planning, and technical pearls. Many of the techniques applied to this case can be applied to similar toric IOL designs on the market.

PATIENT SELECTION

As with any scleral-fixated IOL (SFIOL) technique, appropriate clinical screening is foundational. Favorable candidates have adequate conjunctival and Tenon capsule thickness with good mobility and minimal scarring. Ideally, no prior scleral tunnel exists in the quadrant planned for fixation; however, the toric EnVista IOL can be folded and inserted through a 2.6-mm clear corneal incision when necessary.

PREOPERATIVE MARKING

Toric alignment begins preoperatively by marking the intended axis with the patient seated upright. After sterile preparation and draping, create a 360° limbal peritomy. Place relaxing incisions at the 3 and 9 clock hours, but note that these can be modified to keep them well separated from the toric axis. This reduces the risk of postoperative bacterial migration toward the exposed suture material during conjunctival healing. Marking the intended toric axis prior to making any scleral incisions helps ensure accuracy and reproducibility (Figure 1).

AT A GLANCE

- Many patients who present with a dislocated IOL have either paid (out of pocket) for a premium toric IOL or have significant corneal astigmatism that may benefit from a toric IOL.
- Favorable candidates for a scleral-fixated toric IOL have adequate conjunctival and Tenon capsule thickness with good mobility and minimal scarring.
- In 23 eyes that underwent secondary placement of a toric IOL, 72.7% were within 1 D and 54.5% were within 0.5 D of the planned refractive spherical equivalent target.

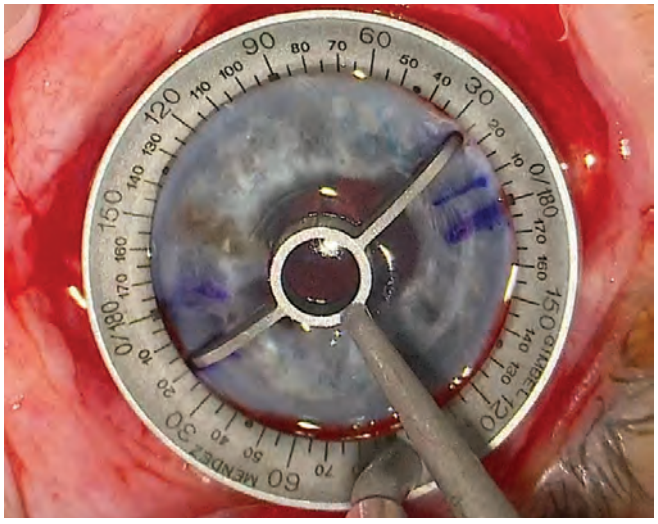

Figure 1. Mark the 180° axis and toric axis prior to any incisions to ensure accurate placement of the scleral marks.

SCLERAL MARKING AND SCLEROTOMY PLANNING

Accurate placement of the scleral fixation points is critical. For toric SFIOLs, orient the scleral marks radially from the limbus rather than the more common tangential orientation for non-toric cases, or fashion a hitch through the eyelet. This helps ensure that the IOL does not rotate away from the correct toric axis. Sclerotomy locations are typically marked in a radial fashion at 1.5 mm and 3.5 mm posterior to the limbus (Figure 2). These marks guide later suture passage; however, you do not create the sclerotomies themselves until later in the case. Depending on the toric axis orientation, an existing sclerotomy used for trocar placement may be used for suture passage.

SCLERAL TUNNEL CREATION AND LENS REMOVAL

Using a crescent blade, create a 6-mm scleral tunnel in the planned quadrant, stopping short of entering the anterior chamber. After a complete vitrectomy, many surgeons apply endolaser to the vitreous base to reduce the risk of retinal tears due to subluxation/dislocation of the original IOL. If the subluxed or dislocated IOL is present, maneuver it into the anterior chamber before completing the scleral tunnel using a keratome and removing the original IOL.

Next, create additional sclerotomies using the trocar inserter via a stab incision at the previous scleral markings. Adding a temporary knot at the scleral tunnel can help prevent iris prolapse when making the additional sclerotomies. At this point, some surgeons consider a peripheral iridotomy to reduce the risk of postoperative pupillary block—while rare, it can be a serious complication.

IOL PREPARATION AND FIXATION

Place the toric EnVista IOL onto the corneal surface and pass polytetrafluoroethylene (Gore-Tex, W.L. Gore) sutures

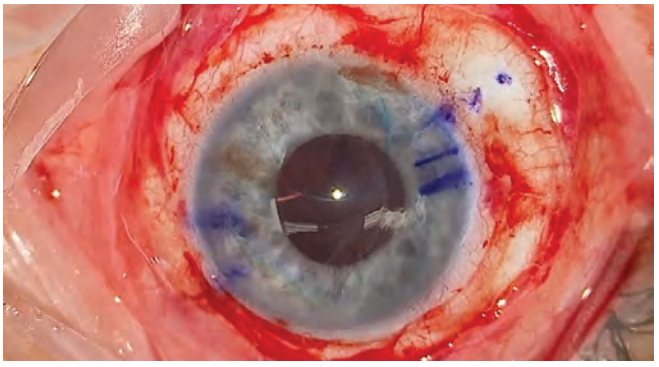

Figure 2. Surgeons should make the sclerotomy markings 1.5 mm and 3.5 mm from the limbus in a radial fashion.

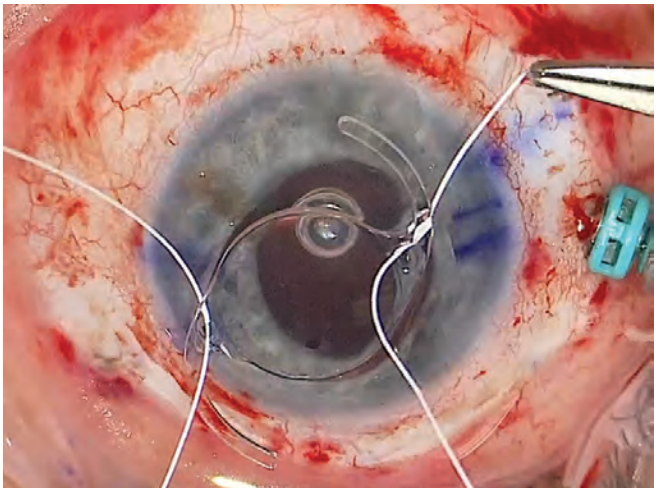

Figure 3. Place the IOL on the cornea in a "reverse S" configuration and thread the suture through the eyelets of the lens.

through the eyelets. Unlike fixation of non-toric EnVista lenses, there is no need to alternate anterior-to-posterior and posterior-to-anterior threading through the eyelets. The radial sclerotomy configuration provides adequate rotational stability and minimizes the risk of IOL tilt.

Some surgeons will then trim the haptics to facilitate passage through the scleral tunnel; this modification is optional and based on individual preference.

Beginning with the posterior sclerotomies and using two forceps with a hand-off technique, pass the suture through the scleral tunnel, through the pupil, and out through the sclerotomy. Repeat the process for the anterior sclerotomy sites, being sure to avoid suture crossing, which could induce unintended IOL tilt or rotation.

Secure the suture ends using slip knots (not locked into place) to allow fine adjustment of centration within the pupillary axis prior to definitive fixation. Once you have confirmed centration, lock the final throws by rotating the last throw 180° and adding an additional throw. Rotate and recess the knot into the scleral wound using forceps to reduce exposure risk.

(Continued on page 57)

MYOPIC TRACTION MACULOPATHY: SURGICAL TIMING AND TECHNIQUES

Part one of this three-part series explores various management considerations when faced with complications of pathologic myopia.

By Taku Wakabayashi, MD, PhD

Myopic traction maculopathy (MTM) is characterized by a spectrum of macular pathologies, including retinoschisis, lamellar macular hole (LMH), and foveal retinal detachment (RD), resulting from anteroposterior and tangential traction in highly myopic eyes. In its early stages, MTM presents as mild foveoschisis, which remains stable for months to years.

However, with persistent traction, the schisis may gradually extend, and the outer retina may separate from the retinal pigment epithelium, resulting in outer LMH and foveal RD. With progression, subsequent rupture of the overlying inner retina leads to a full-thickness macular hole (FTMH) and eventual macular hole RD (MHRD; Figure 1).

Although MTM typically progresses slowly, it may result in severe vision loss if left untreated, highlighting the importance of timely surgery to preserve vision and prevent disease progression. However, because surgery to treat MTM also carries risks, including postoperative FTMH formation,[1] the timing of surgical intervention should be determined carefully.

This review focuses on the optimal surgical timing for the management of MTM without FTMH.

OBSERVATION VERSUS SURGERY

Observation is indicated in the early stages of MTM (Figure 1A), as mild foveoschisis without foveal RD often remains stable and carries a low risk of rapid progression. The proportion of eyes showing progression is much lower in mild MTM (6.7% over 3 years) than in severe MTM (43% over 3 years), and spontaneous resolution may occur in some mild cases (18.9% over 55 months).[2,3]

Clinicians should follow patients with mild MTM every 3 to 6 months, and patients should be advised to visit the clinic earlier if visual symptoms worsen. In eyes that maintain good visual acuity (20/25 or better), or even in those with obvious schisis but preserved vision (20/30 or better) and no symptoms, there is no clear indication to recommend surgery.

Surgery is indicated in eyes with moderate-to-severe MTM with visual impairment or in those at high risk for

AT A GLANCE

- Observation is indicated in the early stages of myopic traction maculopathy (MTM), as mild foveoschisis often remains stable and carries a low risk of rapid progression.
- Surgery is indicated to preserve or improve vision in eyes with moderate-to-severe MTM with visual impairment or in those at high risk for macular hole or macular hole retinal detachment.
- Visual acuity is an important factor when deciding on surgery, since it reflects the severity of schisis, which can also be documented on OCT imaging.

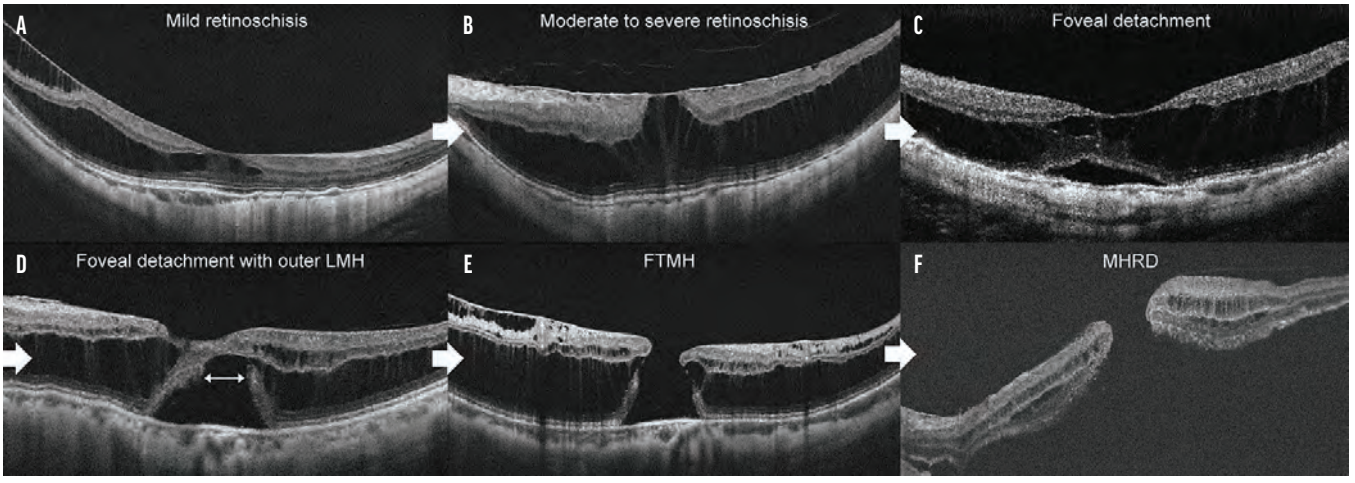

Figure 1. These OCT images document mild retinoschisis with a VA of 20/25 (A), moderate-to-severe retinoschisis without foveal RD with a VA of 20/40 (B), foveal RD without outer LMH and a VA of 20/50 (C), foveal RD with LMH and a VA of 20/60 (D), FTMH with a VA of 20/100 (E), and MHRD with a VA of 20/400 (F). Surgery may be indicated in all cases except A.

MH or MHRD. No guidelines have been established for surgical decision making, and the decision often depends on the combination of visual acuity, retinal morphology on OCT, and the patient's subjective worsening of symptoms.

THE VALUE OF VISUAL ACUITY IN DECISION MAKING

Visual acuity is an important factor when deciding on surgery, as it reflects the severity of schisis. Visual acuity in eyes with MTM ranges widely from 20/20 or better to worse than 20/200.

In our recent study of 193 patients who underwent pars plana vitrectomy (PPV) for MTM, the mean visual acuity significantly improved from 20/76 preoperatively to 20/53 at 12 months ($P < .001$).[4] Postoperative visual acuity correlated with preoperative visual acuity, and more than 80% of the patients in our study achieved postoperative vision equal to or better than their preoperative vision. This raises the question of whether early surgery should be recommended for certain patients with good vision (ie, 20/25 or better).

In general, early surgery is not recommended because approximately 10% to 15% of patients may experience postoperative vision loss of 3 lines or more due to complications, especially postoperative FTMH.[4] Therefore, surgeons must discuss the potential risk of vision loss and reoperation with every patient, as this may significantly affect patient satisfaction.

Surgery should be considered only in appropriate cases that show evidence of ongoing visual deterioration. Anecdotally and based on our study, the risks and benefits of surgery seem optimally balanced for cases with moderate visual impairment of 20/30 to 20/200 (ideally 20/40 to 20/50), as surgery at that time facilitates visual improvement while maintaining relatively good postoperative vision.[4]

Nevertheless, patients who present with very low preoperative vision (worse than 20/200) may still benefit from surgery because they are more likely to experience meaningful visual improvement with minimal risk of further vision loss. Thus, PPV for MTM is generally effective across a wide range of preoperative vision levels.[4] However, eyes with poor preoperative vision may experience lower postoperative vision than those with better preoperative vision. Taken together, surgery should be performed at an appropriate time to avoid operating too early or too late.

THE ROLE OF RETINAL MORPHOLOGY

The severity of schisis seen on OCT imaging is also critical for surgical planning. Although eyes with foveoschisis without foveal RD can often be observed, persistent schisis may cause gradual worsening of vision, even without foveal RD, likely due to cumulative damage to the retina (Figure 1B). In these cases, vitrectomy may be indicated to prevent further vision loss.

In eyes with a gradual MTM progression to foveal RD with worsening vision (Figure 1C and Figure 2), PPV is strongly recommended to prevent progression to FTMH and further vision loss.

MTM with foveal RD and outer LMH, particularly when the fovea is extremely thin, carries a high risk of FTMH formation; therefore, surgery should be considered within 1 to 2 months of diagnosis (Figure 1D).

The chance of visual improvement is substantially lower when MH is present before surgery.[5] Thus, surgery before MH formation is beneficial in eyes with MTM. Close monitoring with serial OCT imaging is essential to determine whether FTMH has developed, as the detection of FTMH alters the surgical approach—favoring fovea-sparing internal limiting membrane (ILM) peeling for MTM and an inverted ILM flap for myopic MH (Figure 1E and F).

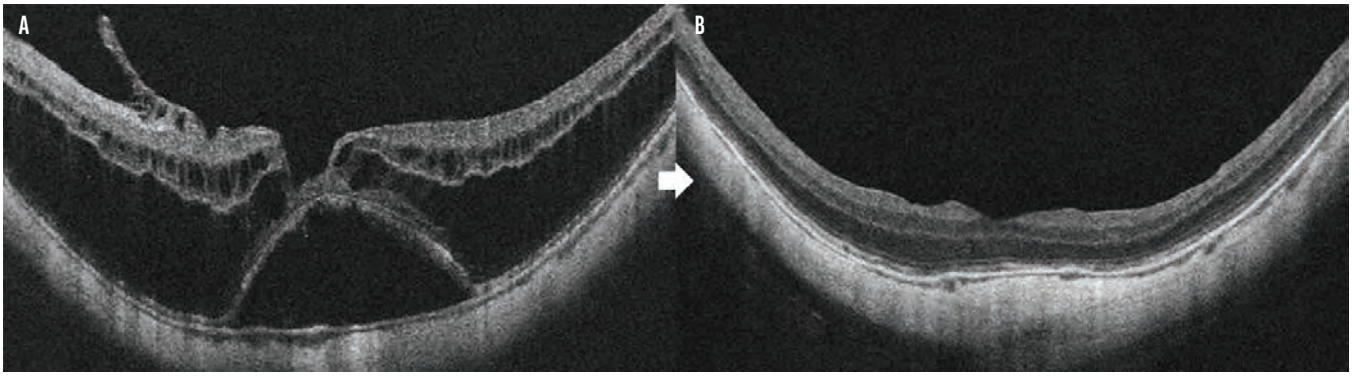

Figure 2. This eye with MTM, foveal RD, and a very thin fovea (A) was treated with PPV, fovea-sparing ILM peeling, and no tamponade (B). VA improved from 20/80 to 20/50 with complete schisis resolution.

SPECIAL CONSIDERATIONS

Some eyes have longstanding MTM or FTMHs with severe macular atrophy, a condition in which visual improvement after surgery is unlikely. In such cases, the benefit of surgery may be minimal, and careful observation may be indicated until the risk of MHRD increases. In cases with MTM in the only-seeing eye, surgical timing should be determined with caution after thorough discussion with the patient, and it should be considered only in cases with a risk of MH or MHRD.

MANAGEMENT OPTIONS

The 2025 Preferences and Trends survey conducted by the American Society of Retina Specialists highlighted current management options for MTM without FTMH. In a scenario involving a 48-year-old man with high myopia (-18 D) and progressive unilateral vision loss from myopic macular schisis (VA declining from 20/40 to 20/200), most retina specialists favored surgical management.

Among US surgeons, PPV with broad ILM peeling was most commonly selected (49.7%), followed by PPV with fovea-sparing ILM peeling (33.5%), observation (11.8%), and macular buckle (2.9%).

In contrast, international surgeons favored PPV with fovea-sparing ILM peeling (57.2%), followed by broad ILM peeling (30.2%), macular buckle (6.1%), and observation (5.2%).

These results indicate PPV as the most common surgical approach, with some variations in ILM peeling techniques and in the use of macular buckle. The goal of PPV is to relieve the traction by removing vitreous cortex remnants, epiretinal membrane, and ILM, thereby achieving schisis resolution and preserving vision.

Tamponade choice has also been debated, but our recent study showed that MTM can be successfully treated without tamponade, with better visual outcomes than those achieved with gas or air tamponade.[6]

The major concern in MTM surgery is postoperative MH formation, which can occur in any type of MTM.[1] The incidence of postoperative MH is approximately 10% after conventional complete ILM peeling compared with approximately 1% to 2% after fovea-sparing ILM peeling. Therefore, PPV with fovea-sparing ILM peeling is preferred. Some surgeons use an ILM flap or ILM peeling and reposition, but their indications and efficacy should be evaluated in future studies. In complex cases such as postoperative MHRD and deep posterior staphyloma, additional techniques—including ILM flap, amniotic membrane, autologous retinal transplantation, and macular buckle—may be considered.

TIMING QUICK TIPS

With MTM, optimal surgical timing is often challenging because of the variations in severity and progression patterns. Observation is indicated in mild cases with stable vision, whereas surgery is considered in eyes with moderate-to-severe MTM before FTMH develops, particularly those with foveal RD, VA of 20/30 or worse, or a high risk of MH formation. However, surgical decisions should be individualized based on subjective symptoms, underlying myopic maculopathy, fellow eye status, and the patient's understanding of risks and benefits. PPV with fovea-sparing ILM peeling is recommended to reduce the risk of postoperative FTMH. ■

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IDENTIFYING EARLY DISEASE AND GEOGRAPHIC ATROPHY RISK FACTORS IN AMD

Functional symptoms, imaging biomarkers, and early referrals support the timely detection and management of GA.

Adrienne W. Scott, MD, FASRS

Age-related macular degeneration (AMD) is a leading cause of irreversible vision loss in older adults. The prevalence is estimated to be 11 to 19 million in the United States and about 170 million globally.[1,2] By 2050, prevalence rates are estimated to increase to 22 million and 288 million for the US and global populations, respectively.[3,4] Intermediate AMD (iAMD) represents a pivotal stage in this disease where drusen and retinal pigment epithelium (RPE) abnormalities can lead to the development of geographic atrophy (GA). In clinical practice, timely recognition of functional symptoms and identification of high-risk imaging biomarkers in iAMD can help clinicians to intervene earlier and prepare patients for the realities of a chronic, progressive macular disease.

Patient-Reported Symptoms and Functional Red Flags

When a patient arrives to the clinic with functional complaints—difficulty driving, problems recognizing faces, and reduced reading speed or inconsistent clarity despite preserved distance acuity—an examination to determine possible progression from iAMD to advanced AMD is warranted. Such symptoms may correlate with foveal-involving disease, which significantly impacts daily activities, or disease that is encroaching on the fovea, even if not fully involving it yet.

Key Biomarkers for GA Progression and Imaging Modalities

Monitoring patients with iAMD for progression to GA is important. In my follow-up visits, I examine the fellow eye to better understand the expected disease trajectory and risk of progression. I also look for structural biomarkers that indicate a higher risk of GA development, including incomplete retinal pigment epithelium (RPE) and outer retinal atrophy (iRORA) and abnormal pigmentation within the macula. I remain alert for subtle signs of choroidal neovascularization, as well as high-risk drusen characteristics like large drusen, pigment migration, and large elevated drusenoid pigment epithelial detachments (PED).

Imaging tools such as OCT and fundus autofluorescence (FAF) are an important adjunct to the clinical exam. With OCT, I can evaluate macular topography and drusen characteristics, assess the presence of iRORA or complete RPE and outer retinal atrophy (cRORA), and characterize PEDs. FAF is used extensively to follow GA progression and foveal involvement, and to evaluate the macula surrounding the GA lesions. These imaging modalities provide longitudinal structural data, support early detection of atrophic changes, and allow retina specialists to compare images across visits (Figure).

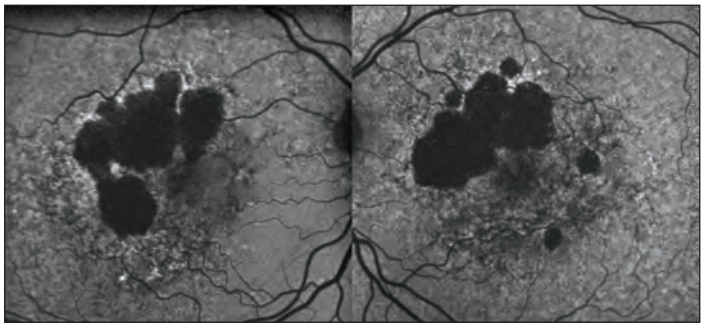

Figure. FAF shows bilateral GA with partial foveal involvement.

Importance of Early Referral

Early collaboration between comprehensive providers and retina specialists is key to optimizing long-term outcomes for patients living with iAMD and those at risk for GA. Early referral offers several advantages: confirming the diagnosis; avoiding misclassification; and conducting a comprehensive baseline exam with multimodal imaging. The baseline visit is also an opportunity to set expectations regarding prognosis, to describe the chronic nature of the disease, and to establish a long-term follow-up plan. Importantly, many patients equate AMD with "going blind," and an early retina specialist visit with me allows me to contextualize the diagnosis, discuss any potential clinical trials for which they may be eligible, and to reassure them that many individuals maintain good vision for quite some time.

Treatment Landscape and Unmet Needs in GA

GA remains an area of significant unmet need. Current therapies have been shown to slow disease progression to a modest extent but they do not restore vision that has already been lost. This can be disappointing for patients who are hoping for vision improvement, so expectation-setting is essential. I explain that preserving remaining vision and delaying further functional loss can have a meaningful impact on quality of life, particularly when the fovea is still spared. ■

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A SHIFT IN THE MANAGEMENT OF EPIRETINAL MEMBRANES

Consider patient symptoms and correlated OCT findings, over visual acuity, when deciding when to operate.

By Lucy V. Cobbs, MD, and Yasha Modi, MD


The greatest challenge of managing epiretinal membranes (ERMs) for the experienced vitreoretinal surgeon is the clinical decision making on when (and when *not*) to peel them. The timing of surgery is nuanced, and practice patterns have shifted over the past decade with the development of new imaging technology.

A CASE EXAMPLE

To demonstrate this change in practice pattern, consider the case of a 25-year-old woman who presented with a VA of 20/15 and an ERM without a posterior vitreous detachment. The vitreous was devoid of cells, and the peripheral examination demonstrated no vascular changes. Fluorescein angiography demonstrated no leakage, and ultrasound biomicroscopy demonstrated no masses; she was diagnosed with an idiopathic ERM, which is rare in this age group.

Over several months, the ERM progressed with increased tangential traction and the development of a cotton ball sign (Figure 1). The patient complained of progressive macropsia despite maintaining a VA of 20/20. She was counseled that her macropsia may not improve with surgery, but membrane peeling would help achieve long-term stability and stop ERM progression.

She underwent 25-gauge vitrectomy, hyaloid elevation, and brilliant blue G dye-assisted ERM peeling. Two months postoperatively, her VA was 20/20 and her symptoms had improved incompletely (Figure 2). Notably, the distortion improved, but the image discrepancy persisted. While this patient is not a typical ERM patient due to her young age, the case demonstrates that visual symptoms and OCT features can be the impetus to operate, even while maintaining excellent visual acuity.

AT A GLANCE

- Historically, visual acuity was the primary driver for surgery with epiretinal membranes (ERMs). However, new OCT-based ERM classifications correlate with vision and can provide prognostic value.
- Increasingly, patient symptoms—such as stereopsis, contrast sensitivity, and reading ability—are important metrics when deciding when to operate.
- Surgeons should follow symptomatic ERMs closely, and if they demonstrate symptomatic or anatomic worsening, even with excellent visual acuity, it may be prudent to consider operating.

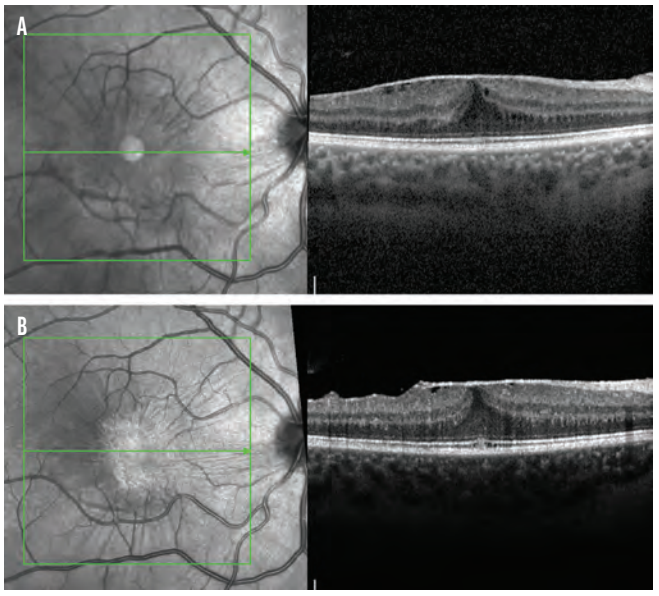

Figure 1. A horizontal raster of a macula OCT from 3 months prior to surgery demonstrates the ERM with loss of a normal foveal contour and trace cystoid changes (A). Note the worsening striae on the near-infrared and the development of a cotton ball sign on OCT (B).

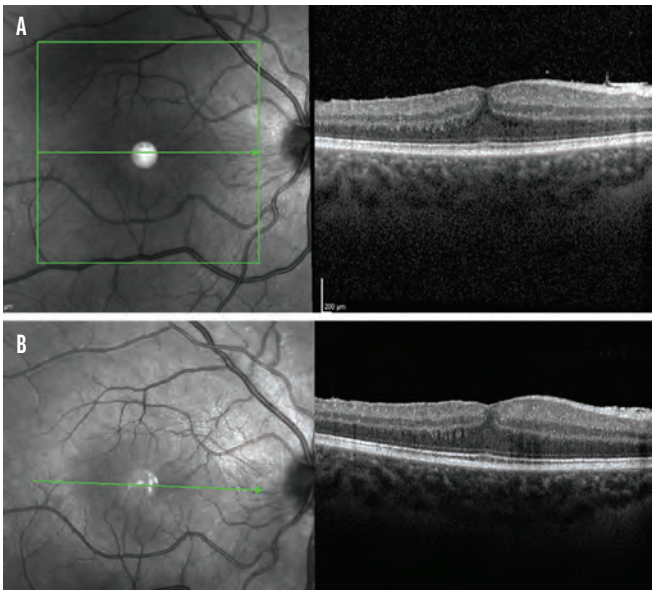

Figure 2. In these OCT images from postoperative month 1 (A) and 2 (B), note the progressive resolution of the cotton ball sign and a gradual trend toward a more normal foveal contour.

IMAGING PEARLS

Historically, visual acuity was the primary driver for surgery. However, the advent of OCT has resulted in new OCT-based ERM classifications that correlate with vision (in a non-linear fashion) and provide prognostic value. One such classification system was devised by Govetto et al, who used ectopic inner foveal layers (EIFL) as the hallmark OCT biomarker of their staging system, rather than the ellipsoid zone (EZ) or external limiting membrane, which have both demonstrated prognostic value.[1]

There are four stages to this system, and, notably, visual acuity does not decline linearly with the Govetto OCT stages.

- Stage 1: an ERM with a normal foveal depression and average VA of 20/21
- Stage 2: loss of the normal foveal contour, widened outer nuclear layer, and average VA of 20/27
- Stage 3: continuous EIFL and average VA of 20/43
- Stage 4: EIFL with disruption of the retinal layers and average VA of 20/81

By the time a patient progresses to stage 3, the prognosis after surgery is guarded, relative to operating at earlier stages. Therefore, using visual acuity alone to drive surgical decision making may not optimize patient outcomes. Considering OCT biomarkers and other functional visual symptoms of metamorphopsia may allow for a more sophisticated approach to ERMs.

ERM: A DEEP DIVE

ERMs occur in approximately one third of individuals over 62 years of age,[2] and over 5 years, 29% of ERMs progress, 26% regress, and 39% remain the same on OCT.[3]

Risk factors for developing an ERM include increasing age, ERM in the fellow eye, and the development of a posterior vitreous detachment.[4] In addition, diabetic retinopathy increases the risk, perhaps due to the effect of hyperglycemia on the vitreous.[5] There is some evidence that cataract surgery may be a risk factor; however, this is confounded by improved visualization and detection of ERMs after surgery.[4] While pseudophakic cystoid macular edema occurs more commonly in eyes with ERMs than in eyes without membranes,[6] there is no increased risk of ERM progression or contraction after cataract surgery.

We have an incomplete understanding of how to predict which ERMs will progress and which ones will remain stable. Persistent vitreomacular adhesion is a risk factor for ERM progression;[7] however, there are no established OCT biomarkers to predict ERM progression.

Although we lack predictive biomarkers, there are OCT features of ERMs that seem to correlate with the development of specific visual symptoms. Metamorphopsia may be related to disruption of the EZ and inner retinal layers.[4] Macropsia and micropsia may correlate with crowding and splitting, respectively, of the photoreceptors, neither of which typically improves after surgical membrane peeling. Visual acuity does not correlate with the presence or severity of patients' metamorphopsia or aniseikonia. However, patients' scores on the National Eye Institute Visual Function Questionnaire-25 decline with severe metamorphopsia.[4]

Traditionally, visual acuity has been the main driver for surgical intervention for ERMs, but increasingly, patient symptoms are considered an important metric. Some of these symptoms, including stereopsis, contrast sensitivity,

and reading ability, may improve after membrane peeling without a gain in visual acuity.[8-11] Certain clinical and OCT features carry a positive prognosis for surgical outcomes, such as shorter duration of symptoms, better presenting visual acuity, and younger age. OCT parameters that are positive surgical prognosticators include thin ganglion cell and inner plexiform layers, longer photoreceptor outer segment distance, intact EZ and interdigitation zone lines, and the absence of an EIFL.[1,12,13]

EARLY VERSUS DELAYED INTERVENTION

This paradigm shift toward symptom-based surgical intervention may lead to operating on ERM patients who have excellent visual acuity. While this remains somewhat controversial, studies have evaluated the merits of early versus delayed surgical intervention to clarify best practices, and an ongoing DRCR Retina Network study will shed more light on this question.[14]

Surgeons must keep in mind that there is a ceiling effect to visual acuity. Patients with very good baseline visual acuity are more likely to maintain rather than gain visual acuity after surgery, while patients with worse baseline visual acuity may have higher BCVA gains that are still inferior compared with those with better baseline BCVA. Therefore, the goals of early surgical intervention are typically maintenance of already excellent (but slowly worsening) visual acuity, possible improvement in visual symptoms, and prevention of progression.

One study by Al-Khersan et al compared immediate versus delayed surgery (if progression occurred) and did not find any significant differences in visual acuity. However, they did not evaluate visual metrics other than acuity.[15] A prospective study by Nakashizuka et al compared surgical outcomes of patients with a VA of 20/20 versus 20/25 to 20/63 and found that surgery in the 20/20 group improved the horizontal metamorphopsia and quality of life scores and prevented worsening of aniseikonia seen in the moderate vision group.[8] While some evidence supports early surgical intervention for symptomatic ERMs, the decision to proceed with early surgery should be tailored to the patient's wishes and balance the risks and benefits.

Once the plan for membrane peeling has been confirmed, surgeons must decide whether to peel the internal limiting membrane (ILM) in addition to the ERM. There are no significant differences in visual acuity or metamorphopsia outcomes after ERM peel alone versus ERM with ILM removal.[16] Although ILM peeling is associated with a lower risk of ERM recurrence, many recurrent ERMs do not require repeat surgery.[17] Because ILM peeling removes the Müller cell footplates, there is a risk of optic nerve fiber layer dissociation or arcuate swelling. While ILM peeling does not disrupt visual acuity, there may be micro-scotomas and decreased retinal sensitivity.[18]

A COMPLICATED DECISION-MAKING PROCESS

There are metrics in addition to visual acuity that may help guide surgeons on the decision to intervene surgically for ERMs. Patient symptoms and OCT prognosticators are important to consider, as visual acuity may not decline linearly with ERM progression. Follow symptomatic ERMs closely, and if they demonstrate symptomatic or anatomic worsening, even if the patient maintains excellent visual acuity, it may be prudent to consider operating. ■

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Membrane Peeling: Tips and Tricks

By Hudson de Carvalho Nakamura, MD

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Get to know outstanding retina fellows from the class of 2026.

Sidra Zafar, MD

***Retina Today (RT):* When did you first know that you wanted to become a retina specialist?**

During medical school, I came to the United States for an observership and worked with several faculty members at the Wilmer Eye Institute, including the retina team. I found retinal pathology to be more fascinating than anything else I had seen. I also realized that retina research was at the forefront of ophthalmic innovation. These early experiences were instrumental in shaping my interest in retina, and my subsequent residency training further reinforced this decision.

***RT:* Who do you look up to as mentors?**

Mentorship has played an invaluable role in my career. I am fortunate to have had mentors who continually supported and guided my professional development. Fasika Woreta, MD, MPH, my residency program director, hired me as her first research assistant, which set off the chain of events that shaped my career. She, along with Michael Sulewski, MD, have been incredible surgical mentors, even today. James Handa, MD, imparted valuable wisdom and instilled in me the importance of always asking "why?". During fellowship, my circle of mentors has expanded even more. As program directors, Arunan Sivalingam, MD, and Richard Kaiser, MD, have been incredibly supportive and have consistently led by example. From Yoshihiro Yonekawa, MD, I learned the importance of precision and efficiency in the OR, while Jordan Deaner, MD, has emphasized the value of trusting—but always verifying—information, recognizing that the truth often lies between differing perspectives. David Xu, MD, has taught me all there is to know about scleral buckling, and Omesh Gupta, MD, is my secondary IOL guru. Samir Patel, MD; Meera Sivalingam, MD; and Joshua Uhr, MD, have shared valuable best practices and pitfalls to avoid, informed by their own experiences.

You cannot help but feel inspired when training at Wills Eye Hospital with strong role models such as Julia A. Haller, MD, and Carol L. Shields, MD.

***RT:* What has been one of the most memorable experiences of your fellowship thus far?**

It's truly been the people. I love my co-fellows and could not have asked for a better group to work alongside. The support staff are exceptional, and I genuinely enjoy working with the faculty, who consistently champion the fellows. During my fellowship, every day has been an enjoyable and fulfilling experience.

***RT:* What advice can you offer to residents who are considering retina?**

Retina is an incredible and deeply fulfilling field. Having strong mentors early on is essential to help guide you in the right direction. Most importantly, pursue what you love and what brings you joy each day. ■

FIRST CAREER MILESTONE

Dr. Zafar is returning to Wilmer Eye Institute to serve as the Assistant Chief of Service.

SIDRA ZAFAR, MD

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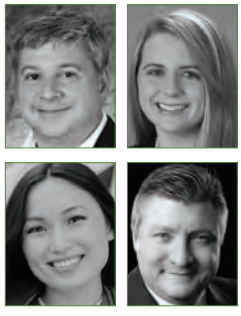
METHOTREXATE: AN EMERGING SURGICAL ADJUVANT

This drug is proving useful for improving outcomes in many retinal pathologies.

By Alan J. Franklin, MD, PhD; Lauren Gibson Snellings, MD; Aly Nguyen, MD; and Christopher Riemann, MD



As a resident, I (A.J.F.) assisted Thomas K. Krummenacher, MD, on a proliferative vitreoretinopathy (PVR) case, and he remarked that we were treating a microscopic disease with macroscopic surgical instruments. This statement really resonated with me. Despite the advent of small-gauge, high-speed instruments and improved visualization in the retina OR since that time, instrumentation remains a macroscopic approach to pathologies that have biological processes that drive disease on a microscopic level.

PVR occurs in 5% to 10% of all retinal detachment (RD) surgeries but accounts for 75% of RD surgery failures.[1] Similarly, eyes with significant posterior segment trauma or eyes with advanced proliferative diabetic retinopathy (PDR) are also at significantly higher risk for postoperative PVR and poor outcomes.[2-4]

Until better therapies become available to target these microscopic processes as pharmacosurgical adjuncts, our success as vitreoretinal surgeons will be limited.

A PHARMACOSURGICAL APPROACH ALREADY HERE

Multiple pharmacologic interventions, such as steroids, antineoplastic agents, colchicine, and retinoic acid, have attempted to establish superiority over surgical interventions to manage PVR without convincing results.[5] However, a novel form of intravitreal methotrexate (MTX) showed a reduction in PVR development and its subsequent complications, both in vitro and in vivo.[6,7] A phase 1b trial also demonstrated that the use of postoperative intravitreal MTX was associated with a reduction in recurrent RD in patients who underwent surgical repair due to PVR or trauma.[6] The pivotal phase 3 GUARD trial found that the use of intravitreal MTX reduced the reoperation rate following surgery for rhegmatogenous RD by 35% to 40%.[8]

Thus, intravitreal MTX is becoming an integral part of our surgical armamentarium to treat RD, trauma, and PDR to prevent recurrent fibrotic proliferation in the posterior segment after vitrectomy.[2,3,9]

The safety and efficacy of intraocular MTX (which costs approximately $4 a dose) has been well-established in the treatment of primary intraocular lymphoma and refractory uveitis. Intraocular MTX can be administered as a 200 µg to 400 µg intravitreal injection or an intraoperative infusion of 40 mg in a 500 cc balanced salt solution bottle.

AT A GLANCE

- A novel form of intravitreal methotrexate (MTX) after retinal detachment repair showed a reduction in proliferative vitreoretinopathy development and its subsequent complications.
- The safety and efficacy of intraocular MTX have been well-established in the treatment of primary intraocular lymphoma and refractory uveitis.
- Interim findings from the FIXER trial show that patients receiving both intraoperative MTX infusion and postoperative MTX injections have had no reoperations 3 months postoperatively.

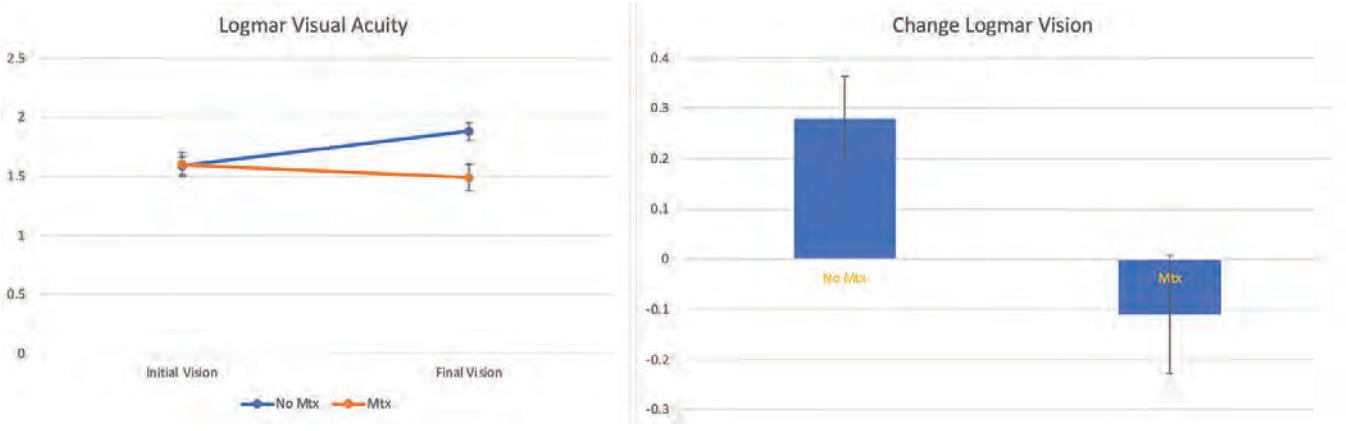


Figure 1. Change in visual acuity after vitrectomy for patients who did or did not receive postoperative MTX. For all patients, the average vision difference was > 3 lines between treated and untreated ($P < .01$).[10]

RECENT MTX DATA

To further explore the utility of MTX in retinal surgery, we performed a retrospective study of 255 patients with complex RDs, either rhegmatogenous RD with large retinal breaks or PVR, as well as patients with advanced PDR or trauma. Our protocol included three to five injections at weeks 1, 2, 4, 7, and 11 postoperatively with a dose of 200 µg. Our primary endpoint was safety, and we also examined the reoperation rate, change in visual acuity, central retinal thickness, and presence of epiretinal membrane.[10]

We found a 57% reduction in the reoperation rate and a 175% higher chance of single-operation success rate for patients who received postoperative MTX injections. Moreover, postoperative MTX led to an average of a 1-line gain in vision compared with an average of 3 lines lost for those who didn't receive injections. Postoperative MTX injections also significantly reduced the risk of a 3-line vision loss, and there was a trend to increase the chance of a 3-line visual recovery. Overall, the injections have been well-tolerated with a less than one in 1,000 risk of post-injection inflammation. In addition, we did not encounter frequent keratopathy as noted with previous studies.[8] Keratopathy incidence was similar in both the study and control eyes.

The Cincinnati Eye Institute had a similar positive experience with MTX and has been using MTX in the setting of PVR as an intraocular infusion since 2006 and as postoperative injections since 2008. Although multiple other groups have reported favorable experiences with MTX for PVR, level one evidence supporting these almost universally positive clinical impressions is lacking.[11,12]

FINDING THE RIGHT PROTOCOL

Given these positive findings, two critical questions remain: 1) Is the best dosing strategy intraoperative MTX infusions, postoperative MTX injections, or both? and 2) Can this drug prevent PVR by administering it in the setting of primary RD repair?

To answer these questions, we initiated the Prevention of ProliFerative Vitreoretinopathy with Intravitreal MethotreXate in Primary Retinal DEtachment Repair (FIXER) trial (NCT06541574). This prospective, multicenter, double-masked phase 2b/3a study is being conducted at three sites in the Cincinnati area. We are randomizing patients with primary RD of less than 6 weeks duration into four arms: 1) intraoperative MTX infusions; 2) postoperative MTX injections on weeks 1, 3, 6, and 10; 3) both intraoperative MTX infusions and postoperative MTX injections; and 4) neither. The primary endpoints at 12 months include the attachment rate at 6 months, the reoperation rate, visual acuity at 12 months, the incidence of epiretinal membrane (ERM), and the incidence of grade C PVR.

Reoperations for missed or new breaks are managed with the same randomization strategy. Reoperations due to PVR were given with MTX rescue therapy.

We have randomized 177 patients to date with excellent follow-up and very little dropout. We recently performed a preplanned safety analysis on the first 107 patients to have reached the 3-month follow-up (Figures 1 and 2). This was first presented at the 2025 annual meeting of the American Society of Retina Specialists in Long Beach, California.[13] Demographics, preoperative examination findings, and surgical details were well-balanced across all groups. Looking at the whole cohort, RD, PVR, and ERM increased over time as expected. Currently, patients receiving combined MTX infusions and MTX injections are doing much better than patients receiving either intervention alone, and all patients who are receiving any intervention are doing better than controls. This correlates to an impressive difference in reoperation rates; in fact, patients receiving both intraoperative MTX infusion and postoperative MTX injections have had no reoperations.

So far, this retrospective study suggests three to five intravitreal MTX injections benefit patients after vitrectomy for advanced PDR, trauma, or complex RD in terms of both anatomic and functional biomarkers.

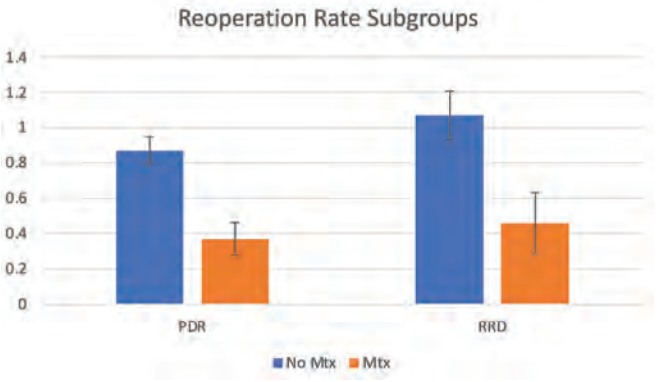


Figure 2. The number of reoperations was reduced by 57% in patients who received postoperative MTX injections compared with those who did not ($P < .01$). This reduction was similar for patients with both PDR and rhegmatogenous RD ($P < .01$). Patients who received MTX injections had a 72% chance of requiring only one operation compared with a 41% single-operation rate for those who did not receive injections ($P < .01$).[10]

THE CHANGING WINDS OF PHARMACOSURGICAL APPROACHES

Many other adjunctive therapies are being developed that include acetyl-salicyclic acid, colchicine, corticosteroids, daunorubicin, 5-fluorouracil, heparin, infliximab, and retinoic acid.[14] The multitude of treatments under investigation underscores the current unmet need for improving surgical outcomes and signals the progress and interest in emerging pharmacosurgical approaches. Research continues to support intravitreal MTX injections as a surgical adjuvant that can positively influence our surgical outcomes.

More than 20 years ago, we could only treat neovascular ocular disease with destructive laser. Anti-VEGF therapy targeting a biochemical pathway represented a monumental change in our ability to influence these pathologies. Intravitreal pharmacosurgical adjuvant therapy is now at a similar stage and is poised to change the treatment paradigm for surgical retinal diseases. ■

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INTRAVITREAL METHOTREXATE IS BECOMING AN INTEGRAL PART OF OUR SURGICAL ARMAMENTARIUM TO TREAT RD, TRAUMA, AND PDR.

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Re-Establishing the Role of Subthreshold Laser in DME Management

The subthreshold laser remains a useful tool for managing diabetic macular edema.

BY MARCO LUPIDI, MD

For many years, ophthalmologists treated diabetic macular edema (DME) primarily with focal and grid laser thermal photocoagulation. With the advent of anti-VEGF therapy, the approach shifted dramatically, and laser therapy lost its place as a first-line treatment. Yet, as laser technology evolved—especially with the introduction of the subthreshold laser (STL)—we began to rediscover its potential.

Here, I will share my clinical experience with Lumibird Medical's SubLiminal® subthreshold laser, a treatment that has proven to be both safe and highly effective in specific cases of DME. When applied properly, this treatment continues to play a valuable role in retinal care.

KEY TAKEAWAYS

- The subthreshold laser (STL) remains a valuable tool for both center-involved and non–center-involved DME, especially when central thickness ≤ 400 µm.
- The STL promotes biological healing through retinal pigment epithelium and Müller cell activation, reducing inflammation and fluid accumulation.
- AI-based analysis provides objective confirmation of the procedure's efficacy and may help standardize outcome measurement.
- When integrated with anti-VEGF regimens, the STL offers a safer, cost-effective, and durable adjunct or alternative therapy for selected DME patients.

HOW LASER THERAPY LOST—AND REGAINED—ITS PLACE

The skepticism surrounding laser therapy dates back to the Diabetic Retinopathy Clinical Research (DRCR.net) Protocol I, which compared prompt and deferred laser treatments combined with ranibizumab (Lucentis, Genentech).[1] After 5 years, results between the groups were similar, but deferred treatment showed better functional outcomes in eyes with poorer baseline vision. This led many to conclude that conventional laser therapy might even be harmful in some DME cases.

Consequently, guidelines shifted. Laser therapy was relegated to a secondary or "relative" indication, reserved for non–center-involved DME, eyes with vasogenic subforms, or persistent microaneurysms identified on fluorescein angiography.

However, these conclusions were drawn from the performance of conventional threshold lasers, not from the newer, non-destructive subthreshold approaches like the SubLiminal® subthreshold laser.

In recent years, studies like the DIAMONDS trial in the UK[2] have shown that STL therapy yields equivalent visual and anatomical outcomes compared with standard laser, but without retinal burns or scarring—a decisive advantage for preserving tissue integrity.

THE SCIENCE BEHIND SUBTHRESHOLD LASER

The rationale for the STL lies in its non-thermal, tissue-sparing mechanism. Unlike continuous-wave lasers, which generate visible burns, an STL delivers short bursts of energy with "off" intervals that allow heat to dissipate. This prevents photoreceptor and RPE damage while triggering beneficial cellular responses.

Mechanistically, the STL stimulates the retinal pigment epithelium (RPE) to produce heat-shock proteins, which suppress VEGF expression and reduce inflammation. It also activates Müller cells,[3] which are central to fluid homeostasis in the retina. One study demonstrated that the STL reduces biomarkers like GFAP and Kir4.1, as well as inflammatory chemokines such as RANTES and FasL.[4]

This dual anti-inflammatory and neuroprotective effect forms the physiological mechanism of action of the subthreshold approach, and it explains how the procedure works with the eye's biology rather than overwhelming it with heat.

A SAFE AND REPRODUCIBLE TREATMENT PROTOCOL

One of the challenges with STL therapy has always been its titration—how to deliver the correct amount of energy without causing damage. "Barely visible" burns are subjective and depend on multiple factors, including pigmentation and media clarity.

To overcome this issue, I devised a fixed-parameter regimen for Lumibird Medical's 577-nm yellow laser in a high-density, fully confluent fashion on the entire macular area:

- **Spot size:** 160 µm
- **Exposure time:** 200 ms
- **Duty cycle:** 5%
- **Power:** 250 mW

I apply this treatment in a high-density, confluent pattern, targeting the entire leaking area rather than isolated microaneurysms.

This standardized approach ensures a uniform therapeutic effect without risking injury to the photoreceptors. It also minimizes variability and increases the procedure's safety profile.

CLINICAL EXPERIENCE: REAL-WORLD CASE STUDIES

Case 1: Persistent Edema After Multiple Anti-VEGF Injections

A patient presented with 20/50 BCVA in the left eye after undergoing seven anti-VEGF injections. The examination revealed a serous neurosensory detachment and mild intraretinal fluid. My team and I applied the STL therapy, carefully avoiding the central fovea.

Within 1 month, the eye's vision improved to 20/32 BCVA, and follow-up imaging showed

- a resolution of the subretinal fluid,
- a reduction of the intraretinal cysts, and
- a decrease in hyperreflective foci (markers of inflammation).

Using AI-assisted analysis via the Ophthal software on the Mr. Doc platform (Mr. Doc s.r.l., Italy), we quantified this patient's improvement: a decrease in both neurosensory detachment volume and intraretinal fluid, which confirmed the laser's anti-inflammatory and stabilizing effect[5] (Figure 1).

This outcome reinforced what we often see clinically following STL treatment, specifically the combination of structural restoration and functional gain without any signs of retinal scarring.

Case 2: Serous Detachment With Outer Retinal Integrity

A patient with a 20/50 baseline BCVA and serous detachment in the left eye underwent the same SMPL protocol. After 1 month, his vision improved to 20/25 BCVA. Structural OCT confirmed the preservation of the outer retinal layers, including the ellipsoid zone, and a reduction of hard exudates—findings that are difficult to achieve, even with repeated pharmacologic therapy (Figure 2).

Slit-lamp examination of the macula showed a clear regression of lipid deposits and hemorrhagic components in the eye, providing evidence of effective fluid resorption and microvascular stabilization.

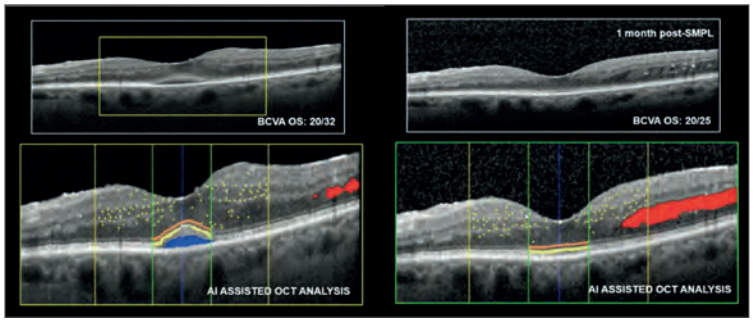

Figure 1. AI-assisted OCT images taken at the 1-month follow-up visit of an eye with serous neurosensory detachment and mild intraretinal fluid after treatment with Lumibird Medical's SubLiminal® laser.

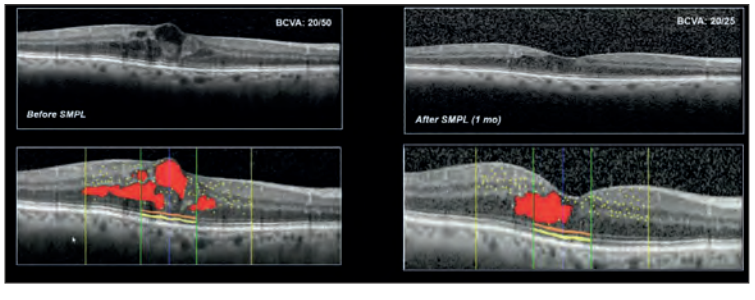

Figure 2. OCT images of an eye with serous detachment taken 1 month after treatment with the SubLiminal® laser show intact outer retinal layers, including the ellipsoid zone, and fewer hard exudates.

LESSONS FROM RESEARCH AND PRACTICE

Clinical trials such as the DIAMONDS study have validated these observations. The study demonstrated equivalent efficacy between subthreshold and conventional lasers for DME with central subfield thickness ≤ 400 µm, in terms of both BCVA change and reduction in central retinal thickness. Furthermore, quality-of-life and visual field outcomes were similar, while the subthreshold group avoided permanent retinal burns entirely.[2]

When combined with anti-VEGF therapy, the STL can also reduce injection frequency, as shown in meta-analyses and real-world data. In my experience, the combination approach offers the best of both worlds: rapid fluid reduction from anti-VEGF and long-term stabilization from the laser's RPE-modulating effects.

SAFETY AND THE FUTURE OF SUBTHRESHOLD THERAPY

What differentiates STL technology from conventional laser therapy is its safety profile and the ability to treat without causing visible burns. When applied properly, the 577-nm yellow SubLiminal® laser achieves therapeutic results without histological damage, allowing repeat treatments if necessary.

Beyond DME, this same principle is being explored for central serous chorioretinopathy (CSC), macular telangiectasia, and other retinal disorders where inflammation and RPE dysfunction play key roles.

CONCLUSION

Our evolving understanding of DME has led us full circle: from destructive lasers to pharmacotherapy and now to biologically intelligent laser modulation. With Lumibird Medical's SubLiminal® technology, we are stimulating repair instead of burning tissue to induce healing. Subthreshold laser therapy represents a step toward a safer, smarter, and more sustainable future in retinal disease management. ■

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CODING ADVISOR
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10 ESSENTIAL STEPS FOR ACCURATE RETINA SURGERY CODING


Keeping these in mind, practices can reduce errors, prevent denials, and maintain accurate billing.

BY JOY WOODKE, COE, OCS, OCSR, AND MATTHEW BAUGH, MHA, COT, OCS, OCSR

Ensuring proper reimbursement for ophthalmic surgery demands more than simply selecting a CPT code—it requires a structured, methodical approach to coding. A consistent review process helps safeguard against denials, clarify complex billing combinations, and accurately reflect what occurred in the OR. The following example shows how to apply 10 necessary steps for successful surgical coding (Figure).

OPERATIVE SUMMARY

The operative note describes a patient who underwent a pars plana vitrectomy (PPV) to address a dislocated posterior chamber IOL in the left eye. The IOL was split into two fragments, and during surgery, each piece was carefully elevated, cut, and removed through a clear corneal incision under the protection of viscoelastic. After clearing the posterior segment, the surgeon placed a new posterior chamber IOL. A peripheral iridotomy was created to remove residual viscoelastic, and subconjunctival injections of dexamethasone and cefazolin were administered.

Step 1: Identify All Possible CPT Codes and Read Full Descriptors

Using the documentation in the operative report, identify every CPT code that could apply to the documented procedures. In this case, there are several initial possibilities (Table 1). The vitrectomy itself aligns with CPT 67036, which describes a mechanical PPV. The implantation of a new IOL—unrelated to cataract surgery—corresponds to CPT 66985, which covers insertion of a secondary IOL without concurrent cataract removal. CPT 66986, an IOL exchange code, is also a possibility. Finally, CPT 67121, removal of intraocular implanted material, could apply. The iridotomy and subconjunctival injections are considered incidental to the other procedures performed in addition to being bundled.

A close reading of the operative note and the full CPT descriptors shows that only 67036 and 66986 accurately describe the work performed. CPT 66985 would not be appropriate, as a lens was already implanted and needed to be removed. CPT 67121 is bundled with 67036 and incorrect, as it is included in the IOL exchange, CPT 66986.

Step 2: Obtain Prior Authorization

Before any surgery is scheduled, it is critical to determine whether the payer requires prior authorization. PPV (CPT 67036) and IOL exchange (CPT 66986) can fall under prior authorization requirements with Medicare Advantage and commercial plans. Confirm authorization requirements during the preoperative process to avoid claim denials.

Step 3: Ensure Payer-Required Preoperative Documentation

Every payer outlines certain documentation expectations that must be met before the surgery is considered medically

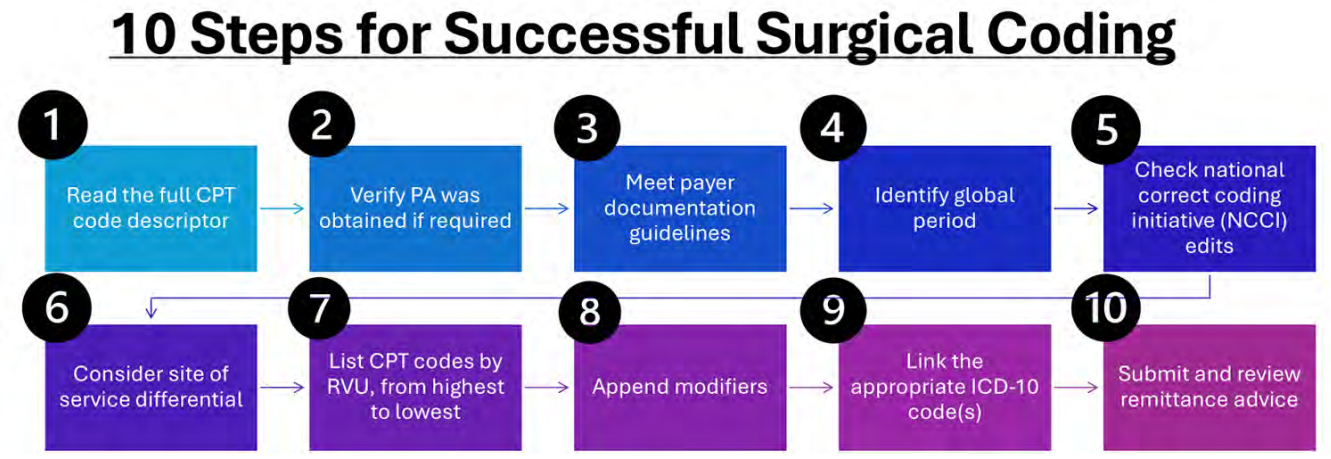

Figure. Following these 10 steps can help surgeons code carefully and enjoy proper reimbursement.

necessary. For posterior segment procedures such as PPV, the record should clearly demonstrate why surgery was needed. Here, the documentation records a dislocated posterior chamber IOL, a condition that can impair vision, cause patient discomfort, or lead to further complications if left unaddressed. The note also supports the need for secondary IOL implantation by describing the lens removal and subsequent aphakia. For some codes—such as CPT 67036—a specific diagnosis matters because only certain ICD-10 codes are payable under Medicare National Coverage Determination (NCD) policies.[1]

Step 4: Determine if Surgery Occurred Within a Global Period

In this case, there is no indication of a recent surgery or that this procedure was performed during the global period on the same eye. The surgeon does not need to append a surgical modifier such as -79 for an unrelated procedure, -78 for a return to the OR for a related procedure, or -58 for a staged/related procedure.[2] The absence of recent surgical activity simplifies this step; no additional modifier is required in addition to the anatomic modifier.

Step 5: Check NCCI Edits

National Correct Coding Initiative (NCCI) edits play a crucial role in determining which CPT code combinations can be billed on the same day. CPT 67121 is bundled with PPV code 67036 and can't be billed separately. CPT 66985—while related to IOL work—is the wrong code. Importantly, CPT 66986 and CPT 67036 are not bundled and can be billed on the same day. NCCI edits can be reviewed on the CMS website or in the Academy Ophthalmic Coding Coach.[3,4]

Step 6: Consider Site-of-Service Differential

Both CPT 66986 and CPT 67036 are assigned facility-only relative value units (RVUs), and there is no alternate non-facility value to consider. All payers expect these procedures to be performed commonly in a facility setting. As a result, the site-of-service differential does not affect these codes.

The site-of-service differential applies to procedures that are typically performed in both the clinic or facility. For example, CPT 67110—repair of retinal detachment by injection of air or other gas (eg, pneumatic retinopexy)—has a 2026 RVU of 26.69 in the office and 20.92 when performed in the facility. The office RVU value is higher to cover the additional practice expenses associated with performing the procedure in the office.

TABLE 1. INITIAL CPT CODE CONSIDERATIONS AND DESCRIPTORS

CPT Code	Descriptor
67036	Vitrectomy, mechanical, pars plana approach
66985	Insertion of IOL prosthesis (secondary implant), not associated with concurrent cataract removal
66986	Exchange of IOL
67121	Removal of implanted material, posterior segment, intraocular

TABLE 2. FINAL CODING SUMMARY

CPT Code	Description	Modifier(s)	Linked ICD-10
66986	Exchange of IOL	-LT	T85.22XA
67036	Pars plana mechanical vitrectomy	-LT	H43.392

Step 7: List CPT Codes From Highest to Lowest RVU

When multiple procedures are billed during the same session, Medicare and most commercial payers reimburse the highest-valued procedure at 100% of its allowable rate, while subsequent codes are typically reduced—often to 50% of their allowable. For this reason, the order of submitted CPT codes matters. Given their respective 2026 RVUs, CPT 66986 (22.87) should be listed first, followed by CPT 67036 (22.72) to appropriately maximize reimbursement. RVUs can be accessed using the CMS Medicare Physician Fee Schedule lookup and in the Academy Ophthalmic Coding Coach.[4,5]

Step 8: Append Modifier(s)

Because the surgery was performed on the left eye, both codes require the anatomic modifier, -LT. No global-period modifier is needed because this case does not fall within another surgical global period. If a global-period modifier was needed, it would go before the anatomic modifier. The final coded procedures therefore appear as CPT 66986-LT and CPT 67036-LT (Table 2).

Step 9: Link to Appropriate Diagnosis Codes

Assigning the proper ICD-10 codes is essential to demonstrate medical necessity. For the lens exchange, CPT 66986, the diagnosis is T85.22XA (dislocation of IOL, initial encounter). For the PPV, CPT 67036, a diagnosis of H43.392 (other vitreous opacities, left eye) is both clinically appropriate and listed as a payable diagnosis under the NCD for this CPT code.[1] ICD-10 code T85.22XA is not a payable diagnosis per Medicare's NCD. Linking each code to its most specific diagnosis ensures clean claim processing.

Step 10: Submit the Claim and Review Remittance Advice

After submission, carefully review the remittance advice to confirm that both procedures were paid correctly and that the multiple procedure reduction was appropriately applied. If either code is denied—whether due to modifier issues, bundling concerns, or diagnosis-linking errors—remittance will help the practice identify the necessary corrections.

ALL PART OF THE PROCESS

Follow this consistent 10-step process to ensure complex ophthalmic surgeries are coded accurately and reimbursed appropriately. By carefully reviewing the operative note, selecting the correct CPT and ICD-10 codes, applying modifiers, and confirming payment, practices can reduce errors, prevent denials, and maintain efficient, compliant billing. ■

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OCULAR TOXICITY FROM NEW ONCOLOGY AGENTS

While these drug innovations are exciting, we need to be on alert for a range of ocular complications with this patient population.

BY SARAH TOUHAMI, MD, PHD

New oncologic medications such as small molecule inhibitors and immunotherapies have transformed cancer treatment by offering targeted approaches and improving patient survival rates. However, these novel agents are associated with various side effects, notably class-specific ocular toxicities ranging from mild, reversible symptoms to serious, vision-threatening conditions, which are more common with combination therapies.

The mechanisms underlying ocular toxicity with newer oncology agents are broadly classified as direct (affecting neuronal and/or glial cells) or indirect (resulting from inflammation or a compromised blood-retinal barrier). It is crucial to establish a definitive connection between the specific medication and adverse event, for which tools such as the World Health Organization classification or the Naranjo criteria can be useful.[1]

This article reviews the commonly reported drug-induced retinal and uveitis-related toxicities linked to modern oncology treatments and describes a multidisciplinary management strategy.

SMALL MOLECULE INHIBITORS

Dysregulation of the mitogen-activated protein kinase (MAPK) pathway is a factor in several cancers. MAPK kinase (MEK) and BRAF gene inhibitors interfere with this signaling pathway, limiting the proliferation, differentiation, and survival of cancer cells. Activation of fibroblast growth factor receptor (FGFR) signaling triggers the MAPK cascade, thereby accounting for the overlapping retinal adverse effects observed with FGFR inhibitors.

MEK inhibitors

MEK inhibitors are used to treat various cancers as monotherapy and in combination with other targeted drugs, such as BRAF inhibitors.[2,3] Despite their high efficacy, these inhibitors are linked to a specific class-effect retinopathy known as MEK-associated retinopathy (MEKAR), which causes self-limiting serous detachments of the neurosensory retina.[4-7] This condition is highly prevalent, affecting up to 90% of patients receiving these drugs, and is generally asymptomatic and reversible.[3] Symptomatic patients may report blurred vision, halos around lights, and colorful spots in their vision.

The toxicity is thought to affect the retinal pigment epithelium (RPE) cells, causing dysfunction by inhibiting the MAPK pathway. This pathway is downstream of the FGFR that is vital for the maintenance, repair, and survival of the RPE.[3,8] Inhibition leads to the buildup of subretinal fluid (SRF), and, as such, MEKAR presents with characteristic patterns of fluid accumulation on OCT, including dome, caterpillar, waves, and splitting.[6]

While these SRF findings resemble those seen in central serous chorioretinopathy (CSC), key differences exist: The fluid's location in MEKAR is between the photoreceptors and an intact RPE, it is typically multifocal and bilateral, and, unlike with CSC, pigment epithelial detachments (PEDs) and fluorescein leakage are absent. Furthermore, MEKAR is not associated with changes in choroidal thickness, and visual acuity is maintained in most cases.[6]

Less commonly, MEK inhibitors may also cause retinal vein occlusion (RVO), which suggests a possible toxicity to endothelial cells.[9,10] Although the prevalence of RVO in patients undergoing MEK inhibition is low (0.5%), it exceeds the 0.1% prevalence in the general population.[11]

There is no current recommendation for routine ocular screening for patients on MEK inhibitors; however, a baseline examination is advised to distinguish preexisting conditions from MEKAR. Management of MEKAR usually involves observation, given its reversible nature. However, in cases of RVO, discontinuing the MEK inhibitor is necessary to prevent sight-threatening bilateralization, alongside standard-of-care treatment for the occlusion.

BRAF Inhibitors

BRAF inhibitors operate upstream of MEK inhibitors, triggering significant apoptosis in cancer cells. This process

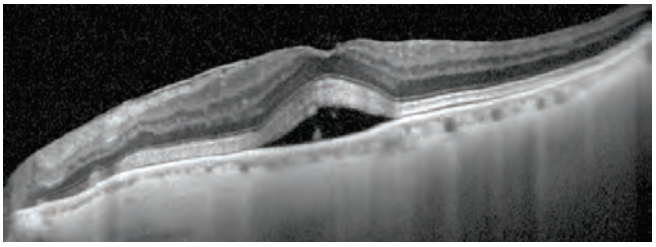

Figure 1. This OCT B-scan shows the left eye of an 81-year-old man being treated with erdafitinib, an FGFR inhibitor, for urothelial carcinoma. The scan reveals a distinct foveal SRD, elongation of the photoreceptor outer segments with subretinal debris, and a surrounding area where SRF appears to separate the retina from the RPE (ie, splitting). The noted lesions were bilateral. Importantly, the choroid appears thin, in contrast to the thickened choroid typically observed in CSC.

can provoke an inflammatory response leading to ocular side effects. The suggested mechanism is mimicry, in which the immune system, activated by dying cancer cells, attacks healthy tissues. Therefore, uveitis is the most common ocular adverse event associated with this drug class, affecting about 4% of patients, although the frequency may vary by the specific drug.[12,13] Anterior, intermediate, posterior, and/or panuveitis can occur, and macular edema may accompany it. Additionally, Vogt-Koyanagi-Harada (VKH)-like syndromes may develop, possibly due to mimicry involving melanomatous cancer cells.[14] Other potential complications include dry eye, conjunctivitis, and subretinal detachment (SRD); SRD is most commonly associated with combined use of BRAF and MEK inhibitors.

The prognosis for BRAF inhibitor-induced uveitis is generally good, with most cases responding well to local corticosteroids.[15] It is important to avoid systemic steroids and immunosuppressants to prevent interference with the anti-cancer immune response. Discontinuation of the drug is reserved for severe, uncontrolled inflammation that becomes sight-threatening.

FGFR Inhibitors

FGFR inhibitors are a class of tyrosine kinase inhibitors that may cause toxicity of the retina and ocular surface. Typical manifestations include:

- Trichiasis, trichomegaly, increased eyelash curling, and changes in hair texture
- Dry eye, blepharitis, and conjunctivitis
- Corneal deposits, keratitis, and limbal stem cell deficiency
- FGFR inhibitor-associated retinopathy

Retinal adverse events have been documented with nearly all FGFR inhibitors, including erdafitinib, infigratinib, pemigatinib, futibatinib, and rogaratinib.[16] The primary mechanism appears to be direct toxicity to RPE cells, as the FGFR pathway is critical for RPE maintenance and survival.[3,8] OCT imaging may show SRF mainly in the form of SRDs; lesions are often bilateral and can be unifocal or multifocal (Figure 1).

In contrast to CSC, FGFR-associated retinopathy features

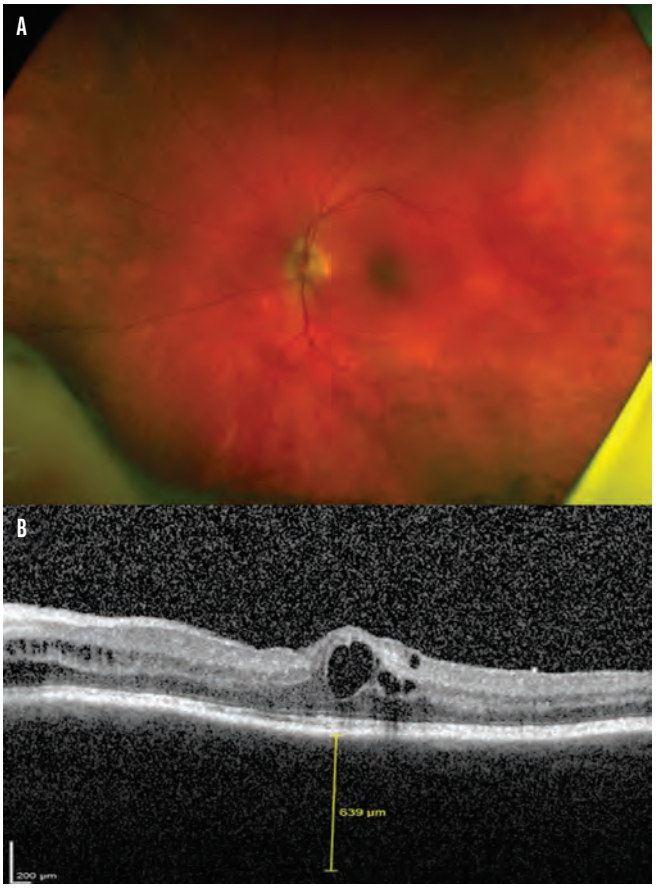

Figure 2. Ultra-widefield fundus imaging shows the left eye of a 72-year-old patient undergoing treatment with nivolumab, a CPI, for metastatic melanoma and demonstrates blurred optic disc margins and vitritis, particularly in the inferior retina (A). An OCT B-scan reveals intraretinal cysts in the macula and interpapillomacular region (B). Note the choroid appears markedly thickened, consistent with diffuse inflammatory infiltration. Bilateral anterior chamber cells were observed on the anterior segment examination.

intact, hyperreflective photoreceptor and RPE layers with sensory retinal detachments but no true PEDs or choroidal thickening, and the condition is most frequently reversible. However, cases of inner/outer retinal atrophy, ellipsoid zone disruption, interdigitation zone thickening, and/or hyperreflectivity near the affected ellipsoid/interdigitation zones corresponding to subretinal deposits have also been described.[16] Management rarely involves drug withdrawal, depending on the agent used, especially if the condition becomes chronic and severely affects vision[16,17]; however, the utility of discontinuing the drug is unclear, given the high rate of spontaneous resolution in such cases.

IMMUNOTHERAPY: CHECKPOINT INHIBITORS

Checkpoint inhibitors (CPIs) are a form of immunotherapy that functions by blocking proteins such as CTLA-4 and PD-1/PD-L1, which normally suppress the immune system. These proteins are also used by cancerous cells to evade the immune response. Thus, CPIs regulate T-cell activation and

THE MECHANISMS UNDERLYING OCULAR TOXICITY WITH NEWER ONCOLOGY AGENTS ARE BROADLY CLASSIFIED AS DIRECT (AFFECTING NEURONAL AND/OR GLIAL CELLS) OR INDIRECT (RESULTING FROM INFLAMMATION OR A COMPROMISED BLOOD-RETINAL BARRIER).

are effective against many malignancies, including metastatic melanoma, small-cell lung cancer, colon cancer, renal cell carcinoma, and more. However, this broad immune activation can cause immune-related adverse events (irAEs) anywhere in the body, including the eye.[13] Furthermore, some of the inhibited molecules, such as PD-L1, are expressed on the cornea, iris-ciliary body, and RPE, where they contribute to the eye's immune privilege; blocking them can thus cause significant ocular inflammation.

Ocular irAEs affect 0.4% to 1% of patients on CPIs,[18] although incidences as high as 4.3% have been reported, suggesting events may be under-documented.[19] Timing of manifestations may vary but usually occurs within 6 months of exposure to the drug. Clinical signs may involve intra-, extra-, and/or periocular structures, with symptoms ranging from dry eye and keratitis to more severe conditions such as orbital inflammation, cranial nerve palsies, optic neuropathy, and myasthenia gravis.[13] When uveitis occurs, it is often anterior, and posterior segment involvement may include vitritis, immune retinopathy, papillitis, vasculitis, and/or choroiditis (Figure 2). Similar to BRAF inhibitors, VKH-like syndromes have also been reported, especially in patients treated for metastatic melanoma.

MULTIDISCIPLINARY MANAGEMENT

The management of ocular toxicities from these cancer drugs requires close collaboration between oncologists and ophthalmologists. The first step is to exclude other potential causes, as oncology patients may have confounding factors such as corticosteroid-induced CSC, immunosuppression-related intraocular infections, or metastatic disease.

For FGFR- and MEK-inhibitor associated retinopathies, observation is the typical approach, with drug withdrawal considered only for chronic cases with severe vision impairment. For MEK inhibitor-associated RVO, the drug must be stopped and the occlusion treated. For uveitis due to BRAF or checkpoint inhibitors, a stepwise strategy is best, starting with local corticosteroids and progressing to systemic corticosteroids or other immunosuppressants. However, this approach should be avoided whenever possible, as it can promote cancer progression. Withdrawing the cancer drug is a last resort. Continued research and strong collaboration are crucial to optimize both visual and oncologic outcomes. ■

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Building the Future of Ophthalmology: YMDC Brings Mentorship, Innovation, and Industry Together at AAO 2025

Early-career ophthalmologists gathered with thought leaders and industry experts at YMDC's capstone event to discuss mentorship and the future of ophthalmic innovation.

YoungMD Connect (YMDC) recently hosted its capstone mentorship and networking event at the 2025 American Academy of Ophthalmology (AAO) Annual Meeting in Orlando, where early-career ophthalmologists connected with key leaders in the field and representatives from top industry organizations. During this event, medical students, residents, fellows, and early-career ophthalmologists were able to experience the power of building connections among peers and mentors, and prepare for a successful future in ophthalmology.

A NIGHT OF CONNECTION AND COLLABORATION

The event brought together 160 attendees, including residents, fellows, medical students, practicing ophthalmologists, and mentors. Throughout the evening, they participated in an inspiring program that featured a panel discussion, interactive mentorship rotations, and a vibrant networking reception (Figure 1).

PANEL INSIGHTS: PARTNERING FOR INNOVATION AND GROWTH

The evening began with an engaging panel led by William B. Trattler, MD (refractive, corneal, and cataract eye surgeon at the Center for Excellence in Eye Care in Miami, Florida) and featured Kelly Vaupel (US Marketing Senior Director at Johnson & Johnson Vision) and Jason Rothenhaus (General Manager, Eye Care, Ocular Surface, and Glaucoma at AbbVie; Figure 2). The discussion emphasized collaboration between surgeons and industry to drive innovation and support early-career ophthalmologists.

Dr. Trattler emphasized the vital role of industry partners in helping early-career ophthalmologists transition from training to independent practice, including facilitating access to new technologies and support in the operating room.

Both panelists highlighted their companies' commitment to mentorship, education, and innovation. Ms. Vaupel introduced Johnson & Johnson Vision's new mentorship pilot program that pairs six mentors with 12 mentees, with plans for expansion. Mr. Rothenhaus discussed AbbVie's Institutions Team, created 3 years ago to directly support residents, fellows, and young ophthalmologists through surgical education and access to innovative treatments.

When speaking on the future of ophthalmology, Mr. Rothenhaus projected major advances in AI adoption, noting that 70% of ophthalmologists plan to use AI for diagnostics in the coming

Figure 1. Attendees enjoyed a warm evening outside during the networking reception.

Figure 2. Panelists Kelly Vaupel (Johnson & Johnson Vision), Jason Rothenhaus (AbbVie), and William B. Trattler, MD, in discussion.

Advice for Early-Career Ophthalmologists

- Engage with mentorship/training programs to accelerate skills and connections.
- Share real-world insights with companies. If you observe study ideas or technique tweaks in practice, reach out. Bi-directional feedback can improve patient care.
- Explore AI readiness. Begin learning and applying AI tools as diagnostic adoption grows.

year. Both panelists agreed the current innovation in cataract and refractive surgery, combined with data-driven care, will reshape practice patterns and improve treatment outcomes for patients.

Dr. Trattler closed the panel by urging young ophthalmologists to engage actively with mentorship and industry programs to accelerate their careers and drive innovation in eye care.

LEARNING FROM LEADERS

Known for its thought-provoking discussion, the mentorship rotations featured 21 faculty members representing retina, cornea, refractive, glaucoma, oculoplastics, and pediatric ophthalmology subspecialties (Figure 3).

These sessions encouraged open discussions in an intimate setting that were conducted in an "ask me anything" format, allowing attendees to cover a range of topics.

Figure 3. Attendees engaged in robust discussion during mentorship rotations.

LOOKING TO 2026

At the core of YMDC events is a goal for members to embrace lifelong curiosity, while building networks across peers, mentors, and industry. The next YMDC Capstone event will take place at the 2026 AAO Annual Meeting in New Orleans, Louisiana.

To stay connected and explore future opportunities, visit **www.youngmdconnect.com.**

(Continued from page 35)

Close the scleral tunnel with nylon, when necessary, and reapproximate Tenon and conjunctiva to the limbus without tension to protect the polytetrafluoroethylene sutures and reduce erosion risk.

TIME TO FOCUS ON VISION

Scleral fixation of toric IOLs represents an expanding frontier in premium lens surgery, allowing us to preserve patients' refractive goals even in the setting of compromised capsular support. But should we, as retina surgeons, pursue this? I would argue that we should, and our practice may evolve to include those who specialize in refractive retina.

Many patients who present with a dislocated lens have either paid (out of pocket) for a premium toric IOL or have significant corneal astigmatism that may benefit from a toric IOL. Eyes without capsular support have limited options from our anterior segment counterparts (eg, anterior chamber IOLs or aphakic contact lenses), and our ability to remove and replace the IOL during vitrectomy allows us to correct as much refractive error as possible during the case.

Correction of astigmatism allows a patient to be as glasses-free as possible, and while our results may not be as accurate as in-the-bag IOL placement, they are very good. In a case series by Swaminathan et al, 23 eyes underwent secondary placement of an EnVista toric IOL, and 72.7% were within 1.0 D and 54.5% were within 0.5 D of the planned refractive spherical equivalent target.[7] With proper counseling and expectation management, correction of a patient's astigmatism should be included in our preoperative assessment of the case, as it can lead to significantly improved vision that would otherwise be corrected with glasses.

If you are ready to dive into the world of refractive retina, start with confidence knowing that, with a small adjustment to your surgical skillset, you can correct more than aphakia. Meticulous patient selection, accurate axis marking, thoughtful sclerotomy planning, and controlled centration are keys to achieving optimal outcomes. With familiarity and refinement of the technique, surgeons can confidently incorporate toric optics into their SFIOL armamentarium and provide patients with durable, high-quality vision. ■

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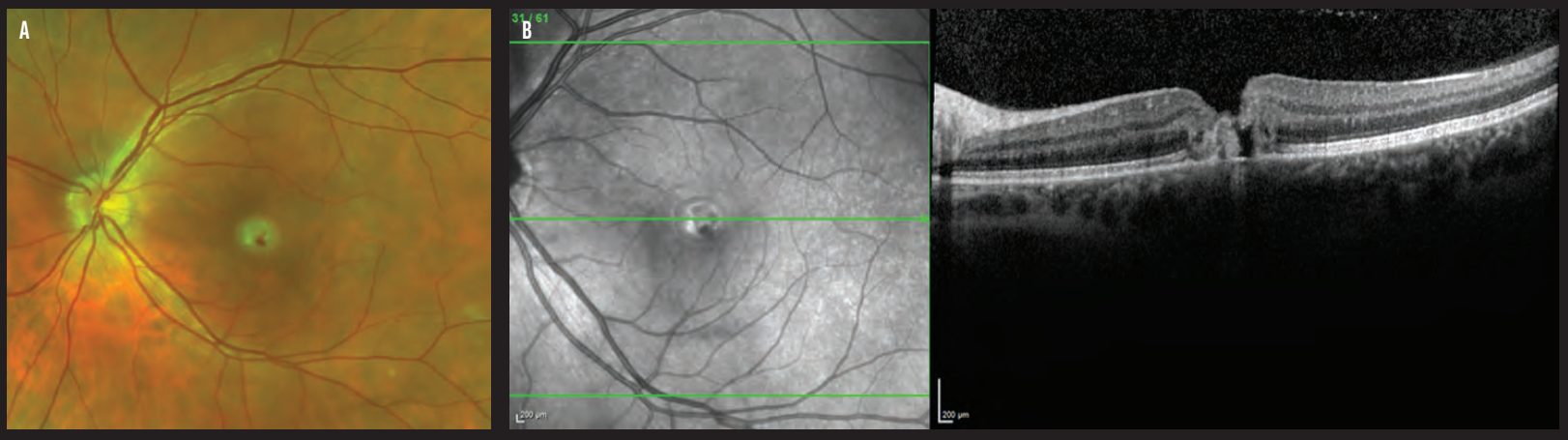


FIGURE 1

PIERCED BY LIGHT: COSMETIC LASER-INDUCED MACULAR INJURY

A workplace injury required surgical intervention to repair a full-thickness macular hole.

BY IRMAK KARACA, MD; MARC MARDELLI, MD; AND TALIA R. KADEN, MD

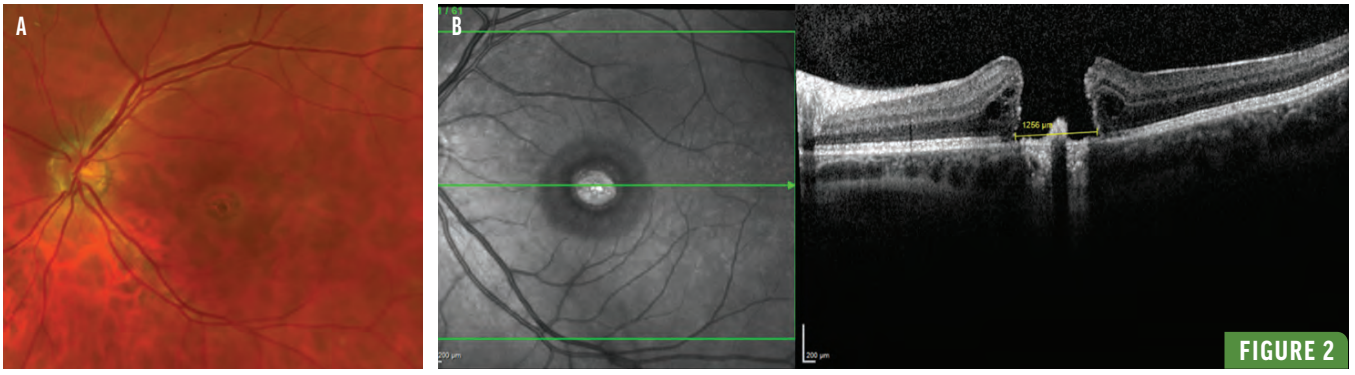
A 34-year-old woman working as a beauty spa technician presented with a central black spot in her left eye following an accidental injury while using a 1,064-nm Q-switched Nd:YAG laser to perform laser hair removal. Her VA was 20/20 OD and counting fingers OS. Slit-lamp examination and IOPs were unremarkable. Fundus examination showed a ~.75 disc-diameter yellow-white circular lesion with a small intraretinal hemorrhage in the central macula (Figure 1A) and an inferior vitreous hemorrhage. OCT of the left eye (Figure 1B) showed central ellipsoid zone and outer retinal loss, increased hyperreflectivity, and disorganization of retinal layers, raising concern for an impending full-thickness macular hole (FTMH). OCT of the right eye was normal.

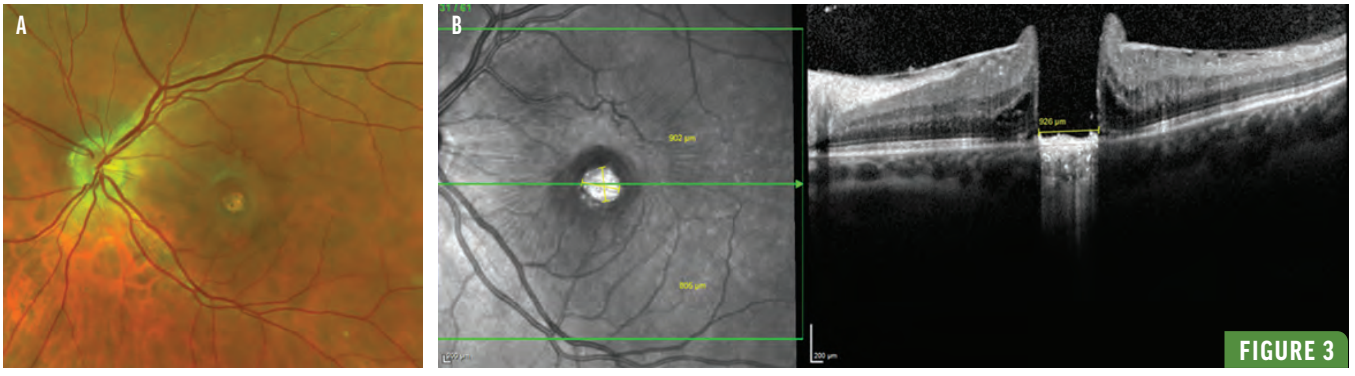
Two weeks after her injury, a FTMH had developed on fundus imaging and OCT (Figure 2A, B). Six weeks after the injury, a progressive tractional epiretinal membrane (ERM) was noted (Figure 3A, B). The patient underwent pars plana vitrectomy and internal limiting membrane peel with rosette creation and 12% C_3F_8 tamponade. One month postoperatively, the FTMH was closed (Figure 4). Nine months later, it remained closed, and her final VA was 20/600 OS.

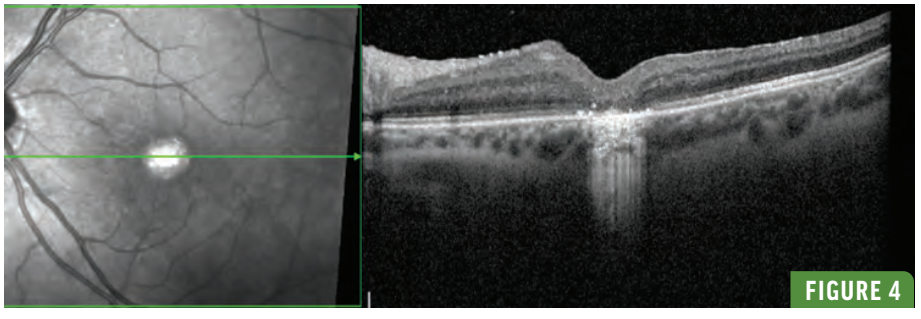
LASER-INDUCED FTMH

While most FTMHs are idiopathic,[1] they may also occur secondary to trauma, including accidental laser exposure. Traumatic MHs result from direct photothermal or photomechanical disruption of the foveal architecture. Unlike idiopathic FTMHs, spontaneous closure is relatively common, particularly in younger patients, making initial observation a reasonable approach.[2,3]

Laser-induced macular injury is a distinct subset of traumatic maculopathies. Accidental exposure to Q-switched Nd:YAG lasers, which are widely used in dermatologic and cosmetic procedures, can cause immediate photothermal and photodisruptive retinal damage.[4,5] Clinical findings







often include foveal whitening, small intraretinal hemorrhages, and outer retinal disruption on OCT. Secondary complications, such as FTMH formation or chorioretinal scarring, may develop over days to weeks. Although some traumatic MHs may close spontaneously, surgical intervention should be considered when closure is unlikely or delayed, particularly in the presence of additional factors, such as progressive traction from an ERM, large hole size, or persistent visual deficit.[4-6]

OBSERVATION VERSUS SURGERY

This case underscores the importance of using protective eye wear and following safety protocols while using cosmetic laser devices. Bear in mind that even with successful anatomic closure, visual recovery may remain limited due to the severity of initial photothermal injury with subsequent chorioretinal scarring. Careful OCT monitoring is essential to guide management and optimize outcomes. ■

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The Valeda Light Delivery System is intended to provide improved visual acuity in patients with best-corrected visual acuity of 20/32 through 20/70 and who have dry age-related macular degeneration (AMD) characterized by:
• The presence of at least 3 medium drusen (> 63 µm and = 125 µm in diameter), or large drusen (> 125 µm in diameter), or non-central geographic atrophy, AND
• The absence of neovascular maculopathy or central-involving geographic atrophy
After about two years, the Valeda Light Delivery System treatment provides improved mean visual acuity of approximately one line of visual acuity (ETDRS) compared to those not receiving the treatment.
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As a precaution, patients have not been tested and should not be treated with Valeda if they have any known photosensitivity to yellow light, red light, or near-infrared radiation (NIR), or if they have a history of light-activated central nervous system disorders (e.g., epilepsy, migraine). In addition, patients should not receive treatment within 30 days of using photosensitizing agents (e.g., topicals, injectables) that are affected by 590, 660, and/or 850 nm light before consulting with their physician.
Precautions
Safety and effectiveness in patient populations and/or conditions excluded from the clinical study has not been established. This includes the following: patients under the age of 50, pregnant or nursing women, current or history of neovascular maculopathy, presence of center involving geographic atrophy (GA) within the central 1mm diameter, media opacities, including cataracts, which might interfere with visual acuity or imaging in the eye, posterior capsule opacification, which might interfere with visual acuity or imaging in the eye, ocular disorder or disease that partially or completely obstructs the pupil, any visually significant disease in any ocular structure apart from dry AMD.
An analysis of the primary effectiveness endpoint (mean BCVA change from baseline for the PBM arm – the mean BCVA change in the Sham arm) showed the following differences between arms for the subgroup of pivotal study patients with early AMD (Beckman Clinical Category Classification):
- At Month 13: +1.90 letters
- At Month 21: -0.10 letters
- At Month 24: +0.29 letters

The eyecare practitioner should consider the observed benefit/risk profile for this sub-population, when contemplating treatment of patients with this classification of Early AMD.
It is possible that treatment benefit may not persist significantly after treatment is stopped. The clinical study provided no significant data concerning the safety and effectiveness of the device should treatments be applied more frequently than described in this manual, or if more than 54 total treatments are delivered per eye. Twelve (12) eyes (12.9%) in the PBM group and 4 eyes (7.3%) in the Sham group had a fellow eye that had neovascular AMD (nAMD). Of these 5 (41.7%) of 12 eyes in the PBM-treated group converted to nAMD, and 1 (25.0%) of the 4 eyes in the Sham group converted to nAMD. The eye care practitioner should consider the benefit/risk profile in this sub-population and should closely monitor patients whose fellow eye has nAMD.

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