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OCTOBER 2025 VOL. 20, NO. 7
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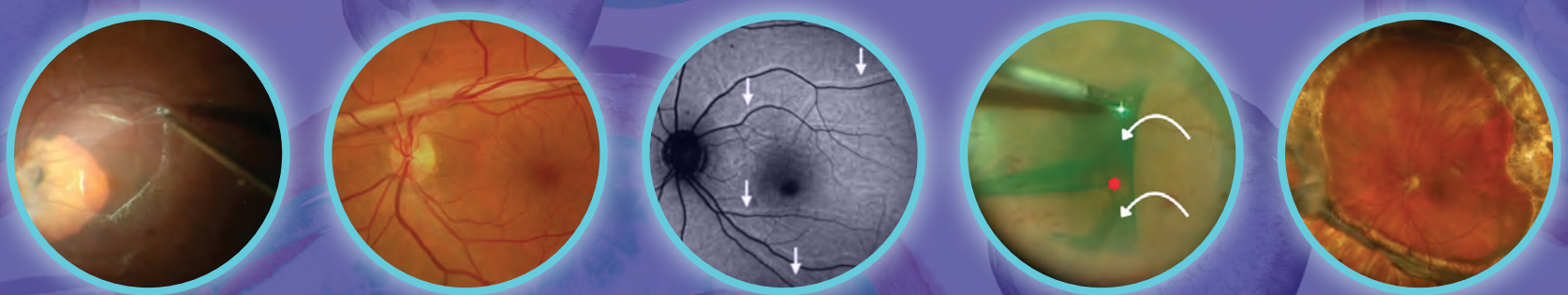

Experts share the latest techniques transforming their ORs.

AN ATLAS OF INTERNAL LIMITING MEMBRANE FLAPS

AN ILLUSTRATIVE GUIDE TO INTRAOPERATIVE OCT

RESCUE TECHNIQUES FOR DISLOCATED IOLS

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Vitreoretinal
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Experience Extraordinary

Superior Efficiency for Vitreoretinal and Cataract Surgery.*

*Based on bench testing.

Reference: 1. Alcon data on file, 2024.

UNITY® VCS and CS Important Product Information
Caution: Federal (USA) law restricts this device to sale by, or on the order of, a physician.
Indications / Intended Use: UNITY VCS: The UNITY VCS console, when used with compatible devices, is indicated for use during anterior segment (i.e., phacoemulsification and removal of cataracts) and posterior segment (i.e., vitreoretinal) ophthalmic surgery. In addition, with the optional laser this system is indicated for photocoagulation (i.e., vitreoretinal and macular pathologies), iridotomy and trabeculoplasty procedures. **UNITY CS:** The UNITY CS console, when used with compatible devices, is indicated for use during anterior segment (i.e., phacoemulsification and removal of cataracts) ophthalmic surgery. **Warnings:** Appropriate use of UNITY VCS and CS parameters and accessories is important for successful procedures. The console supports various accessories to perform various surgical procedures. Accessories include handpieces and probes, as well as tips and sleeves when necessary. Different accessories are required for different procedures and operating modes. Test for adequate irrigation and aspiration flow, reflux, and operation of each accessory prior to entering the eye. The consumables used in conjunction with ALCON® instrument products constitute a complete surgical system. To avoid the risk of a patient hazard, do not mismatch consumable components or use settings not specifically adjusted for particular consumable component combinations. **AEs/Complications:** Inadvertent activation of functions that are intended for priming or tuning accessories while the accessory is in the eye can create a hazardous situation that could result in patient injury. During any ultrasonic procedure, metal particles may result from inadvertent touching of the ultrasonic tip with a second instrument. Another potential source of metal particles resulting from any ultrasonic handpiece may be the result of ultrasonic energy causing micro abrasion of the ultrasonic tip. **ATTENTION:** Refer to the Directions for Use for the accessories/consumables and User Manual for a complete listing of indications, warnings, cautions and notes.

Alcon

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TABLE OF CONTENTS

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FEATURED ARTICLES

DEPARTMENTS

VALEDA®

Light Delivery System

The First and Only FDA-Authorized Treatment for Dry AMD that Improves Vision

It's Time for Patients to See Their Future

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Refer to the Valeda User Manual for indications for use and important safety information.

PROTECT THE OR!


For many of us retina specialists, the OR is where we fell in love with the retina. Browse through our *Rising Stars* and *One to Watch* honorees (online at www.retinatoday.com), and you will see just how many admit that they were hooked after watching a membrane peel or foreign body removal for the first time.

However, like most relationships these days, it's complicated. We might love the OR, but it doesn't always love us back. A new study by Li and Adelman found that, between 2000 and 2021, the service volume experienced a statistically significant decrease for 20 of 38 retina procedures. While intravitreal injections increased more than 1,000-fold (remember, anti-VEGF agents came to market in 2006) and vitrectomy procedures increased from 71,039 to 95,429, panretinal photocoagulation declined from 104,865 to 48,533 procedures, and scleral buckling plummeted from 6,502 to 587 procedures.[1] Perhaps even more telling is the reimbursement: In the same timeframe, reimbursement decreased by a statistically significant amount for 29 of those 38 procedures.[1]

The ongoing discussion of limited OR access for retina procedures—although rampant in conference halls—has yet to seep into the peer-reviewed literature, as it's hard to quantify. Still, it's adding even more pressure to those who practice in academic centers equipped to handle emergency cases. It's also changing how we practice (choosing a tap-and-inject for endopthalmitis in lieu of vitrectomy, for example).[2]

Thus, retina surgery has become more of a labor of love than one might expect. Despite the grim aura surrounding reimbursement, surgical volume, and OR access, surgical intervention is often vital to preserve patients' vision. And it's an ever-evolving field with an onslaught of cool innovations poised to change the field forever. In fact, retina surgery is booming.

As we write this editorial, we are also filling our calendars with AAO Retina Subspecialty day sessions, and we cannot wait to learn about eye transplant surgery, office-based surgery, modern vitrectomy platforms, the growing field of robotic surgery, the use of amniotic membranes in vitreoretinal surgery, and novel secondary IOL techniques, to name just a few. There are also lectures on the latest surgical approaches to historically medically managed (or not managed at all) diseases, such as AMD, diabetic macular edema, and macular telangiectasia type 2. We are innovating in the OR more than ever before.

IN THIS ISSUE, WE LAUD THE GRIT AND CREATIVITY THAT DEFINES THE RETINA OR.

In this issue, we laud the grit and creativity that defines the retina OR—the reason we still do what we do. Stratos Gotzaridis, MD, FASRS, and Niki Zabogianni, MD, discuss the best techniques to ensure anatomic *and* functional success after retinal detachment repair (hint: Slower reattachment is better!), and Avni P. Finn, MD, MBA, and David L. Zhang, MD, provide a wonderful atlas of internal limiting membrane flaps to consider for macular hole repair. Jason Hsu, MD, and Sidra Zafar, MD, share pearls for handling proliferative vitreoretinopathy in the OR, and William E. Smiddy, MD, details the various ways to adapt scleral fixation for nearly any IOL style. Lastly, Audina M. Berrocal, MD, and Daniel A. Balikov, MD, PhD, describe several cases that benefitted from intraoperative OCT.

These are all new approaches our colleagues are implementing in their ORs right now, and we hope they reinvigorate your own curiosity and drive to innovate and improve our surgical practice. The more we improve outcomes, preserve patients' vision, and treat those who used to hear "sorry, there's nothing we can do," the more weight we have when advocating to save our OR times and increase reimbursement rates. It's a win-win—for us and our patients. ■

1. Li ES, Adelman RA. Trends in Medicare reimbursement and service volume of vitreoretinal procedures: 2000 to 2021 [published online ahead of print November 8, 2024]. *J Vitreoretin Dis*.
2. Schwartz SG, Flynn HW Jr. "Real world" management of acute-onset postoperative endophthalmitis with presenting visual acuity of light perception. *Ophthalmol Retina*. 2024;8(11):1033-1034.

ALLEN C. HO, MD
CHIEF MEDICAL EDITOR

ROBERT L. AVERY, MD
ASSOCIATE MEDICAL EDITOR

The **first and only** FDA-approved treatment for adults with idiopathic macular telangiectasia type 2 (MacTel)[1]

ENCELTO™

(revakinagene taroretcel-lwey)

implant, for intravitreal use

Proven to **slow disease progression** in two phase 3 studies[1,2]*

*Based on two phase 3, randomized, multicenter, sham-controlled studies (Study A and Study B). Both studies evaluated the rate of ellipsoid zone (EZ) area loss (macular photoreceptor loss) in 228 adults with MacTel type 2 over 24 months. Results for ENCELTO: 54.8% reduction in retinal degeneration in Study A (P<0.0001); 30.6% reduction in Study B (P=0.0186).[1,2]

The permanent J-code for ENCELTO is now available: **J3403**

Scan the QR code for more information about accessing ENCELTO

INDICATIONS AND USAGE

ENCELTO is an allogeneic encapsulated cell-based gene therapy indicated for the treatment of adults with idiopathic macular telangiectasia type 2 (MacTel).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ENCELTO is contraindicated in patients with active or suspected ocular or periocular infections, and in patients with known hypersensitivity to Endothelial Serum Free Media (Endo-SFM).

WARNINGS AND PRECAUTIONS

ENCELTO implantation surgery and/or implantation related procedures have been associated with the following:

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.

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 adjacent pages.

References: 1. ENCELTO [prescribing information]. Cumberland, RI. Neurotech Pharmaceuticals, Inc. **2.** Data on file. Neurotech Pharmaceuticals, Inc. Cumberland, RI.

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.

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ENCELTO is contraindicated in patients with:

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

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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

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

RT NEWS

OCTOBER 2025

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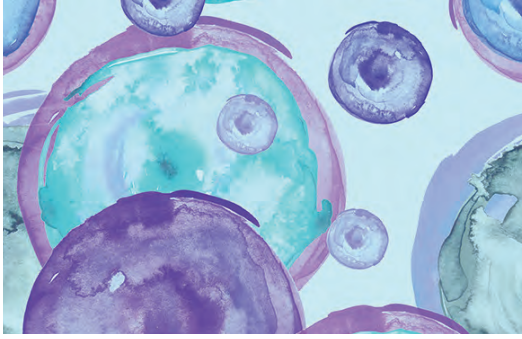


GLP-1 RA USE ASSOCIATED WITH A LOWER RISK OF UVEITIS

A recent retrospective cohort study found that treatment with glucagon-like peptide-1 receptor agonists (GLP-1 RAs), commonly used for weight loss and glycemic control in diabetes, was associated with a lower risk of developing uveitis. Researchers at the Cleveland Clinic Cole Eye Institute initiated the study to better understand the effects of the antiinflammatory properties associated with GLP-1 RAs, particularly as they pertain to the eye.[1]

The study included patients with and without diabetes who were prescribed GLP-1 RAs, metformin, insulin, or sodium-glucose cotransporter 2 (SGLT-2) inhibitors. Of the 516,052 patients included in the study, 258,026 were prescribed GLP-1 RAs and 258,026 were in a control group.[1]

The researchers found that the GLP-1 RA cohort had a reduced risk of uveitis compared with controls (risk ratio [RR]: 0.48), a finding that was consistent among patients with (RR: 0.54) and without (RR: 0.52) diabetes. Compared with the patients taking metformin (RR: 0.58) and insulin (RR: 0.57), GLP-1 RAs were associated with greater protection against uveitis. However, GLP-1 RA use was associated with a slightly increased uveitis risk compared with SGLT-2 inhibitors (RR: 1.17). The use of SGLT-2 inhibitors was also associated with a reduced uveitis risk compared with controls (RR: 0.52).[1]

The researchers concluded that the findings suggest a potential antiinflammatory benefit, and further investigation is required to better understand the role GLP-1 RAs play in various ocular inflammatory diseases.[1]

1. Mohan N, Srivastava SK, Schulgit MJ, Nowacki AS, Kaelber DC, Sharma S. Glucagon-like peptide-1 receptor agonists and risk of uveitis [published online ahead of print August 28, 2025]. *JAMA Ophthalmol.*

RESEARCH CONTINUES ON METFORMIN USE AND AMD RISK

A team of researchers recently discovered that metformin use was not associated with significant development or progression of AMD.[1] Although metformin has proven protective against several systemic diseases (eg, cancer and cardiovascular disease) and retinal diseases (eg, diabetic retinopathy and choroidal neovascularization), the literature remains unclear about its effect on AMD. Several studies have suggested a potential protective effect of metformin use on AMD development,[2-4] while others found metformin had no effect on reducing the progression of GA.[5]

To better understand the relationship between metformin use and the development of any AMD and progression to geographic atrophy and/or wet AMD, researchers used the TriNetX database to evaluate 297,008 participants who had been exposed to metformin and 1,269,644 participants who had not. They divided the metformin group into two cohorts: patients without an AMD diagnosis and those with early or intermediate AMD to evaluate any potential progression to geographic atrophy or wet AMD. They then calculated risk ratios (RRs) to compare outcomes at 5 and 10 years and any time after meeting the criteria for the development or progression of AMD.[1]

The team found that, after propensity score matching, patients who were prescribed metformin had a comparable risk of developing AMD compared with patients who were not prescribed metformin (RR: 0.90); the risk remained similar at 5 years (RR: 0.94) and 10 years (RR: 0.91). In addition, the risk of AMD progression was comparable between those who had and had not been prescribed metformin over 5 and 10 years: the RR was 0.87 for geographic atrophy and 1.03 for wet AMD.[1]

The team concluded that, based on their data, metformin is not associated with significant development or progression of AMD. They note that further research is necessary to evaluate the effect of dosage and longevity of metformin use on the development and/or progression of AMD.[1]

1. Jindal DA, Hanna J, Shaia JK, et al. Metformin and the development of age-related macular degeneration [published online ahead of print September 18, 2025]. *JAMA Ophthalmol.*
2. Blitzer AL, Ham SA, Colby KA, Skondra D. Association of metformin use with age-related macular degeneration: a case-control study. *JAMA Ophthalmol.* 2021;139(3):302-309.
3. Aggarwal S, Moir J, Hyman MJ, Kaufmann GT, Flores A, Hariprasad SM, Skondra D. Metformin use and age-related macular degeneration in patients without diabetes. *JAMA Ophthalmol.* 2024;142(1):53-57.
4. Huh MD, Le SN, O'Brien KS, Keenan JD, Stewart JM. Potential efficacy of metformin for age-related macular degeneration: a systematic review and meta-analysis. *Ophthalmol Sci.* 2025;5(4):100741.
5. Shen LL, Keenan JD, Chahal N, et al. Metformin for the minimization of geographic atrophy progression (METforMIN): a randomized trial. *Ophthalmol Sci.* 2023;4(3):100440.

4DMT

At the **4FRONT** of wet AMD

4D Molecular Therapeutics (4DMT) is a late-stage biotechnology company focused on unlocking the full potential of genetic medicines. We're advancing durable and disease-targeted therapeutics to transform treatment paradigms.

Our lead retina program, **4D-150**, is a potential backbone therapy designed to provide multi-year sustained delivery of anti-VEGF (aflibercept and anti-VEGF-C) targeted to the retina with a single intravitreal injection. **4D-150** utilizes our retinotropic intravitreal vector, **R100**, which is designed for routine low dose intravitreal delivery to all layers and regions of the retina.

4D-150 is currently being studied in the global **4FRONT** Phase 3 program for the treatment of wet age-related macular degeneration.

Learn more at www.4DMT.com

Eyewire+ Pharma Update

- **AAVantgarde Bio** announced that the phase 1/2 LUCE-1 trial of AAVB-081, a gene therapy for Usher syndrome type 1B-associated retinitis pigmentosa, showed good safety and tolerability and signs of clinical benefit after more than 180 days of follow-up.
- **Ashvattha Therapeutics** reported 40-week results from a phase 2 trial of migaldendranib, its investigational anti-VEGF candidate for the treatment of diabetic macular edema, showing reduced treatment burden, a 6.1-letter gain in BCVA, and a reduction of 23.3 µm in central subfield thickness.
- **Inflammasome Therapeutics** announced early results from a first-in-human trial showing that K8, its lead ophthalmic candidate for inflammasome inhibition delivered via a sustained-release intraocular implant, reduced geographic atrophy lesion area growth by an average of 53% after 3 months of treatment compared with a control group (P = .03).
- **Kalaris Therapeutics** initiated patient enrollment of a phase 1b/2 multiple ascending dose trial of TH103, its investigational anti-VEGF therapy for wet AMD. Participants will receive four monthly doses of the investigational drug, followed by an extension phase.
- **Valitor** announced that VLTR-559, its long-acting anti-VEGF biologic in development for the treatment of wet AMD, showed positive preclinical safety and tolerability data and early signs of drug durability in a non-human primate toxicology study.
- **Klinge Biopharma,** the global commercialization rights holder for Formycon's FYB203 (an aflibercept biosimilar), has entered into a semi-exclusive license agreement with Horus Pharma. Klinge partnered with Teva Pharmaceuticals in January to commercialize FYB203 under the brand name Ahzantive across most of Europe and Israel. With this two-brand strategy, Teva and Horus can market the same biosimilar under different labels, Ahzantive and Baiama.
- **Roche** recently received the European Union's (EU) CE mark for its port delivery platform containing Susvimo, branded as Contivue in the EU. Susvimo (ranibizumab injection) 100 mg/mL is under review by the European Medicines Agency for the treatment of wet AMD.
- **Oculis** presented positive phase 2 data from its ACUITY trial investigating privosegtor (OCS-05) for the treatment of acute optic neuritis. The topline results showed clinically meaningful improvements in vision with 18 letters at 3 months, as well as preservation of retinal structure and a favorable safety profile.
- **Vyome** announced encouraging preclinical results for VT-1908, a topical formulation of mycophenolate (an established systemic immunosuppressant) designed to treat uveitis. Twice-daily eye drops led to significantly reduced uveitis scores and matched the efficacy of a clinically used steroid. The company is planning a phase 1/2 clinical trial.

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

NEW DATA ON ALCON'S UNITY VITREORETINAL CATARACT SYSTEM

Alcon recently announced the results from two multicenter studies demonstrating workflow efficiencies with the new Unity Vitreoretinal Cataract System (VCS) compared with the Constellation Vision System and the Centurion Vision System.[1]

In one prospective multicenter study, researchers compared the Unity VCS (n = 92) with the Constellation Vision System (n = 87) for 25-gauge vitrectomy. The team found an increase of 16% in overall workflow efficiency with the Unity VCS, as well as a 33% faster console setup and 38% faster teardown with the Unity VCS compared with the Constellation system.[1]

A second observational multicenter analysis evaluated cataract surgery turnover (n = 303) with the Unity VCS compared with the Centurion Vision System (n = 161). This study found a 6% reduction in cataract surgery turnover time, a 35% reduction in total energy into the eye, and an 8% decrease in ultrasound time with the Unity VCS compared with the Centurion system.[1]

1. Alcon presents new data showing OR efficiency with Unity Vitreoretinal Cataract System [press release]. Eyewire+. September 16, 2025. Accessed September 17, 2025. eyewire.news/news/alcon-presents-new-data-showing-or-efficiency-with-unity-vitreoretinal-cataract-system

NICE APPROVES TREATMENT FOR LEBER HEREDITARY OPTIC NEUROPATHY

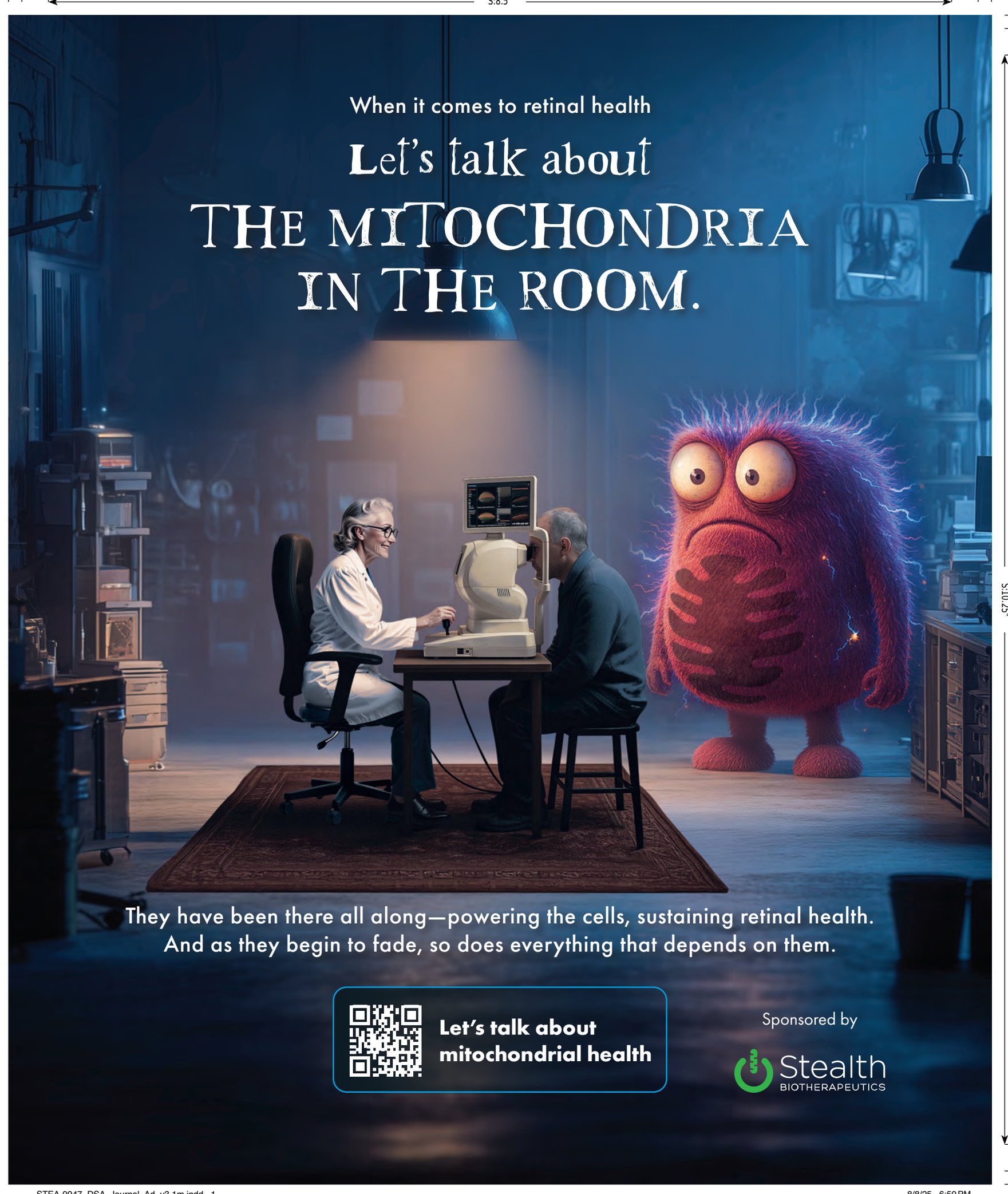
The UK-based National Institute for Health and Care Excellence (NICE) recently approved idebenone (Raxone, Chiesi Pharmaceuticals) for the treatment of Leber hereditary optic neuropathy (LHON) in patients 12 years of age and older. This is NICE's first endorsement of a therapy for any mitochondrial condition.[1]

LHON, a rare mitochondrial disorder that causes rapid, painless central vision loss and affects the optic nerve cells, is one of the most common mitochondrial diseases and often progresses to legal blindness within weeks.[1]

Idebenone is an oral antioxidant therapy taken three times a day. By supporting mitochondrial function, it is designed to boost cellular energy production in the optic nerve, helping to reduce damage and preserve vision.[1]

Already available in Wales and Scotland, idebenone was approved by NICE based on clinical studies led by NIHR Moorfields Biomedical Research Centre and long-term genetic research funded in part by Moorfields Eye Charity.[1]

1. NICE approves first NHS treatment for Leber hereditary optic neuropathy (LHON). September 11, 2025. Accessed September 17, 2025. eyewire.news/news/nice-approves-first-nhs-treatment-for-leber-hereditary-optic-neuropathy-lhon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BIOTHERAPEUTICS

OPTOS INVESTS IN AI TO ESTIMATE AGE BASED ON OCULAR IMAGING

Optos recently entered into an agreement with Toku to integrate the company's BioAge solution into Optos Daytona, Monaco, Monaco Pro, and California devices, without having to replace any existing hardware.[1]

BioAge uses AI to estimate a patient's biological age by analyzing the vascular and metabolic markers in the retina. Research suggests estimating age based on retinal scans has the potential to reveal a retinal age gap (the difference between the retinal age and biological age), highlighting accelerated aging, which correlates with mortality risk across several models.[2]

"We are delighted to offer our customers the ability to seamlessly integrate BioAge into their workflow," said Masayuki Numako, director and executive vice president, and head of the healthcare business division at Optos. "This collaboration allows eye care professionals to deliver greater value to their patients through a deeper understanding of overall wellness."[1]

The integrated BioAge solution debuted at Vision Expo West in Las Vegas, September 17 – 20.[1]

1. Optos and Toku partner to bring ai-powered "BioAge" to U.S. eye care practices [press release]. Eyewire+. September 17, 2025. Accessed September 19, 2025. eyewire.news/news/optos-and-toku-partner-to-bring-ai-powered-bioage-to-us-eye-care-practices
2. Grimbly MJ, Koopowitz SM, Chen R, Sun Z, Foster PJ, He M, Stein DJ, Ipser J, Zhu Z. Estimating biological age from retinal imaging: a scoping review. *BMJ Open Ophthalmol.* 2024 Aug 24;9(1):e001794.

FDA GRANTS FAST TRACK DESIGNATION TO AMD GENE THERAPY

The FDA has granted fast track designation to Sanofi's SAR402663, an investigational one-time intravitreal gene therapy for the treatment of wet AMD.[1]

SAR402663 is designed to deliver genetic material encoding soluble FLT01, a protein that inhibits VEGF. By targeting the underlying disease pathology, this gene therapy aims to prevent abnormal choroidal neovascularization, reduce vascular leakage and retinal damage, and decrease treatment burden by reducing the need for frequent intravitreal anti-VEGF injections.[1]

Sanofi is currently evaluating SAR402663 in a phase 1/2 clinical trial (NCT06660667) to assess safety, tolerability, and preliminary efficacy. The trial includes two parts, a dose-escalation study and a dose-expansion study, with a total enrollment of approximately 66 patients.[1]

1. FDA grants fast track designation to Sanofi's investigational gene therapy for wet AMD [press release]. Eyewire+. September 11, 2025. Accessed September 17, 2025. eyewire.news/news/fda-grants-fast-track-designation-to-sanofis-investigational-gene-therapy-for-wet-amd

TOPCON INVESTS IN SENSEYE MENTAL HEALTH DIAGNOSTIC PLATFORM

Topcon Healthcare announced an investment in Senseye, a company developing a mental health diagnostic platform that uses AI and computer vision to analyze pupil dynamics and eye movement captured with a smartphone camera. These ocular signals are translated into validated digital biomarkers to help support the diagnosis and monitoring of post-traumatic stress disorder, major depressive disorder, and generalized anxiety disorder.[1]

For eye care professionals, the technology opens the possibility of detecting neuropsychiatric risk factors during routine eye examinations and facilitating more timely referrals to primary care providers.[1]

The collaboration lays the foundation for embedding Senseye's technology into Harmony, Topcon's connected care platform. With this addition, Harmony may help clinicians achieve a more holistic view of each patient's physical and mental health status.[1]

1. Topcon Healthcare invests in Senseye to advance mental health diagnostics through the eye [press release]. Eyewire+. September 9, 2025. Accessed September 22, 2025. eyewire.news/news/topcon-healthcare-invests-in-senseye-to-advance-mental-health-diagnostics-through-the-eye

SUTURELESS IOL IMPLANTATION DEMONSTRATES GOOD VISUAL OUTCOMES

A prospective, multicenter study reported the 2-year outcomes of sutureless intrascleral fixation of a foldable single-piece IOL. This technique is specifically designed for eyes lacking adequate capsular support and demonstrated good visual, refractive, and anatomic results, as well as a low rate of complications.[1]

The study included 234 eyes of 232 patients who underwent secondary IOL implantation using a standardized sutureless intrascleral fixation technique. At 24 months, mean BCVA and spherical equivalent had improved, and a refractive prediction error within ±1.00 D was achieved in 77% of eyes.[1] Mean absolute surgically induced astigmatism remained stable, and IOL tilt and decentration showed no significant change over time; endothelial cell density was also unchanged. Visual decline occurred in 2.56% of eyes, and no cases of IOL dislocation or endophthalmitis were noted.[1]

The study authors concluded that for eyes without proper capsular support, sutureless intrascleral fixation of a foldable single-piece IOL may be a viable surgical approach for secondary implantation, leading to sustained visual and anatomic improvement with good tolerability.[1] ■

1. Marolo P, Parisi G, Conte F, et al. Two-year visual, refractive, and anatomical outcomes of sutureless intrascleral one-piece IOL fixation: a prospective study. [published online ahead of print September 19, 2025]. *Ophthalmol Retina.*

THE BUSINESS OF RETINA AT ARDS 2025

Two sessions covered efficiencies in clinical practice and how to avoid lawsuits.

BY DANIEL A. BALIKOV, MD, PHD

At the 53rd annual ARDS meeting, held March 1 – 5, 2025, John Kitchens, MD, delivered two lectures with broad applicability to the retina community (Figure). Here, I summarize his pearls for improving efficiencies in and out of the OR and how to avoid lawsuits.

EFFICIENCIES IN THE OR AND CLINIC

Dr. Kitchens' first lecture was a masterclass in building habits and systems that save time, reduce errors, and improve outcomes—all rooted in the idea that true efficiency is not about speed but intention, preparation, and precision.

One of the first practical tips he shared was his preference for a 26-gauge, 3/8-inch needle. Shorter and stiffer than other options, this tool offers better control for delicate procedures such as silicone oil infusion and subretinal fluid drainage. Dr. Kitchens also shared an innovative technique for cryodepression. Rather than first marking retinal breaks and then treating them, he uses the cryo-probe to identify and immediately treat the break. While the probe is still frozen to the eye, his assistant marks the spot, eliminating an entire step without sacrificing precision.

Biome buckling was another technique highlighted that provides a vitrectomy-like wide-angle view, which improves visualization, teaching, and safety. A surprisingly effective trick came not from a colleague but from an industry representative: When the biome lens fogs up mid-surgery, simply lift and swipe the lens with a gloved finger. It's a tiny move that helps maintain momentum during surgery.

When addressing macular holes, he uses what he calls the *soft tip pucker* technique. With high IOP and a soft tip cannula open to air, he gently nudges the edges of large or flat macular holes to break adhesions, enhancing the likelihood of closure.

On the postoperative side, Dr. Kitchens has simplified his regimen dramatically. For nearly all surgeries (with the exclusion of IOL-related procedures), he now prescribes only antibiotic ointment twice daily for a week. This

Image courtesy of Kevin Caldwell Photography

Figure. Dr. Kitchens had the ARDS audience scrambling to take note of his pearls that could help improve their OR and clinic efficiency.

streamlined protocol reduces patient burden and avoids high pharmacy costs. His institution's data, presented at ARVO 2024, confirmed there was no significant difference in outcomes using this approach.

Perhaps most intriguing was his integration of nutraceuticals into postoperative care. Inspired by Sharon Fekrat, MD, Dr. Kitchens began prescribing curcumin to patients with retinal detachments. The data suggest a reduced risk of proliferative vitreoretinopathy and epiretinal membrane formation,[1] all for roughly $100 per 6-month course.

Dr. Kitchens' talk then transitioned to the theme of simplification in clinical practice. He emphasized the

often-overlooked value of scribes. He praised his own scribe for anticipating needs, answering patient questions, and flagging clinical concerns before he even stepped into the room.

Dr. Kitchens next dove into AI, describing it as a versatile assistant that can summarize medical literature, draft patient handouts, and translate complex terms into plain language. He showed how ChatGPT Pro's "Deep Research" mode could simulate a digital research assistant, retrieving expert commentary and patient perspectives across the web.

Of the many anecdotes provided, one memorable example involved using ChatGPT to explain retinal detachment to a patient in Korean. In another instance, he had AI interpret a rare OCT finding from a smartphone photograph and deliver a spot-on diagnostic explanation.

AI's administrative potential was also on display, as Dr. Kitchens used it to craft polished and accurate emails to peers. He even fed a clinic schedule into ChatGPT and asked it to optimize flow for 80 patients in a half-day; he received a detailed, workable plan in return.

AVOIDING LAWSUITS: LESSONS FROM AN EXPERT WITNESS

During his second presentation, Dr. Kitchens cited statistics showing that between 75% and 99% of physicians will face a malpractice lawsuit, with about 7% sued annually.[2] The financial stakes are substantial: Average malpractice payouts range from $200,000 to $400,000, he said. Despite this, Dr. Kitchens reassured the audience that most malpractice cases never go to trial or are dismissed, and even when they do reach a jury verdict, physicians win approximately 95% of the time. This framed the talk's main objective: strategies to avoid getting sued altogether.

Dr. Kitchens identified common reasons why ophthalmologists get sued, including misdiagnosis, surgical and medication errors, failure to treat, lack of proper informed consent, and mismanagement of postoperative complications. Based on his experience as an expert witness, Dr. Kitchens noticed three recurring themes in lawsuits: the patient suffered a poor outcome, the patient had a strained relationship with the physician, and there was poor or absent documentation. He explained that if one of these elements is missing, the physician usually survives the lawsuit, but when all three are present, litigation is almost certain.

Next, Dr. Kitchens discussed the legal concept of *standard of care*, which refers to the quality of care expected from a competent practitioner under similar circumstances. Expert witnesses often argue whether a physician's actions met this standard. He recommended surgeons avoid performing surgeries that are not clearly indicated, as unnecessary or overly aggressive surgery increases risk.

He stressed that poor documentation is a major contributor to malpractice claims. The old adage, "If it's not documented, it wasn't done," remains true. Lack of detailed and accurate records increases the risk of successful lawsuits and larger payouts. Never alter the medical record after a lawsuit is filed, he said, noting that forensic methods can detect changes, and such actions can worsen the legal situation. Overall, he recommended documenting key clinical details clearly and warned against using ambiguous or nonstandard abbreviations that can confuse reviewers who are not specialists.

Informed consent is another major source of malpractice claims. Dr. Kitchens emphasized that patients rarely retain all information explained preoperatively, especially when anxious about vision loss. He advised simplifying the explanation, involving family members in the discussions, and ensuring all staff provide consistent messaging. Consent should cover diagnosis, treatment options, risks, benefits, and alternatives in a routine, repeatable format, tailored slightly for specific cases.

Dr. Kitchens recommended dictation to improve documentation. He himself dictates notes in front of patients and promptly sends copies to patients and referring doctors. He criticized the use of generic OR templates, which often fail to document unexpected complications or deviations, and stressed that every case deserves a unique, dictated operative note with justification for the procedure and explanation of options discussed.

Dr. Kitchens also addressed the crucial role of the doctor-patient relationship in malpractice risk. Research shows that busy surgeons with high surgical volumes and a history of lawsuits tend to get sued more, not necessarily because they perform more surgeries, but because they appear rushed or indifferent. Effective communication by physicians and their staff is vital. Patients may sue for perceived neglect or poor communication even if the clinical care was appropriate. He underscored the importance of humility and apology. Patients appreciate when doctors acknowledge poor outcomes and express regret sincerely.

SAVE THE DATE

The meeting was packed with other clinical pearls and top-notch panel discussions. Head to retinatoday.com to catch up on other meeting summaries, including: *ARDS 2025: Surgical Pearls* and *Top Panel Discussions at ARDS 2025*. And don't forget to register for the 54th annual ARDS meeting in Snowmass Village, set for February 28 – March 4, 2026! ■

1. Zheng Y, Valikodath N, Woodward R, Allen A, Grewal DS, Fekrat S. Oral curcumin to reduce risk of proliferative vitreoretinopathy following rhegmatogenous retinal detachment repair. Retina. 2024;44(10):1741-1747.
2. Jena AB, Seabury S, Lakdawalla D, Chandra A. Malpractice risk according to physician specialty. *N Engl J Med*. 2011;365(7):629-636.

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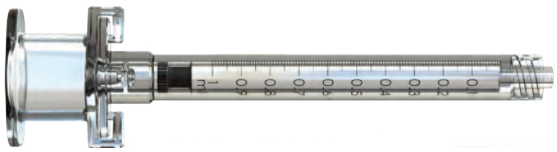

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DUKE fAVS/AVS COURSE

A PEEK AT THE 2025 DUKE FAVS AND AVS COURSES

This year's meetings hit it out of the park with top-notch sessions, a wet lab, and networking opportunities.

BY VENKATKRISH M. KASETTY, MD; YUXI ZHENG, MD; LINUS SHEN, MD; AND ANGELA LI, MD

The 23rd Duke Advanced Vitreous Surgery (AVS) Course, held May 16 – 17, 2025, included an excellent series of lectures and panel discussions from leaders in vitreoretinal surgery, medical retina, uveitis, inherited retinal disease, and ocular oncology. The 11th annual fellows AVS (fAVS) Course, which occurred the day prior, focused on critical tips for first-year vitreoretinal surgery fellows. Led by Course Director Lejla Vajzovic, MD, and Co-Diretors Dilraj Grewal, MD; Xi Chen, MD, PhD; and Durga S. Borkar, MD, MMCi, both courses boasted world-renowned faculty. Here, we share highlights from both events.

FELLOWS EDUCATION AND PARTICIPATION

The fAVS Course involved a day of curated lectures focused on fellow education and an exciting wet lab experience. The course also invited residents to attend following a rigorous selection process.

The day started with talks by Carl C. Awh, MD; Sharon Fekrat, MD; and Avni P. Finn, MD, MBA, on financial pearls for retina specialists and tips and tricks for new retina surgeons. Lizzy Rossin, MD, PhD, highlighted the importance of scleral buckling and then discussed how to choose the right patients for the procedure, the best buckling elements for certain cases, and the steps to the procedure itself.

Next, Nick Ulrich, MD, and Jason Fan, MD, PhD, discussed billing and retinal detachment (RD) repair costs, respectively, giving attendees a glimpse into the economics of practice.

The remaining lectures focused on a variety of topics ranging from biosimilars (by Stefanie G. Schuman, MD) and retinal vein occlusion (by Michael J. Allingham, MD, PhD) to inherited retinal disease (by Oleg Alekseev, MD, PhD), retinoblastoma (by Arpita S. Maniar, MBBS, MD), dry AMD (by Eleonora G. Lad, MD, PhD), and autoimmune retinopathy (by Ramiro S. Maldonado, MD).

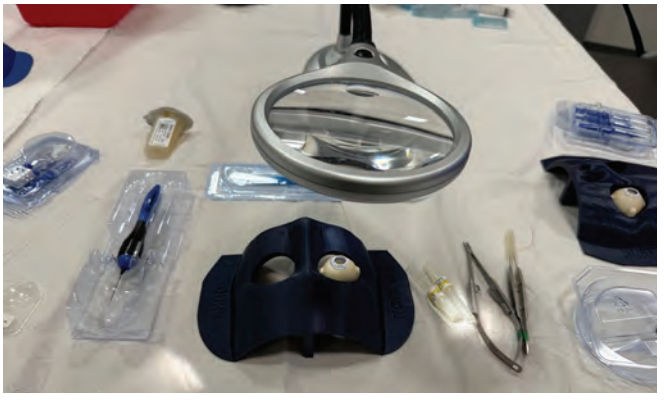

Figure. The scleral fixation wet lab station was a popular stop for attending retina fellows.

During the hands-on wet lab, attendees rotated through 14 stations to practice key aspects of retina surgery under the guidance of world-renowned mentors. The lab featured vitrectomy systems from Alcon (including the new Unity system), Bausch + Lomb, and DORC; it also featured the newly FDA-approved revakinagene taroretcel-lwey implant (Encelto, Neurotech Pharmaceuticals) for macular telangiectasia type 2. Other stations were dedicated to membrane peeling, subretinal delivery, RD repair, and scleral fixating IOLs (Figure). Dr. Fekrat and Jason Hsu, MD, led a station for virtual reality implant placement of the port delivery system (PDS; Susvimo, Genentech/Roche), while Cynthia A. Toth, MD, and Daniel S.W. Ting, MD, PhD, led a station demonstrating intraoperative OCT. Another station focused on 3D visualization systems and diagnostic vitrectomy.

The course concluded with "The Great Job Search Panel" moderated by Dr. Fekrat and Glenn J. Jaffe, MD. During this well-loved annual panel, faculty in different career stages and different practice settings shared their pearls for first-year fellows who are about to embark on their job search.

ATTENDING EDUCATION

The AVS Course started with talks focused on suprachoroidal buckling, timing and techniques for RD repair, proliferative vitreoretinopathy management, and laser light sources. The next scientific session highlighted new treatment paradigms with talks on the PDS, gene therapy, complement inhibition, Fas inhibition, and AI. A fellows' surgical video panel then featured five fellows from around the world highlighting their surgical talent, which left the audience in awe.

The afternoon boasted a macular surgery section, during which Dr. Awh shared ways to minimize peel-induced maculopathy, which may be associated with decreased retinal sensitivity. Javier Elizalde, MD, PhD, discussed traumatic macular holes and his preferred approach: vitrectomy and dye-assisted internal limiting membrane peeling. Dr. Finn presented several types of flaps, including inverted, temporal, hinged, cabbage leaf or star, and free flaps. Dr. Ulrich discussed techniques for complex macular holes, including plugging/scaffold techniques, autologous retinal transplant, and amniotic membrane grafts.

The second day of the AVS Course opened with talks on diabetic retinopathy (DR). Dr. Allingham presented emerging therapeutic approaches for DR, including anti-VEGF agents, the PDS, gene therapy, small molecules, receptor tyrosine kinase inhibitors, steroids, and oral drugs. He emphasized that diabetic eye disease stands to benefit from treatments targeting multiple mechanisms of action. Majda Hadziahmetovic, MD, then discussed the effect of glucagon-like peptide-1 receptor agonists on DR. Other talks by Sally Ong, MD, and Shohista Saidkasimova, FRCOPhth, focused on the surgical management of proliferative DR.

The next session touched on secondary IOLs, intraocular tumors, and uveitis. Dr. Elizalde shared his technique for transvitreal biopsy of choroidal tumors that are posterior to the equator. He uses 27-gauge vitrectomy, makes a focal retinotomy, obtains a sample with the mouth of the vitrector port while maintaining good hemostasis with IOP control, and then back-flushes the contents into a collection tube.

Gavin Tan, MD, PhD, then discussed his surgical technique for endoresection of choroidal melanoma, which can be an alternative to enucleation for tumors too large for plaque brachytherapy or as salvage therapy after brachytherapy. Miguel A. Materin, MD, explored the risk stratification in uveal melanoma with PRAM testing and possible new treatments. Dr. Grewal gave an overview of new uveitis therapeutics in the pipeline, including a systemic JAK1/TYK2 inhibitor brepocitinib (currently in phase 3), intravitreal IL-6 inhibitors, and a new topical therapy, dazdotuftide.

In the next session, Dr. Hsu discussed treatment options and outcomes for patients with submacular hemorrhages, followed by Andrea Govetto, MD, PhD, who discussed metamorphopsia in epiretinal membrane (ERM) and strategies to optimize surgical outcomes. William E. Smiddy, MD, then discussed how ERMs stabilize after formation and rarely require early removal. His conclusion: If visual acuity is good, observe; if it's poor, consider surgical intervention.

Dr. Tan then presented on myopic tractional maculopathy and macular holes. He emphasized that vitrectomy is considered in cases with outer foveal detachment, progressive schisis, or declining BCVA with anatomic changes. His surgical technique involves the use of brilliant blue dye and intraoperative OCT to guide membrane peeling.

The AVS Course finished with a pediatric retina session. Dr. Chen shared her tips and tricks for tackling the pediatric hyaloid, as it can be very adherent, and vitreoschisis is common. She also discussed how more than one surgery is needed to repair a pediatric RD and the importance of placing a scleral buckle in young patients, especially those without a posterior vitreous detachment.

Dr. Vajzovic highlighted the many manifestations of pediatric retinal diseases in adulthood, and she emphasized the importance of genetic testing for Stickler syndrome in any patient with a family history of RDs, considering that these patients can receive prophylactic laser.

Finally, Dr. Chen discussed how handheld OCT in preterm infants can guide our understanding and management of retinopathy of prematurity. In particular, OCT can highlight the presence of macular edema, whether an RD involves the fovea, and the difference between retinoschisis and RD.

Fellows and practicing retina specialists left the course invigorated and refreshed with new knowledge and techniques to bring back to their various institutions, with the overall goal of enhancing patient care. ■

SAVE THE DATE: MARCH 27 – 28, 2026
12th Annual Duke fAVS Course

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- Prolonged use of a topical ocular anesthetic may produce permanent corneal opacification and ulceration with accompanying visual loss.
- Do not touch the dropper tip to any surface as this may contaminate the gel.
- IHEEZO is indicated for administration under the direct supervision of a healthcare provider. IHEEZO is not intended for patient self-administration.
- The most common adverse reactions in studies following IHEEZO administration (incidence greater than or equal to 5%) were mydriasis, conjunctival hyperemia, and eye irritation.
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Please see the Full Prescribing Information for IHEEZO at www.iheezo.com/prescribinginformation.

REFERENCES: 1. Data on file. Harrow IP, LLC; 2023.
2. IHEEZO. Prescribing information. Harrow IP, LLC; 2022.

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6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

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

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

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

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

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

8.2 Lactation

Risk Summary

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

8.4 Pediatric Use

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

8.5 Geriatric Use

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

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

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

12.3 Pharmacokinetics

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

Elimination

Metabolism

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

Excretion

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

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

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

Mutagenesis

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

Impairment of Fertility

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

14 CLINICAL STUDIES

14.1 Study 1 and Study 2

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

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

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

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

Efficacy results of Study 1

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

Efficacy results of Study 2

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

14.2 Study 3

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

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

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

17 PATIENT COUNSELING INFORMATION

Eye Care Precaution

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

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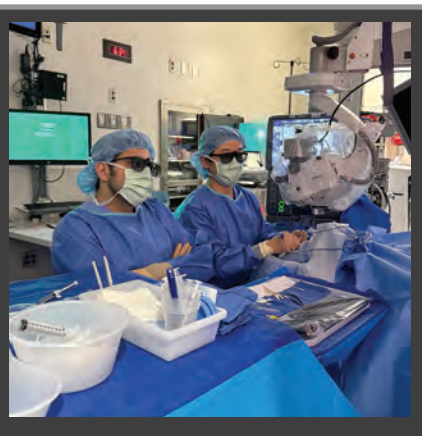
Henry Feng, MD



Dr. Feng's advice: Consider both professional and personal goals when deciding on your career path. Balancing these factors will hopefully lead to a happier and more sustainable professional career.

WHERE IT ALL BEGAN

I grew up in Southern New Jersey near Philadelphia. My mother was a software engineer, and my father has a PhD in food science; therefore, education was always a core value throughout my childhood. I attended the University of Chicago for my undergraduate degree in biochemistry, and then returned to New Jersey for medical school at Rutgers Robert Wood Johnson Medical School.

MY PATH TO RETINA

During my undergraduate studies, I was initially drawn to basic science and had been looking for a summer position as a biology lab assistant. However, I ended up applying to a work-study program in the medical retina clinic at the University of Chicago, which at the time was led by Michael A. Grassi, MD. This was my first true exposure to clinical practice, and, to my surprise, I was fascinated by the eye.

In particular, I was intrigued by how many systemic conditions manifested findings within the retina. It was exciting to witness how the synthesis of careful examination techniques and various retinal imaging modalities could reveal underlying vascular diseases, systemic infections, and even rare autoimmune conditions.

This early exposure to retina paved the way for my ongoing interest in ophthalmology during medical school and influenced my eventual decision to pursue a career in vitreoretinal surgery at Duke University.

SUPPORT ALONG THE WAY

I would consider all the retina faculty at the Duke Eye Center to be my mentors throughout ophthalmology residency and retina fellowship. In particular, Lejla Vajzovic, MD, and Sharon Fekrat, MD, have been truly instrumental in fostering my development as a clinician, surgeon, and scientist in retina.

AN EXPERIENCE TO REMEMBER

My most memorable moment occurred during fellowship while operating on an emergency patient overnight with an intraocular foreign body that was embedded in the retina after having penetrated the sclera and damaged the lens. Prior to retina fellowship, there was always a fear of encountering the vitreous during cataract surgery or other anterior segment procedures. That evening, however, I felt confident in my ability to operate on any part of the eye. Fortunately, the intraocular foreign body was embedded in the peripheral retina, and the the patient did well after surgery.

Even today, impactful experiences from my own fellowship continue to motivate me in training the next generation of vitreoretinal surgeons. ■

Henry Feng, MD, is a vitreoretinal surgeon at Illinois Retina Associates in and around Chicago and an assistant professor of Ophthalmology at Rush University Medical Center in Chicago. He can be reached at **fengretina@gmail.com.**

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AN OMD RETINA CASE

While subtle, certain signs and symptoms are characteristic of occult macular dystrophy.

BY MARIA LUDOVICA RUGGERI, MD, FEBO

In medicine, some conditions can be hard to detect. In the field of retina, some of the most challenging cases to diagnose are those with inherited retinal disease (IRD). These are chronic conditions that affect the retina and/or choroid and involve progressive retinal pigment epithelium (RPE) and photoreceptor loss.[1] While most IRDs are identifiable by characteristic fundus traits, further confirmed by structural and electrofunctional examination, others can be challenging to diagnose.

Here, I present the case of a patient diagnosed with occult macular dystrophy (OMD), a rare condition affecting the photoreceptors and causing loss of central vision.

THE CASE

A 32-year-old woman was referred to our genetics clinic for optic atrophy in each eye. She reported low visual acuity since childhood but overall stability for as long as she could remember. She noted that her mother suffers from progressive vision loss that started at 57 years of age and progressed to severe vision loss at 70 years of age and that her grandmother had mild vision loss associated with wet AMD and was treated with anti-VEGF injections.

Upon examination, the patient's BCVA was 20/50 OU. No abnormalities were noted during the anterior or posterior segment examination, except for the presence of trace temporal pallor in each eye.

Fundus autofluorescence, microperimetry, and OCT imaging were unremarkable. A more detailed examination revealed an indistinct ellipsoid zone (EZ; Figure 1). A full-field electroretinogram (ERG) was performed, and its findings were compatible with moderate, generalized cone dysfunction in each eye. A multifocal ERG showed bilateral foveal suppression (Figure 2).

Genetic testing revealed the presence of a heterozygous variant in the *RP1L1* gene, which is known to be associated with OMD.

DISCUSSION

First described in 1989, OMD is an inherited macular dystrophy characterized by central cone cell dysfunction

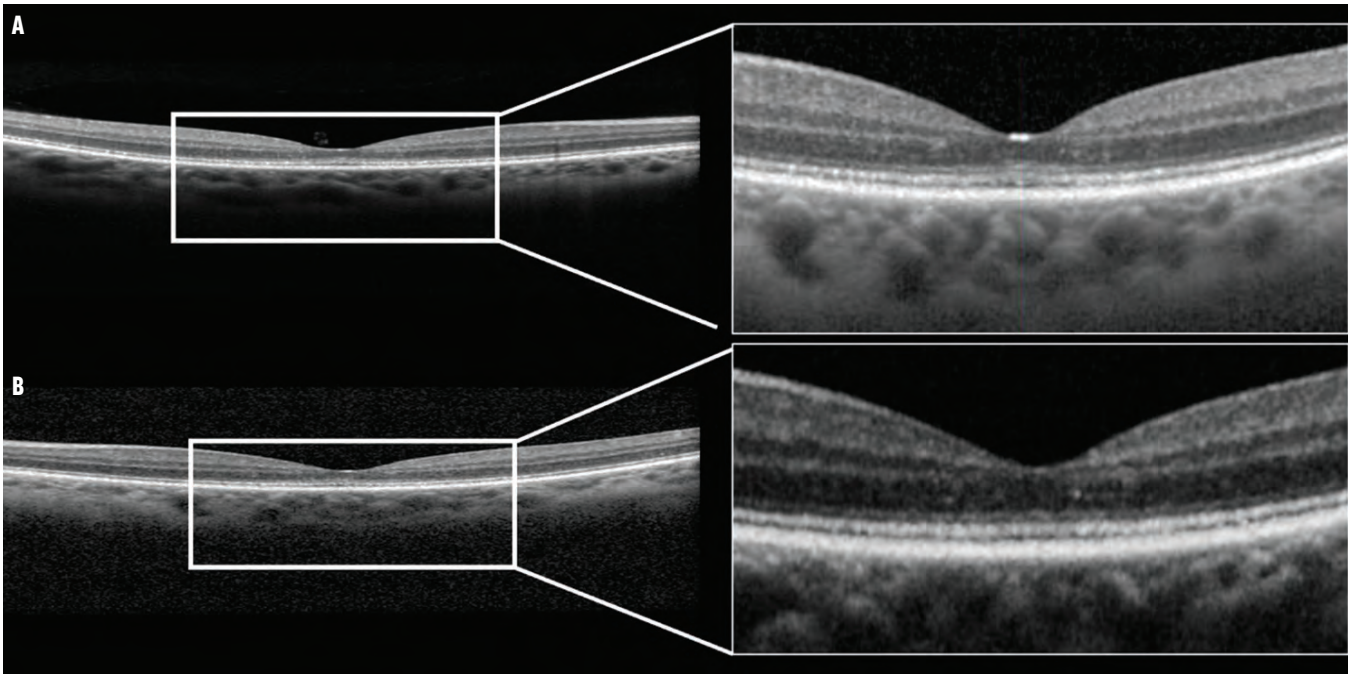

Figure 1. The OCT scans of the right (A) and left (B) eye show a disrupted EZ.

ALTHOUGH RARE, OMD CAN HAVE A SIGNIFICANT CLINICAL EFFECT. PATIENT SYMPTOMS OF PROGRESSIVE VISION LOSS DESPITE A NORMAL FUNDUS APPEARANCE SHOULD RAISE SUSPICION FOR OMD.

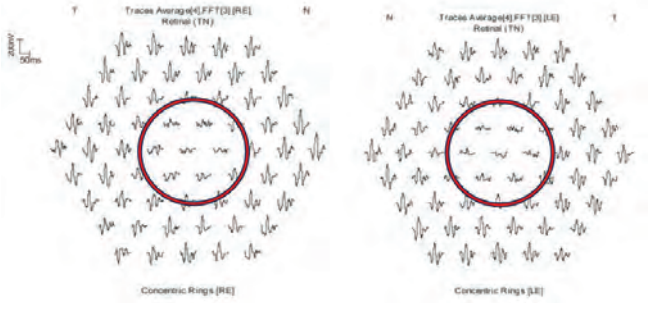

Figure 2. Multifocal ERG shows central foveal suppression in each eye (red circles).

resulting in loss of vision in the absence of striking abnormalities on fundus examination.[2,3] The disease is caused by a mutation in the *RP1L1* gene, whose expression is specific to the retina. Studies conducted on mice have shown *RP1L1* to be located in the outer segments and connecting cilia of the photoreceptor cells, affecting photosensitivity and outer segment morphogenesis of the rod photoreceptors.[4] Due to its rarity, its precise epidemiology is unknown.[5]

Patients often present with a gradual decrease in visual acuity, frequent photophobia, and light sensitivity.[6-8] Classic OMD is characterized by a blurred EZ and the absence of the interdigitation zone on OCT. Based on the severity of interdigitation zone and EZ involvement, the clinical presentation of OMD can be categorized into three stages, which appear to be related to the duration of disease onset.[6,9,10] In late stages, studies have reported thinning of the outer nuclear layer with preservation of the RPE.[11-13] Full-field ERG may show a reduced cone response (although variable), and multifocal ERG often shows a reduced response in the foveal area, playing a key role in OMD diagnosis.[6]

Interestingly, the use of adaptive optics in OMD patients was associated with an increase in cone spacing, resulting in a reduction in cone density.[14] This appears to be related to the cone deficits evidenced on full-field ERG.

Other studies have reported variability in the phenotypical spectrum of *RP1L1* deficiency.[10,15] Some research has shown that a single nucleotide polymorphism located on the *RP1L1* gene plays a protective role in diabetic retinopathy.[3] Further studies are required to better characterize the disease spectrum of OMD.

READ THE SIGNS

Although rare, OMD can have a significant clinical effect. Patient symptoms of progressive vision loss despite a normal fundus appearance should raise suspicion for OMD. Confirmation with genetic testing helps avoid an unnecessary and burdensome diagnostic workup for quicker, accurate diagnosis. ■

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- Financial disclosure: None

TREATING GEOGRAPHIC ATROPHY IN REAL-WORLD PRACTICE: A CASE EXAMPLE

One patient's experience with progressing GA demonstrates the role of complement inhibition therapy.

By Carl J. Danzig, MD, FASRS

Following patients in real-world clinical practice is markedly different than clinical trial settings. Aside from the fact that the absence of strict follow-up protocols inherently alters when and how often patients are seen in the clinic, other considerations, such as how far a patient lives from the office, tend to take on greater prominence. As well, other medical concerns may complicate the risk-benefit analysis of offering treatment. Below is an example case from my practice that demonstrates one patient's experience with geographic atrophy (GA), showing how real-world factors figure into the treatment algorithm.

Case Presentation

In April of 2022, a 71-year-old woman presented to my clinic with a history of GA OD. She was (and is) a current smoker who lives alone 4.5 hours away from my office. She reported that her daughter and granddaughter live closer to my office; nevertheless, the need to travel to my clinic would be a complicating factor. Relevant findings at the time of the exam were a history of fibrotic scar and neovascular AMD (nAMD) OS that has never been treated. The presenting BCVA was 20/40 OD and CF OS. Fundus autofluorescence (FAF) at the time of the exam showed multifocal lesions surrounding the fovea (Figure 1).

The patient was next seen in my office in October 2022, and she was examined a few times more before undergoing cataract surgery OU in July 2023. When she came to see me in August of 2023, FAF photos showed enlargement of the atrophic area (Figure 2) compared to April 2022. OCT captured during this visit demonstrated hypertransmission defects corresponding with the GA lesions (Figure 3). BCVA was 20/30 OD, CF OS. We discussed starting complement inhibition therapy at this visit, and we started treating her right eye with avacincaptad pegol (Izervay; Astellas) in November 2023.

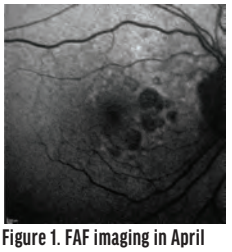

Figure 1. FAF imaging in April 2022 showed extrafoveal multifocal GA.

Figure 2. FAF in August of 2023 showed progression of the GA lesions compared to the initial visit in April 2022 (as seen in Figure 1).

During a January 2024 visit, after 2 monthly injections of avancincaptad pegol, the patient complained of worsening vision OD. On OCT, she was found to have new cystoid macular edema, subretinal fluid, and subretinal hyperreflective material (Figure 4). She was diagnosed with new onset wet AMD and was treated with bevacizumab (Avastin). BCVA at this visit was 20/40. She returned a month later for follow-up, at which time the anatomy had improved, but BCVA was still 20/40 (Figure 5). A second bevacizumab injection was administered.

Additional Follow-Up and Long-Term Prognosis

This patient was subsequently seen a month later; BCVA at that time was 20/40. At this point, treatment for the GA was redosed with avacincaptad pegol, as the wet AMD appeared to be stable. Currently, the patient is treated on alternating months with bevacizumab and avacincaptad pegol. BCVA at the latest follow-up had improved to 20/30. Because complement inhibition therapy is intended to slow down the rate of GA progression (rather than restore vision), the goal of treatment with this patient is to preserve the remaining vision for as long as possible. This case highlights managing both wet AMD and GA in a monocular patient, and fortunately, for this patient, she has had a result thus far. ■

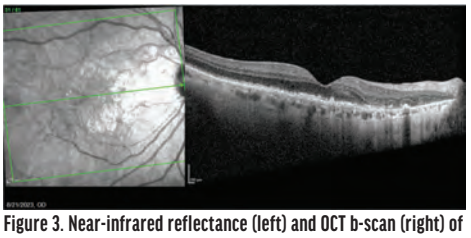

Figure 3. Near-infrared reflectance (left) and OCT b-scan (right) of the patient in August 2023.

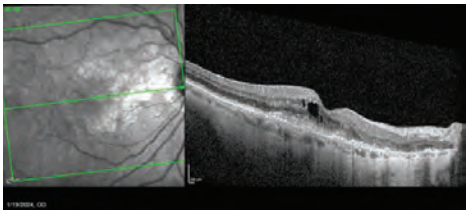

Figure 4. In January 2024, OCT (right) showed cystoid macular edema, subretinal fluid, and subretinal hyperreflective material consistent with wet AMD.

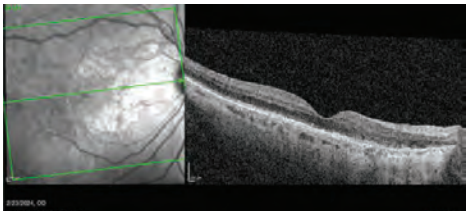

Figure 5. OCT of the patient in February 2024, 1 month after injection of an anti-VEGF agent to treat the wet AMD.

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- Financial disclosures: Consultant (4DMT, AbbVie, Adverum, Alimera, Eyebio, Eyepoint, Galimedix, Genentech, Inc., Iveric Bio/Astellas, Kodiak, Ocular Therapeutix, Oculis, Ocuphire, OcuCool, Regeneron, RegenxBio, Roche, Stealth); Grant support (4DMT, Adverum, Alexion, Astellas, Aviceda, Bayer, Cognition, Curacle, EyeBio, Eyepoint, Genentech, Inc., Gyroscope, Kodiak Sciences, Novartis, Ocular Therapeutix, Regeneron, RegenxBio, Rezolute, Roche, Unity); Speaker (Astellas and Genentech, Inc.)

RD REPAIR: SLOW AND STEADY WINS THE RACE

A look at the evidence supporting slow reattachment in retinal detachment repair.

By Stratos Gotzaridis, MD, FASRS, and Niki Zabogianni, MD


At the end of the 20th century, during the era of 20-gauge pars plana vitrectomy (PPV) and scleral buckling to repair retinal detachment (RD), the final success rate ranged from 70% to 85%.[1,2] Today, our surgical instruments—including gauge size, vitrectomy consoles, illumination systems, and visualization—have improved dramatically, and so have our single-surgery success rates, up to 95%.[3] Now that we can confidently achieve anatomic success, the next goal is improving patients' postoperative quality of vision. For example, we can now use OCT to identify complications such as cystoid macular edema (CME) and epiretinal membrane formation (ERM), both of which can compromise vision.

Regardless of the instruments we use, the principles for a successful operation remain the same: Act immediately, do as little harm as possible, properly evaluate the periphery, and treat with precision.

TREATMENT CONSIDERATIONS

We recommend draining through the existing break because it provides shorter operating time. We also avoid using diathermy, additional laser, and perfluorocarbon liquids (PFCL). Doing so provides better functional vision, reduces the risk of ERM formation or proliferative vitreoretinopathy, and lowers the cost.

In addition, surgeons can leave some subretinal fluid at the end of the operation. During scleral buckling surgery, we find the break, perform cryotherapy or laser retinopexy, and may or may not drain; sometimes, we allow the retinal pigment epithelium (RPE) pump to aspirate the fluid and flatten the retina naturally. Surgeons often feel the need to flatten the retina at the end of the operation to avoid creating retinal folds either outside of the macular area or, in rare cases, in the macula (Figures 1 and 2). However, during PPV to reattach the retina, we have found that if we do not force the retina flat at the end of the operation, we have fewer complications, such as residual PFCL bubbles under the retina, especially in the macula, which can be

AT A GLANCE

- To ensure a successful retinal detachment repair, act immediately, do as little harm as possible, properly evaluate the periphery, and treat with precision.
- Fundus autofluorescence can identify microscopic displacements of the retinal vessels after a successful retinal detachment repair operation.
- To avoid microscopic displacement of retinal vessels, leave some subretinal fluid to be aspirated naturally, allowing the retina to settle back to its original positioning.

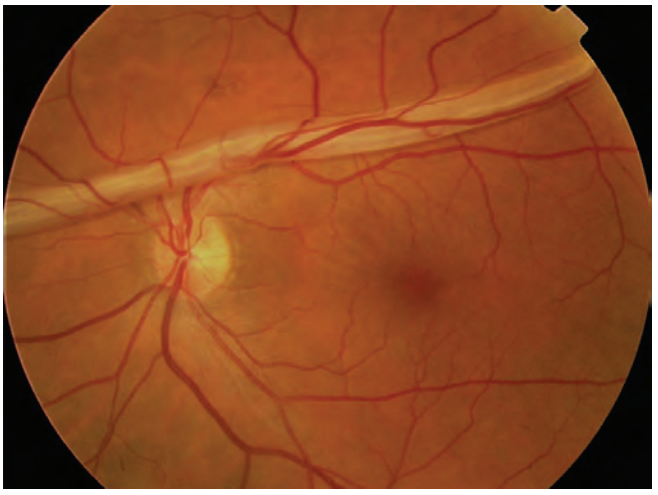

Figure 1. This fundus image shows a superior retinal fold after a successful RD surgery.

devastating. As another benefit, we have no additional inflammation from the diathermy and laser, which are applied to the drainage retinotomy.

OUR PREFERRED TECHNIQUE

The technique we are using in RD cases is 25-gauge PPV, after which we remove as much subretinal fluid as possible through the existing retinal break and apply laser or cryotherapy over the break. At the end, we inject 2.5 ml of pure SF_6, which becomes diluted to 50% due to preexisting air in the eye. The SF_6 bubble expands by 1.25 ml in 24 hours, effectively covering the space as the subretinal fluid is absorbed by the RPE pump or escapes into the vitreous cavity and, from there, the anterior chamber. Thus, in 24 hours, surgeons can expect a flat retina and a sufficient gas bubble volume that will fill the eye for the first 7 days. Postoperatively, we place the patient on the side of the break for up to 2 hours and then ask them to maintain face-down positioning for the following few days.

THE DATA

We have used this technique for more than 20 years and published the results in 2016.[4] At that time, we had two groups of patients treated with either 20- or 25-gauge PPV. Both groups had equally good anatomic and functional results. Unfortunately, the number of patients limited our ability to create a quality analysis to prove our hypothesis that this approach led to fewer postoperative complications.

In 2022, other researchers published a prospective study that included three groups of 100 patients each with macula-off RD.[5] In the first group of patients, the subretinal fluid was drained through the existing peripheral retinal break; in the second group, the retina was flattened with

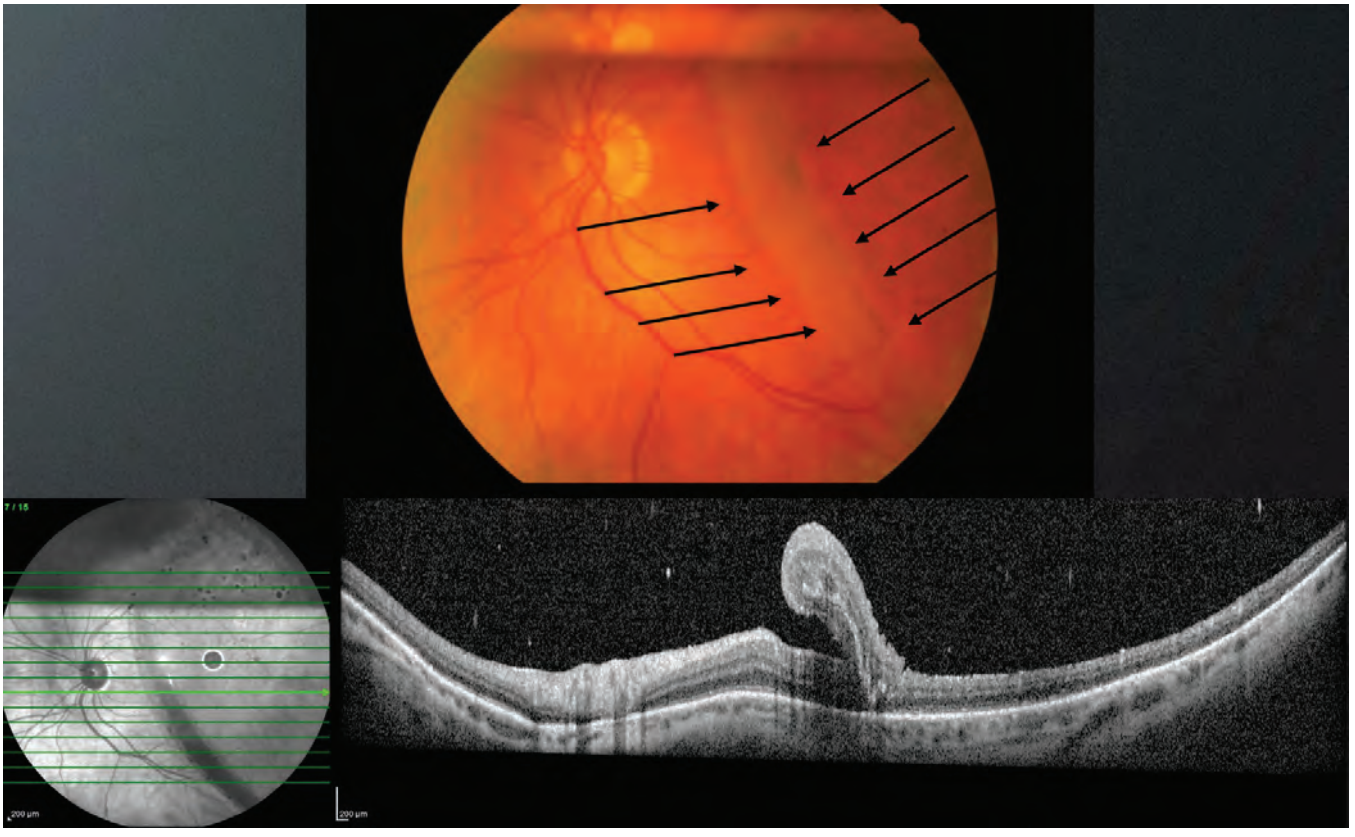

Figure 2. Fundus imaging captures a macular fold after RD repair (arrows), confirmed on OCT imaging.

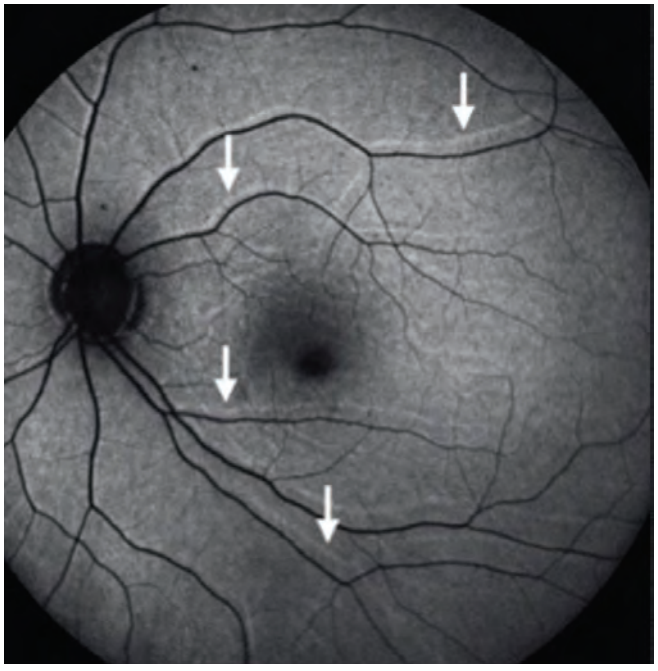

Figure 3. The hyperautofluorescent lines on FAF imaging (arrows) are thought to represent the original position of retinal vessels prior to the RD repair, referred to as *ghost vessels*.

the use of PFCL; and the third group underwent a drainage retinotomy. Visual acuity testing and spectral-domain OCT were performed 3, 6, and 12 months postoperatively. Primary outcomes of the study included visual acuity and the discontinuity of the external limiting membrane, ellipsoid zone interdigitation zone, and RPE at 1 year.

The researchers found that the visual acuity was better in the group who underwent fluid drainage through the existing retinal break compared with the PFCL group.[5] ERM formation was higher in the group who underwent a drainage retinotomy, and CME formation was higher in the group treated with PFCL, supporting the hypothesis that additional diathermy and laser application to the drainage retinotomy creates inflammatory factors that lead to ERM formation. In addition, the chemical component of the PFCL, although proven to be neutral, together with the turbulences of the fluid during the injection and aspiration, may promote inflammation that leads to CME formation.

These results suggest that draining the fluid through the existing break may reduce the risk of complications and provide better functional vision.

IMAGING PEARLS

Although OCT is useful for diagnosing and tracking CME and ERM formation in early stages, fundus autofluorescence (FAF) can be particularly helpful for identifying changes in the posterior pole after a successful RD repair surgery.

For example, FAF can identify microscopic displacements of the retinal vessels after a successful RD repair. The original position of the vessel before RD repair surgery appears as a hyperautofluorescent line and is known by several names in the literature, including *retinal vessel printing*,[6] *RPE vessel ghost lines*, or simply *ghost vessels* (Figure 3).

These ghost vessels may explain some of the complaints patients may have after a successful RD repair, such as distortion of image size (dysmetropsia), metamorphopsia, binocular diplopia, asthenopia, and anisoiconia.[6-11]

In extreme cases, we have known some affected patients to partially occlude the operated eye despite good postoperative acuity.

FOCUS ON THE VESSELS

Many studies have documented the existence of ghost vessels, surgical approaches to avoid them, and postoperative visual disturbances if they happen.[7-11] Most researchers have concluded that flattening the retina at the end of the operation produces microscopic displacement of the macular area. Thus, surgeons should instead leave some subretinal fluid to be aspirated by the RPE pump, allowing the retina to settle back to its original positioning. To help with this, surgeons can position the patient postoperatively either face down immediately or on the side of the break to help prevent microscopic displacement of the retinal vessels.[8-14] ■

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RISING STARS IN RETINA

Retina Today
YoungMD>Connect

Get to know outstanding retina fellows from the class of 2025.

Lucie Y. Guo, MD, PhD

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

More than a decade ago, when I was a medical student at the University of Pennsylvania, I spent a day shadowing Joshua L. Dunaief, MD, PhD, in his retina clinic where I was inspired by the life-changing effect of anti-VEGF injections and the strong longitudinal relationships he formed with his patients. I also shadowed Benjamin J. Kim, MD, in the OR and was astounded by the precision necessary for retina surgery and the ability to visualize a crucial part of the central nervous system. My residency at Stanford clinched my decision to pursue retina. I loved the intellectual rigor of being a diagnostician, and I realized that the dilated fundus examination is one of the most powerful examinations in medicine because the retina can harbor signs of many systemic diseases.

***RT:* Who do you look to as mentors in the field?**

I am thankful for mentors from my residency and fellowship at Stanford, particularly Prithvi Mruthyunjaya, MD, MHS, and Carolyn K. Pan, MD, who inspired and supported me from day one. I am indebted to our incredible teachers and surgical gurus at Stanford, including: Diana V. Do, MD; Steven Sanislo, MD; Charles DeBoer, MD, PhD; Loh-Shan Bryan Leung, MD; Theodore Leng, MD; Chase A. Ludwig, MD, MS; Ramsudha Narala, MD; Stephen Smith, MD; Ehsan Rahimy, MD; G. Atma Vemulakonda, MD; Karen M. Wai, MD; Quan Dong Nguyen, MD, MSc; Darius M. Moshfeghi, MD; Natalia F. Callaway, MD; Vinit B. Mahajan, MD, PhD; Edward H. Wood, MD; Ira H. Schachar, MD, MSc; and Mary Elizabeth Hartnett, MD. Their collective clinical acumen, surgical prowess, and compassion have shaped me into the physician I am today. I have also been mentored by senior residents and retina fellows who inspired me with their strong knowledge base and work ethic.

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

Dr. Mruthyunjaya and Sunil Srivastava, MD, created the Cole Eye Institute and Byers Eye Institute Surgical Retina Rounds for fellows to present surgical cases. During the 2024 AAO annual meeting in Chicago, I presented a difficult case of intraocular foreign body removal, ruptured globe repair, and retinal detachment repair complicated by subfoveal perfluoron. By sharing and discussing one of my most challenging surgical moments with a live audience, I experienced the camaderie of our retina community. It was a moment of reflection on my journey—how much I had grown, and become part of a community defined by mentorship, shared challenges, and a deep commitment to patient care.

***RT:* What are you hoping to accomplish once you are in practice?**

I hope to provide the same high-quality, compassionate patient care that I would want for my own family members. As an academic clinician-scientist, I plan to lead a laboratory to develop new disease insights and therapeutics to help fill the unmet needs in our field.

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

The training is intense, but rewarding. As your knowledge and experience grow, hold fast to your compassion, accessibility, and willingness to listen. Even in a fast-paced clinic, the rapport you build with your patients will make a lasting effect. Residents and fellows are not only learners but also vital members of the care team, adding value to every encounter. ■

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AN ATLAS OF ILM FLAPS

This illustrative guide can help you repair macular holes using different internal limiting membrane flap techniques.

By David L. Zhang, MD, and Avni P. Finn, MD, MBA


Macular hole (MH) surgery aims to release vitreoretinal tractional forces to close full-thickness defects of the foveal neurosensory retina. The conventional approach involves pars plana vitrectomy, lifting the hyaloid (if attached), internal limiting membrane (ILM) peeling, gas bubble placement, and postoperative head positioning.[1] This well-established method is highly effective in patients with small- to medium-sized MHs (usually less than 400 µm), but cases of large, chronic, or refractory MHs remain a surgical challenge.[2]

ILM flaps may be useful in cases of more challenging holes, such as those that are larger than 400 µm, chronic holes, holes in high myopes, or MHs that have failed traditional surgical techniques. ILM flaps—which involve ILM peeling followed by placement of the residual ILM over the MH to promote closure[3]—are hypothesized to act as a scaffold for migration and proliferation of Müller cells, which secrete neurotrophic and growth factors that enhance the survival of retinal neurons.[4] Since the first description of the inverted ILM flap in 2010,[3] a variety of techniques have been developed and have shown favorable outcomes in MH closure and postoperative vision, making them a promising alternative for larger, chronic, and myopic MH. Here, we review several commonly used ILM flap techniques.

INVERTED AND TEMPORAL INVERTED ILM FLAPS

First introduced by Michalewska et al,[3] the ILM flap is peeled in a circular fashion approximately 2 disc diameters around the MH but is left attached to the edges of the hole. After a segment of the peeled ILM is trimmed with vitreous cutters, the remaining central segment is gently massaged over the MH until the ILM is inverted to cover the hole.

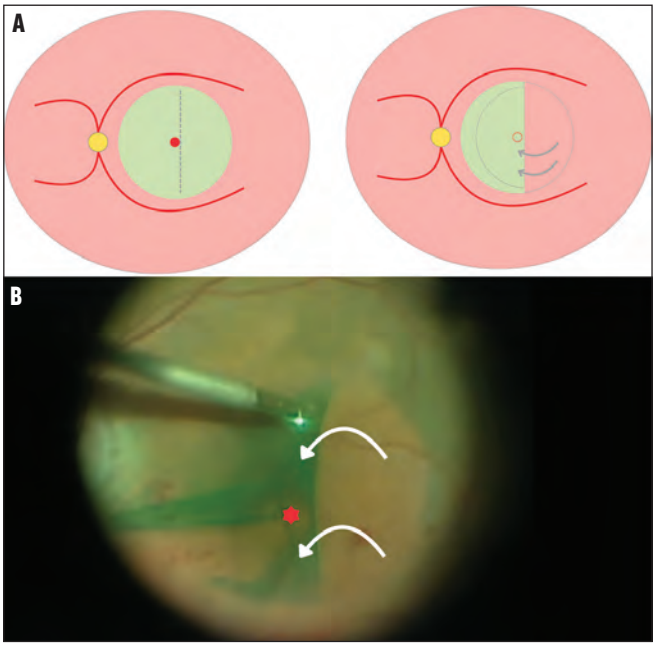
The temporal inverted flap variation is created using the same method, but the ILM temporal to the fovea is peeled nasally so that the flap covers the hole during fluid-air exchange (Figure 1).[5] This helps decrease the risk of dissociated optic nerve fiber layer.

RETRACTING DOOR AND HINGED FLAPS

The inverted ILM flap technique can be challenging in highly myopic eyes or those with posterior staphyloma because the flap is difficult to manipulate. Fluid-air exchange and fluid currents during surgery can also risk loss or displacement of the flap. The ILM retracting door technique

AT A GLANCE

- Internal limiting membrane (ILM) flaps may be useful in cases of macular holes that are larger than 400 µm, chronic, present in high myopes, or that have failed traditional surgical techniques.
- Several common ILM flap techniques include inverted and temporal inverted flaps, retracting door and hinged flaps, cabbage leaf or star flaps, and free flaps.
- ILM flaps have become a valuable option for primary repair, with a higher reported closure rate of 93% compared with 74% for ILM peeling alone.



Surgical image courtesy of Avni P. Finn, MD, MBA

Figure 1. The diagram depicts a temporal inverted ILM flap (A), while the surgical view (B) shows the stained ILM folded nasally (arrows) to cover the MH (asterisk).

was introduced as a technically easier procedure and allows for the confirmation of ILM placement over the MH.[6]

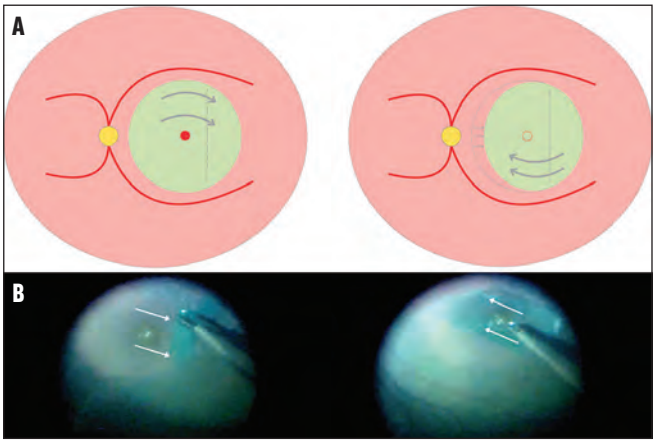
First, a Finesse Flex loop (Alcon) is used to create a large flap of ILM starting nasal to the MH. After the nasal edge is created, ILM forceps are used to peel the flap temporally over the fovea and temporal macula. The flap is then left attached temporally and draped back over the area of the hole. Thus, the previously taut ILM relaxes and retracts as it is draped back over the retina, allowing the nasal portion to cover the MH (Figure 2). Variations of the retracting door technique allow for hinging on various sides of the MH. For example, the ILM can be peeled to create a superior hinge to then drape back over the hole (Figure 3).

CABBAGE LEAF OR STAR FLAP

Instead of a circular ILM peel, the ILM can be peeled in separate areas to create three separate flaps with bases attached at the edge of the MH, creating a star-like shape.[7] The flaps are trimmed and inverted over the macular hole, one on top of the other similar to the layers of a cabbage (Figure 4). This technique allows the flaps to stay over the hole and prevent displacement during fluid-air exchange.

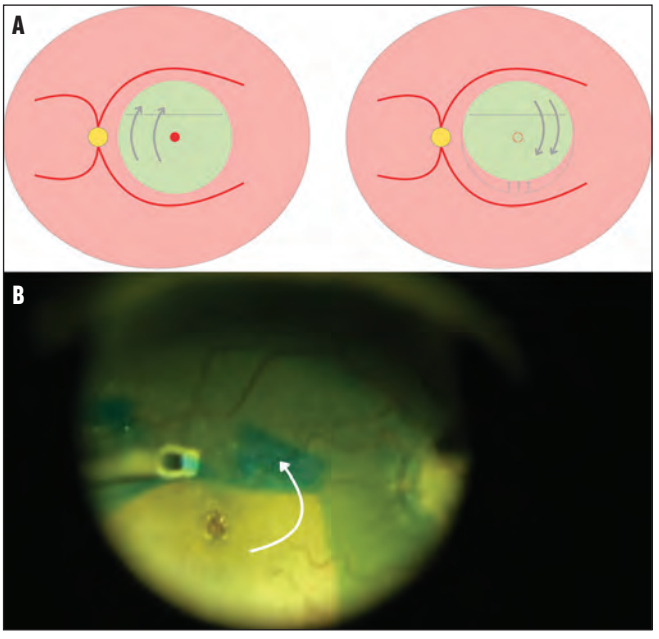
FREE FLAP

When a hinged flap is not possible due to a prior ILM peel, a free flap may be a useful option. In this technique, a small piece of the ILM is peeled to create a free flap with a diameter similar to the MH and then placed inside the hole (Figure 5).[8] Given the ILM's affinity for the retina, surgeons should drag the flap across the retinal surface with a loop to the hole. A low molecular weight viscoelastic placed over



Surgical image courtesy of Avni P. Finn, MD, MBA

Figure 2. The diagram shows a retracting door flap, hinged temporally, which is peeled and placed back down to retract over the hole (A). The surgical view demonstrates peeling of the ILM temporally (arrows) followed by replacement over the hole (B).



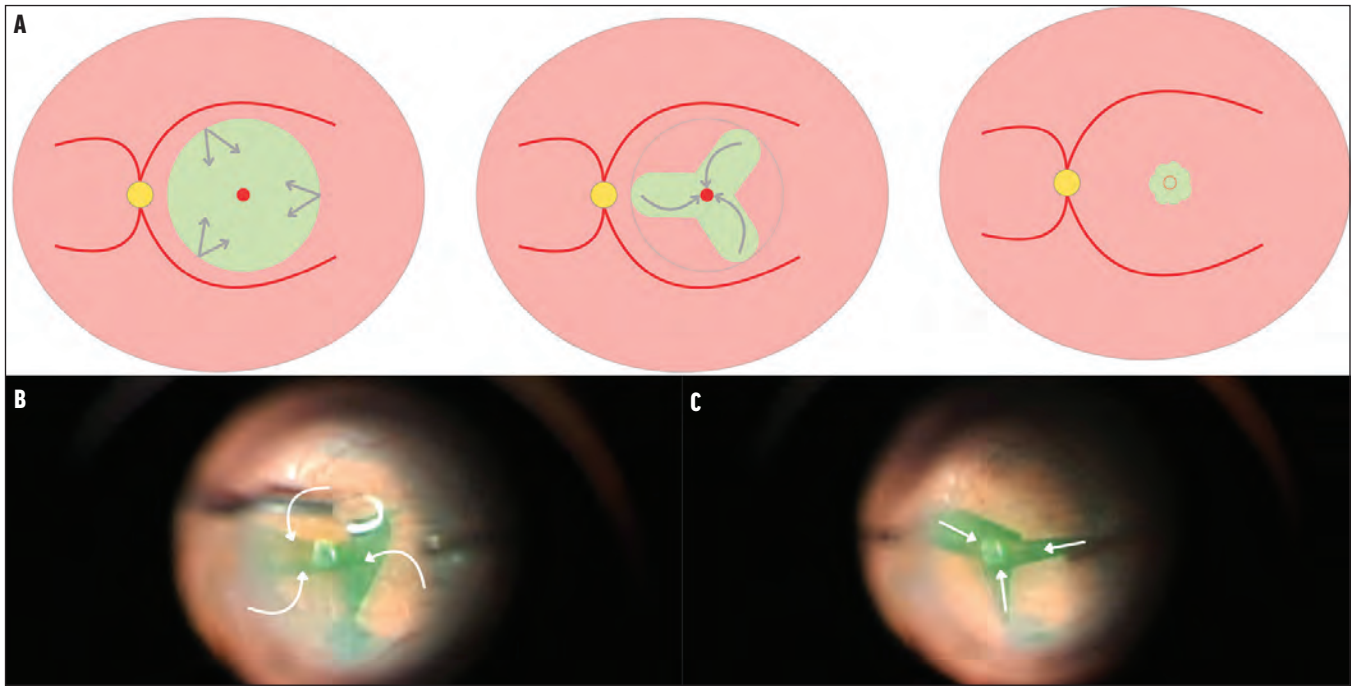
Surgical image courtesy of Prethy Rao, MD

Figure 3. The diagram shows a superiorly hinged retracting door flap (A). The surgical view demonstrates an ILM peel in the superior direction with a hinged fold (B, arrow).

the flap can stabilize it and avoid losing it in the eye. During fluid-air exchange, surgeons should dry slowly and keep the extrusion needle away from the macula. Challenges with the free flap include proper placement and frequent displacement during surgery or even postoperatively, although this may be ameliorated with perfluorocarbon liquids, viscoelastic plugs, or autologous serum as tissue adhesives.

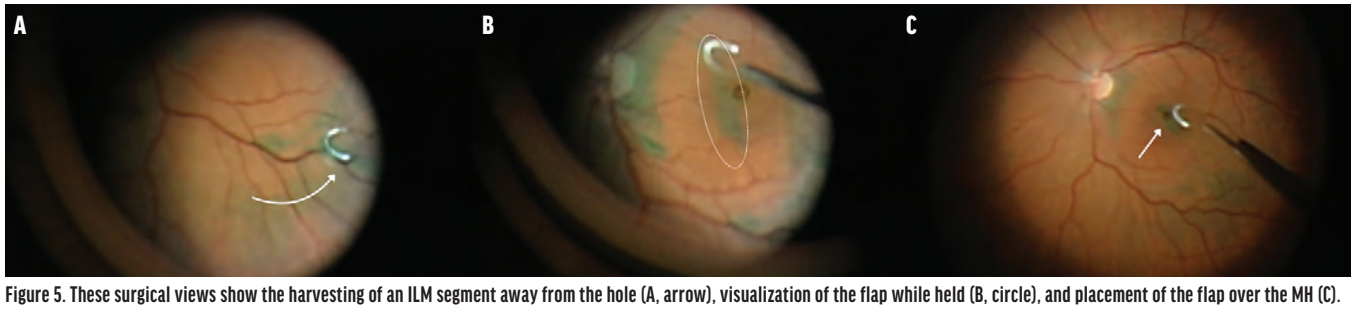
BOOST YOUR CLOSURE RATES

Although ILM flaps are often reserved for large, myopic, or refractory full-thickness MHs that have failed ILM peeling, a recent review found that they are a valuable option for primary repair, with a higher reported closure rate of approximately 93% compared with 74% for ILM peeling alone as



Surgical image courtesy of Avni P. Finn, MD, MBA

Figure 4. The diagram of a cabbage leaf/star flap shows that the peeling is initiated in multiple directions, followed by placement of each arm of the flap over the hole (A). The surgical view shows the ILM peel directions (B, arrows) followed by the star configuration prior to placing the flaps over the MH (C, arrows).



Surgical image courtesy of Avni P. Finn, MD, MBA

Figure 5. These surgical views show the harvesting of an ILM segment away from the hole (A, arrow), visualization of the flap while held (B, circle), and placement of the flap over the MH (C).

well as better postoperative visual acuity at 3 to 6 months.[4] The researchers found that the odds of closure are particularly high for holes greater than 500 µm, although the benefit likely applies over a broad range of MH sizes. The same review also showed no significant differences between ILM flap techniques, suggesting general use of a flap in these cases is the key to maximizing the chances of a good outcome.[4]

No ILM peel is the same, and it is critical to adapt the flap to the circumstances of each individual case. Ensuring a thorough vitrectomy and posterior vitreous detachment is essential for a successful surgery, as is the use of dyes to help visualize the ILM. A familiarity with these techniques allows surgeons the necessary flexibility in their flap approaches to maximize anatomic and functional outcomes for each patient. ■

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TAMING THE BEAST: SURGICAL TACTICS FOR PVR

Careful preoperative planning and a low threshold for adding a buckle can optimize outcomes.

By Sidra Zafar, MD, and Jason Hsu, MD


Proliferative vitreoretinopathy (PVR) is the leading cause of surgical failure following primary rhegmatogenous retinal detachment (RRD) repair with a reported incidence of 5% to 10%.[1] PVR can be characterized as an exaggerated and maladaptive wound healing process of the retina defined by cellular proliferation, membrane formation, and intraretinal fibrosis, resulting in contraction and foreshortening of the retina and, eventually, recurrent RRD.[2]

PREOPERATIVE PLANNING FOR HIGH-RISK RRD

Preoperatively, it is important to identify primary RRDs with high-risk features for developing PVR, as the surgical method of repair may influence outcomes, including single surgery anatomic success (SSAS). High-risk features that have been identified include preoperative PVR grade A or B (Figure 1), vitreous hemorrhage, more extensive RRDs (ie, involving at least 50% of the retinal area), multiple breaks (ie, presence of three or more retinal breaks), choroidal detachment, prior cryotherapy, and/or more chronic RRD (ie, duration of more than 2 weeks).[3]

Salabati et al evaluated 389 eyes with high-risk RRDs at their institution and found a much lower SSAS rate in these eyes at 71.5%.[4] However, eyes that underwent pars plana vitrectomy (PPV) combined with scleral buckle (SB) in their study had a significantly higher SSAS rate compared with eyes that underwent PPV alone (80.8% vs 67%, respectively).[4] This effect was driven primarily by patients younger than 65 years of age, where SSAS was 85.6% in the PPV/SB group versus 67.9% in the PPV group ($P = .003$). In patients 65 years of age or older, there was no significant difference in SSAS for PPV/SB and PPV (68.6% vs 66.1%, $P = .99$). Storey et al similarly found a higher surgical success rate in the PPV/SB cohort versus PPV alone among 65 eyes with high-risk features (75% vs 48.3%, respectively).[5]

AT A GLANCE

- In eyes with rhegmatogenous retinal detachment (RRD) that are high-risk for the development of proliferative vitreoretinopathy (PVR), strongly consider adding a scleral buckle, particularly among patients younger than 65 years of age.
- Early surgical intervention for repairing PVR RRDs can optimize visual outcomes.
- Lens removal may not be necessary in all PVR RRDs, especially in cases with an adequate view.

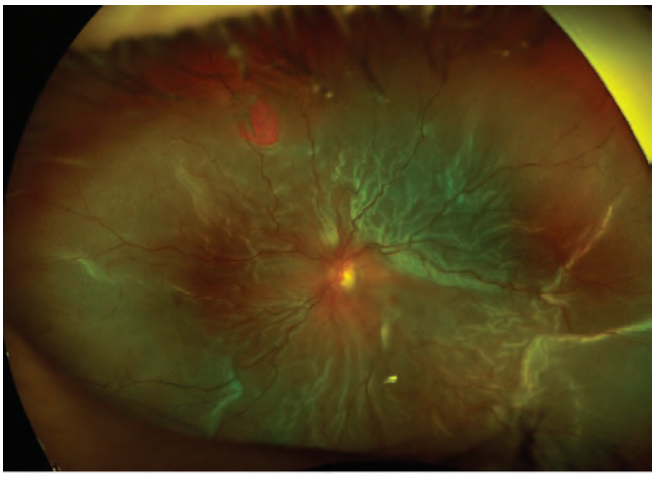

Figure 1. This phakic patient with an RRD and high-risk features would benefit from the addition of an SB.

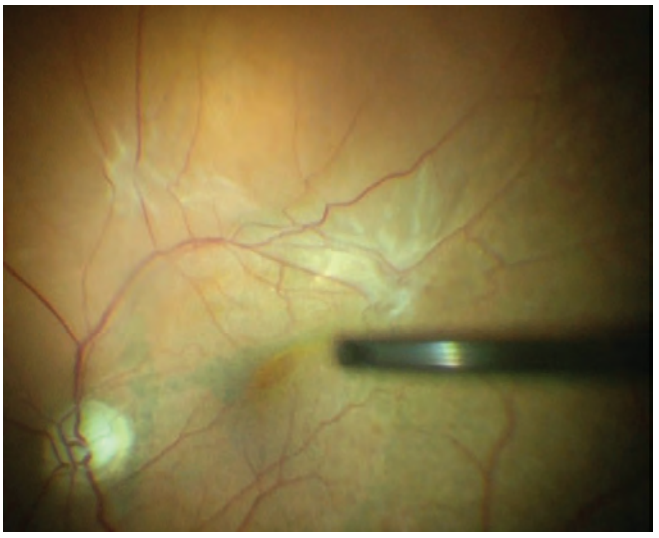

Figure 2. During surgery for a PVR RRD, surgeons can use ICG to stain the ILM and posterior PVR membranes.

SURGICAL TIMING

Eyes with PVR RDs are often treated differently compared with eyes with primary RRDs. Traditionally, there is less urgency to repair PVR RDs due to the perceived notion that the visual outcomes will be poor regardless, particularly in macula-off detachments. In fact, one school of thought suggests that it may be better to wait for further maturation of the membranes to help make membrane peeling easier and potentially lower the chance of future redetachments. There may also be less inflammation present if surgery is delayed, again lowering the risk of PVR recurrence.

However, in a retrospective study of 5,355 eyes with primary RRD, of which 345 developed PVR, time to surgery from the diagnosis of a recurrent RRD was the only modifiable factor that was associated with good visual acuity in eyes that had PVR RDs and underwent retinectomies.[6] This was independent of whether the macula was on or off. There were significantly fewer days between recurrent RD diagnosis and time to repair in eyes achieving good VA (mean Snellen equivalent 20/42) compared with eyes with worse VA (mean Snellen equivalent 20/693), regardless of macula status (mean 2.9 days vs mean 5.8 days).[6]

APPROACHING PVR DETACHMENTS INTRAOPERATIVELY

The initial step when managing PVR detachments is determining whether to proceed with PPV alone or in combination with an SB. Placing an SB helps relieve anteroposterior and circumferential traction. Therefore, in most cases, an SB should be strongly considered, except in situations where a 360° retinectomy may be needed (eg, to repair a funnel-shaped RD with a pronounced anterior loop). Even if a 180° retinectomy is done, the SB still supports the remaining vitreous base and the anterior edges of the retinectomy.

The main goal of surgery in PVR cases is to reattach the retina and release all traction, both from the preretinal membranes and subretinal fibrosis. Triamcinolone can be helpful to ensure the hyaloid is up and highlight both posterior and more peripheral membranes for peeling.

During the surgery, look for star folds. Pinching with forceps while aiming for the center of the fold can often help initiate the peel because there is often a fibrous band. Alternatively, a Finesse Flex Loop (Alcon) can be used to gently massage the surface of the retina and identify additional membranes or edges from which to initiate a peel. Surgeons should consider using a chandelier light with dual Flex Loops, particularly in areas of contraction, to help identify preretinal membranes. The membranes can be very adherent in certain cases, making it difficult to peel, especially if the underlying retina is bullously detached. A lighted pick and forceps may be useful in this situation.

ICG or brilliant blue can also be used to stain the internal limiting membrane (ILM) and reveal negative staining of posterior membranes (Figure 2). In a recent multicenter international study of 370 eyes with grade C PVR, ILM peeling, and extended ILM peeling in particular, was associated with higher SSAS at 3 months (86.6% vs 73.2%, respectively) and 6 months (75.2% vs 65.3%, respectively) and significantly better visual acuity compared with eyes that did not undergo ILM peeling.[7]

All membranes should be peeled, if possible, prior to considering a retinectomy. If a retinectomy cannot be avoided, the more posterior membranes that have been removed the better so that the retinectomy can remain as anterior as possible while removing the intrinsic fibrosis (Figure 3). Diathermy should be used to demarcate the area of planned retinectomy. Careful diathermy during the retinectomy is important to achieve good hemostasis, as hemorrhage is a risk factor for PVR proliferation. A small initial PFO bubble can be used to stabilize the retina and protect the macula from any inadvertent subretinal hemorrhage prior

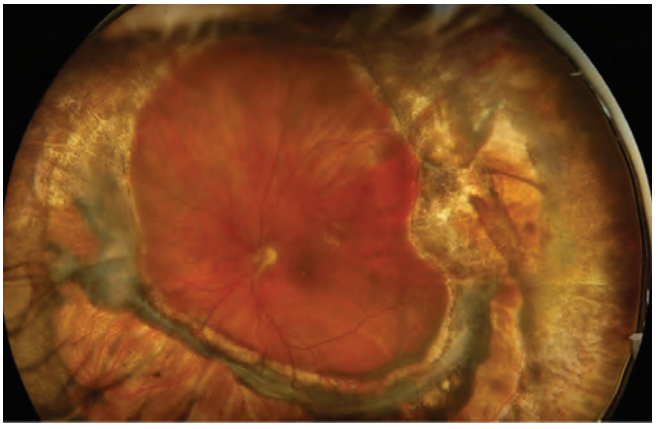

Figure 3. This ultra-widefield fundus photograph depicts the eye of a patient who underwent 360° retinectomy for RD repair.

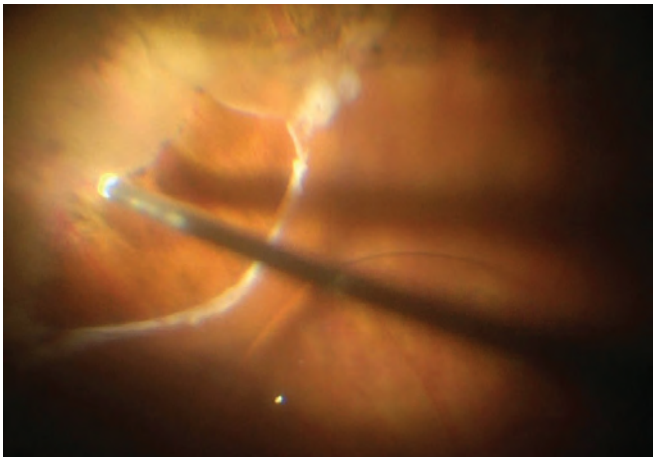

Figure 4. Before performing a retinectomy in eyes with PVR RRD, surgeons can instill a small PFO bubble to protect the macula.

PVR DETACHMENTS ARE COMPLEX, AND THEIR MANAGEMENT BEGINS EVEN BEFORE THE PATIENT ENTERS THE OR.

to initiating the retinectomy (Figure 4). Surgeons should make sure this initial bubble is small enough such that tilting the eye during the retinectomy does not lead to small PFO bubbles going into the subretinal space.

LENSECTOMY OR NOT

For phakic eyes with PVR, surgery can be performed with or without lens removal. Lensectomy has the advantage of improved visualization during surgery, and it also allows for a closer vitreous base shave. Alternatively, lens removal increases surgery duration, can be proinflammatory, and may be associated with a greater incidence of postoperative complications such as cystoid macular edema and corneal edema. A retrospective study by Mahmoudzedah et al evaluated outcomes of vitrectomy with retinectomy without lensectomy for grade C PVR RRDs in phakic eyes.[8] In their study, visual and anatomic outcomes were similar to prior studies where lensectomies had been performed.[8]

However, if a lensectomy is needed, it is essential to remove the entire capsule, as preservation of the anterior capsule may provide a scaffold for PVR over the ciliary body, increasing the risk of hypotony and compromising clinical outcomes. However, it is unclear whether this is an issue if the posterior capsule is preserved as in a standard phacoemulsification procedure with IOL implantation.

PLAN CAREFULLY

PVR detachments are complex, and their management begins even before the patient enters the OR. Take time to evaluate if the patient is at elevated risk for PVR and could benefit from SB placement unless there are plans for a retinectomy. Incorporate surgical adjuncts such as triamcinolone and dyes to improve intraoperative visualization and facilitate a smoother procedure. Find instruments that give you the most flexibility. Hemostasis is key to mitigate further PVR risk. Unless the cataract substantially limits intraoperative visualization, remember that a lensectomy may not be required in all PVR cases. ■

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THE VALUE OF INTRAOPERATIVE OCT: AN ILLUSTRATIVE GUIDE

Expanding the frontiers of adult and pediatric retinal surgery through imaging.

By Daniel A. Balikov, MD, PhD, and Audina M. Berrocal, MD


OCT is a well-established imaging modality to diagnose and monitor treatment of retinal diseases in the clinic. However, its utility in the OR is less established, as clinicians struggle to integrate the tool into their surgical workflows and OR technology platforms.

At Bascom Palmer Eye Institute, we have successfully integrated intraoperative OCT (iOCT) and find it useful in many cases. For imaging under anesthesia, we placed a Heidelberg Spectralis system on a multi-axis mounting arm and have found that this setup allows for maximum flexibility to patient anatomy during examination under anesthesia when clinical imaging can't be obtained during routine visits due to age, ability to cooperate with the imaging specialist, and potential need for anesthesia. For iOCT, the Rescan system (Carl Zeiss Meditec) provides good quality imaging to evaluate and monitor pathology in real time during surgery, which can be particularly helpful with surgical management decisions. Here, we highlight a few examples of these advantages.

MEMBRANE PEELING IN ADULTS WITH AN IOL

Many adult patients opt for multifocal IOLs at the time of their cataract surgery. While these lenses can provide excellent vision, they make it difficult to visualize macular pathology, particularly for membrane peeling procedures. When a multifocal IOL is present, the surgeon must constantly shift focus to account for the different optical zones of the IOL. In our ORs, we use the Finesse Sharkskin forceps (Alcon) to maintain a firm grip on the membranes and minimize re-grabbing or slippage that may occur due to the shift in focal planes. However, the view through a

AT A GLANCE

- During membrane peeling surgery, surgeons can use real-time, high-resolution intraoperative OCT imaging to confirm that the membrane is completely peeled.
- Intraoperative OCT can reveal tractional hemorrhage caused by persistent hyaloid tension mimicking a central retinal vein occlusion.
- During pediatric lens cases, surgeons can use intraoperative OCT to ensure optimal vitrector positioning as the capsule collapses.

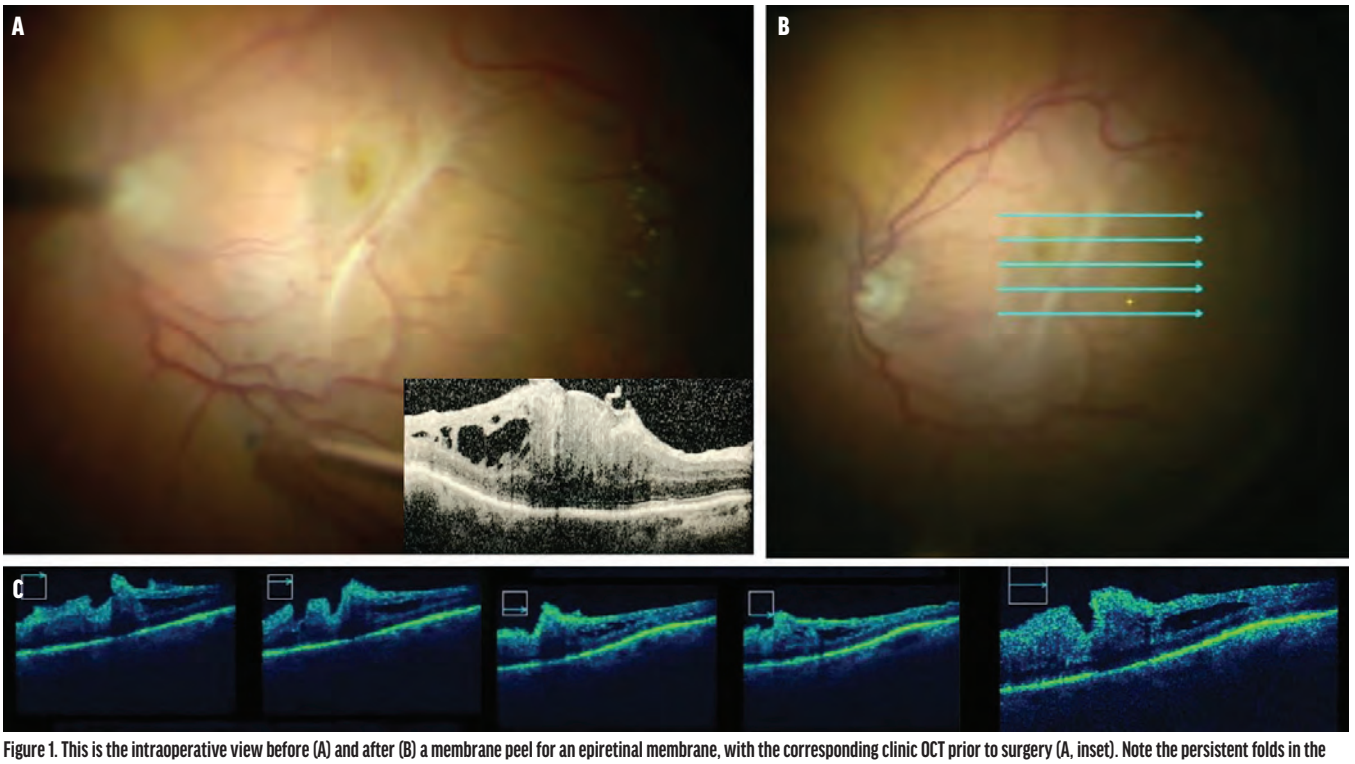

Figure 1. This is the intraoperative view before (A) and after (B) a membrane peel for an epiretinal membrane, with the corresponding clinic OCT prior to surgery (A, inset). Note the persistent folds in the retina. In the B-scan images of each iOCT roster scan in B, the persistent retinal folds are visualized with some cystoid changes due to chronicity but no remaining epiretinal membrane is seen (C).

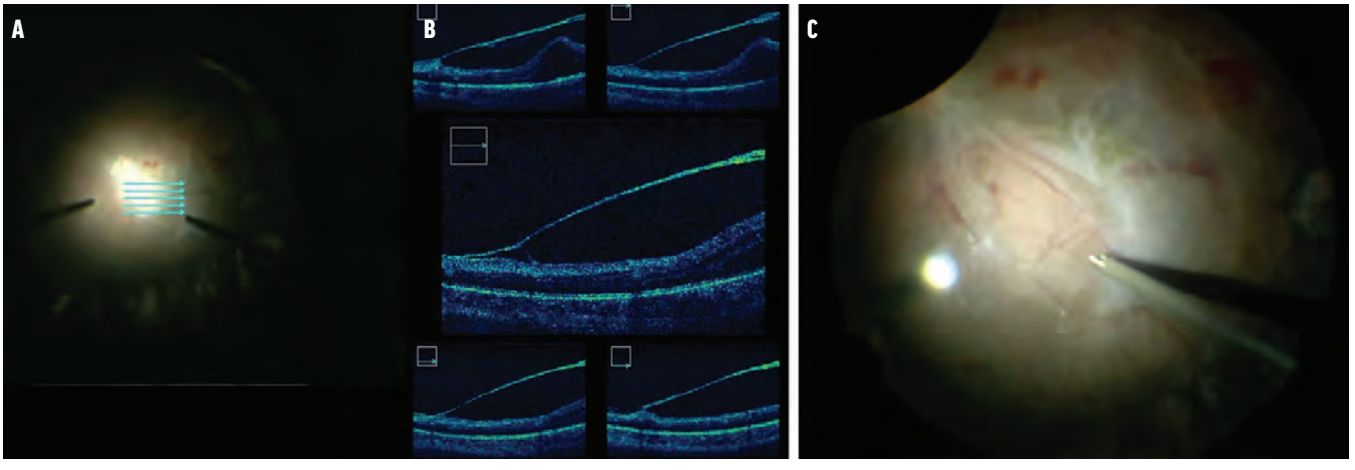

Figure 2. During surgery in the eye of a 7-year-old with a suspected CRVO (A), the iOCT roster scans demonstrate a mature tractional membrane over the macula and a potential surgical plane (B). After initiating membrane removal with the vitrector (C), note the small loop of fibrotic material that released after entering the surgical plane.

multifocal IOL can be deceptive, and it can be challenging to know whether the entire membrane was removed despite having good surgical tools and honed surgical technique.

As seen in Figure 1, the retina does not immediately relax following peeling of a mature epiretinal membrane in an eye following cataract surgery. This can leave the surgeon wondering if the entire membrane was successfully removed. In these cases, surgeons can use real-time, high-resolution iOCT imaging to confirm that the membrane is completely peeled and ensure that, with time, the retina will flatten, thus maximizing the surgical outcome.

CHALLENGING PEDIATRIC CASES REIMAGINED

Pediatric cases present with their own challenges, given that the patients are young and their fibrotic tissue responses are robust. Intraoperative imaging can be helpful to ensure that membrane peeling for complex detachments or profound inflammatory reactions to underlying pathology is complete.

For example, as illustrated in Figure 2, a 7-year-old patient with a history of retinopathy of prematurity had been referred for a suspected central retinal vein occlusion (CRVO). During the surgery, iOCT revealed the true etiology

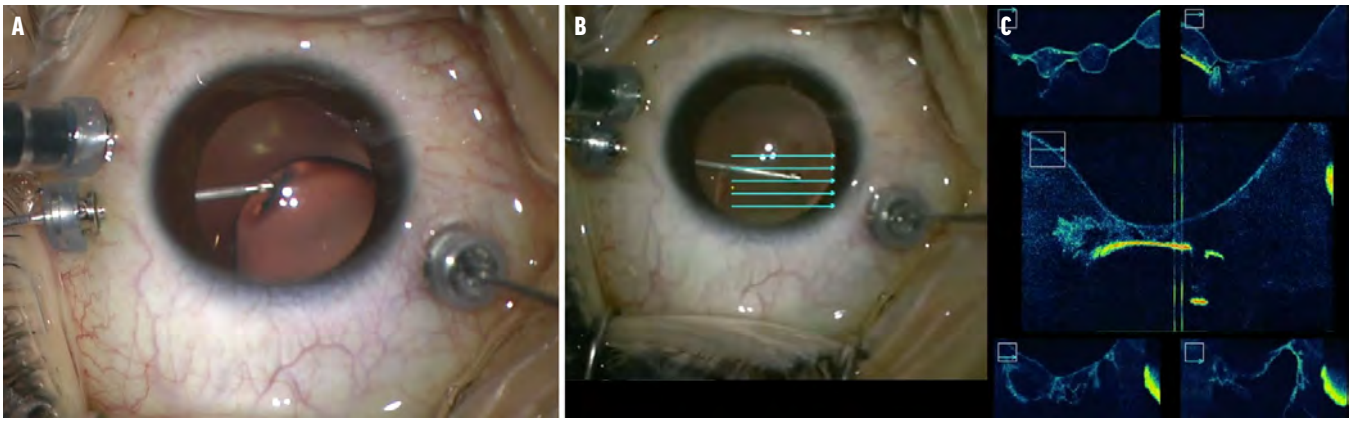

Figure 3. This case of optic pit maculopathy is obvious due to the hypopigmentation around the nerve with significant involvement of the nasal macula (A). Dilute Kenalog was used to visualize the hyaloid before using a Finesse Flex Loop. iOCT confirmed the removal of the hyaloid from the macula (B). Note the single vitreous strand attached to the nerve. The vitrector was used to cut the remaining vitreous band and propagate the posterior vitreous detachment (C).

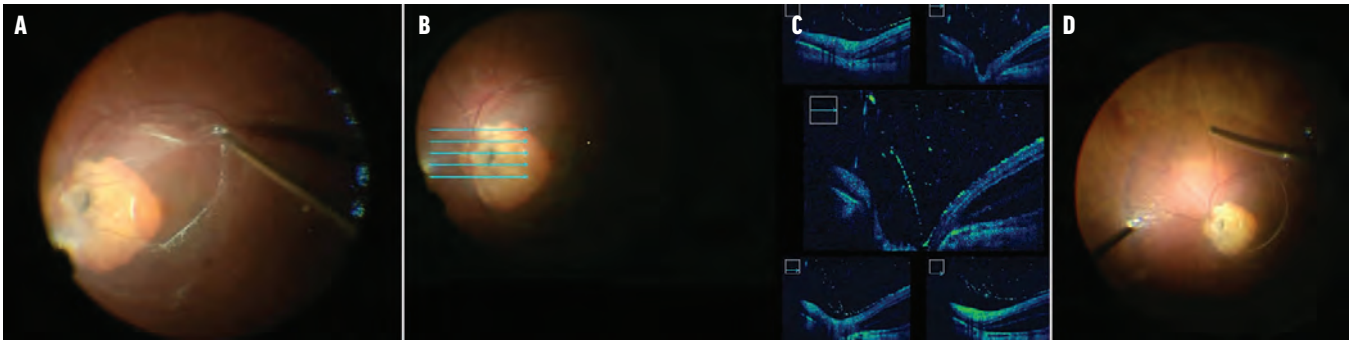

Figure 4. This pediatric patient presented with a superotemporally subluxed crystalline lens (A). During surgery, the vitrector mouth is placed facing the capsule, and aspiration is used to fill the vitrector mouth before cutting an opening in the capsule. The vitrector removes the crystalline lens material (B), and the surgeon uses iOCT to verify that the vitrector is fully within the capsule as illustrated by the increased hyperreflective signal corresponding to the vitrector surface (C, D).

for the patient's vision loss: a tractional hemorrhage caused by persistent hyaloid tension on the retinal vessels, mimicking a CRVO. With the help of iOCT, the surgeon can address the membranes with the vitrector alone to minimize trauma from repeat cycling of instrumentation through the cannulas. The same OCT imaging modality could subsequently confirm all tractional components are removed prior to ending the surgery, again maximizing long-term stability of the retina and a successful surgical outcome.

The same surgical principles can also be applied to optic pit maculopathy cases when the surgeon needs to confirm that the posterior hyaloid over the macula and nerve is separated before propagating a posterior vitreous detachment (Figure 3). These cases are best set up by starting with a Finesse Flex Loop (Alcon) and moving radially from the center before initiating the lifting of the posterior hyaloid to the nerve.

INTRAOPERATIVE LENS ASPIRATION IN MARFAN SYNDROME

We have also found iOCT useful in pediatric lens cases. Figure 4 shows a pediatric patient with a subluxed lens due to Marfan syndrome. During crystalline lens removal, it can be challenging to efficiently penetrate the capsule without dislocating the lens capsule complex into the vitreous chamber, thus increasing risk and prolonging the surgery. Using iOCT, the surgeon can localize the cutter onto the anterior capsule, aspirate, cut, and then smoothly enter the capsule to remove the lens material before taking the capsule. All these maneuvers can be done under iOCT to ensure optimal vitrector positioning as the capsule collapses.

PERSISTENT FETAL VASCULATURE: COMPLEX ANATOMY, REAL-TIME DECISIONS

Persistent fetal vasculature remains one of the more intricate diseases in pediatric retina, as residual fibrotic material can serve as a nidus for tractional membrane formation. We have found that careful dissection around the hyaloid artery followed by confirmation with iOCT minimizes this risk. Furthermore, as these patients have poor vision initially, assessing the macula, and the foveal structure in particular, can aid in prognostication of vision potential after the immediate postoperative period. This is helpful not only for the surgeon but also for the parents

(Continued on page 50)

RESCUE TECHNIQUES FOR ATYPICAL DISLOCATED IOLs

You only need a few tried and true approaches to reposition almost any lens.

By William E. Smiddy, MD

When vitreoretinal surgeons encounter a dislocated IOL, they have three management options: observe, exchange, or reposition.[1,2] Observation is a viable option when the symptoms are minimal or if the fellow eye serves the patient's needs. Many exchange techniques exist, with a general trend toward using posterior chamber techniques rather than exchanging for an anterior chamber IOL. Although many would consider scleral suturing, surgeons are also using newer approaches, such as using polytetrafluoroethylene (Gore-Tex, W.L. Gore) sutures to insert an Akreos IOL (Bausch + Lomb) or sutureless techniques involving externalizing a PMMA haptic (ie, the Yamane technique).[3-5]

Exchange techniques involve more surgical maneuvers, likely contributing to the risk of corneal decompensation. Perhaps more importantly, they involve an *open* repair, which may be more difficult in the setting of other ocular conditions. When the patient has a history of a corneal transplant or glaucoma surgery, an open repair presents additional risks and difficulties.

CHOOSING THE RIGHT TECHNIQUE

Thus, many retina surgeons may prefer IOL repositioning whenever possible. When there is sufficient residual anterior capsule, it is relatively easy to reposition the IOL into the sulcus, although that can introduce its own set of complications. When the dislocated IOL involves an endocapsular dislocation, the zonules and peripheral capsule are often too compromised to permit sutureless sulcus fixation.

When presented with a dislocated IOL, retina surgeons could benefit from having one technique that is applicable to a broad range of IOL styles. Focusing on one or two specific techniques enables the surgeon to hone the surgical steps and become more effective and efficient in the OR.

For me, that technique is scleral sutured IOLs, which has been reported and widely used for decades.[1,2] Briefly, the

AT A GLANCE

- When managing a patient with a dislocated IOL, it is advantageous to employ a technique that is applicable to a broad range of IOLs used by cataract surgeons.
- Almost all IOL styles can be repositioned with classic scleral fixation, with a few customized modifications.
- To modify the scleral suture technique for IOLs with silicone plate haptics, the Envista MX60 (Bausch + Lomb), or Raynor style IOLs, surgeons can use a handshake maneuver.

technique involves looping the haptic with a 9-0 polypropylene suture (introduced with a 27-gauge needle 3 mm posterior to the limbus) through scleral flaps (usually placed at the 2 and 8 clock hour positions), tying externally while pinning the haptic internally, and later passing the polypropylene suture needle through the base of the flap to fixate the IOL (on both sides). This approach is well suited for three-piece IOLs (PMMA or acrylic optics) and even older one-piece PMMA IOLs (eg, CZ70BD [Alcon] style IOLs).

Here, I discuss minor modifications to the classic scleral suturing technique that allow its applicability to a much broader array of IOL types.

ONE TECHNIQUE, MANY LENSES

The Crystalens IOL (Bausch + Lomb) can be scleral sutured using the standard technique but requires a wider polypropylene suture loop to lasso the T-shaped haptic (Figure 1).[6] A key element of the standard technique is to use intraocular forceps to grasp the optic and guide it through the loop. For the Crystalens, surgeons must first use the forceps to create more slack in the intraocular polypropylene loop-to-haptic complex. However, the Crystalens haptic complex is fragile and requires a gentler looping maneuver.

The standard scleral suture technique is easily adapted to one-piece acrylic IOLs such as the AcrySof SA60AT (Alcon) and other similar styles (Figure 2), despite their design for bag fixation (ie, shorter lateral dimension and non-independent haptic extensibility compared with three-piece IOLs with PMMA haptics).[7] When adapting this technique to one-piece IOLs, avoid over tightening the initial knot that affixes the polypropylene to the haptic because it is easy for the suture to cut through the haptic (ie, *cheesewire*). An important modification is to internalize the haptic suture knot to suspend the IOL, as the lens dimensions are too small to pin the haptic to the eye wall without creating tilt. In addition, if the IOL is pulled too hard when pulling the IOL toward the opposite side, the suture can cut through the haptic. Other IOL designs use the same concept of some lens suspension.

An important feature of any IOL that allows permanent fixation is for the haptic to be either long enough or have a reverse taper with the haptic being broader at the tip than at its apex. The Tecnis Symfony IOL (Johnson & Johnson) does not have this taper, so the modification for scleral suture fixation requires securing the polypropylene suture to the haptic proximal to the optic, taking advantage of the notch at the optic-haptic junction (Figure 3).[8] While this requires the polypropylene suture be more internal, the distal haptics still function as spacers to avoid IOL twisting.

Several other IOL designs can be scleral sutured with the right modifications. For IOLs with silicone plate haptics, the Envista MX60 (Bausch + Lomb), or Raynor style IOLs, surgeons can use a handshake maneuver in which the polypropylene suture-containing 27-gauge needle is directed

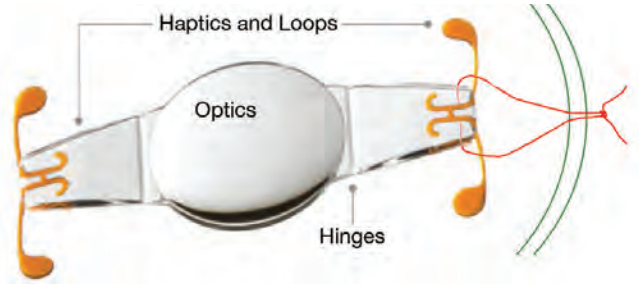

Image courtesy of Bausch + Lomb

Figure 1. A rescued Crystalens IOL can be scleral sutured using the standard technique with a slightly wider polypropylene suture loop to lasso the broader haptic. Note that the lens haptics are fragile and require gentle handling.

Image courtesy of Alcon

Figure 2. The AcrySof SA60AT, although designed for bag fixation, can be scleral fixated; surgeons should allow the haptic suture knot to be internalized to suspend the IOL.

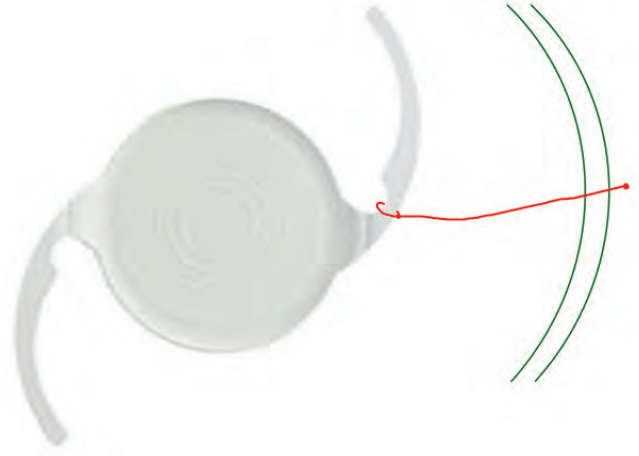

Image courtesy of Johnson & Johnson

Figure 3. Because the Tecnis Symfony IOL does not have a reverse taper (ie, the haptic is broader at the tip than at the apex), surgeons must use the notch at the optic-haptic junction to secure the suture to the haptic proximal to the optic.

through a hole in the haptic and the forceps holding the optic is released and used to grasp the suture (Figure 4).[9] A separate, 25-gauge (or smaller) forceps is introduced anterior to the initial 27-gauge needle stab site to grab the suture from the first forceps (the handshake) and pulled externally. Then, the suture is temporarily tied until the other side is secured to allow the flexibility to center the optic. Although a similar technique can be used if there is a capsular tension ring, often it is better to remove the capsular tension ring and denude the haptics for repositioning.

For IOL designs without holes, the initial polypropylene-containing 27-gauge needle can be used to pierce the IOL at the broader zone at the optic-haptic junction and a similar

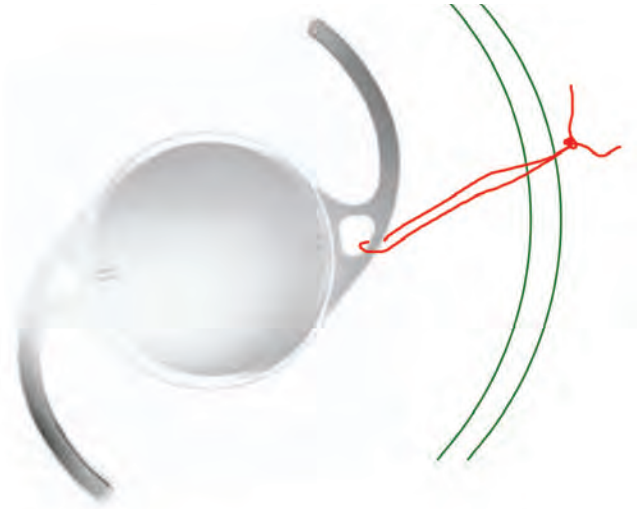

Image courtesy of Bausch + Lomb

Figure 4. To scleral fixate the Envista MX60, surgeons can use a handshake maneuver to suture through a hole in the haptic.

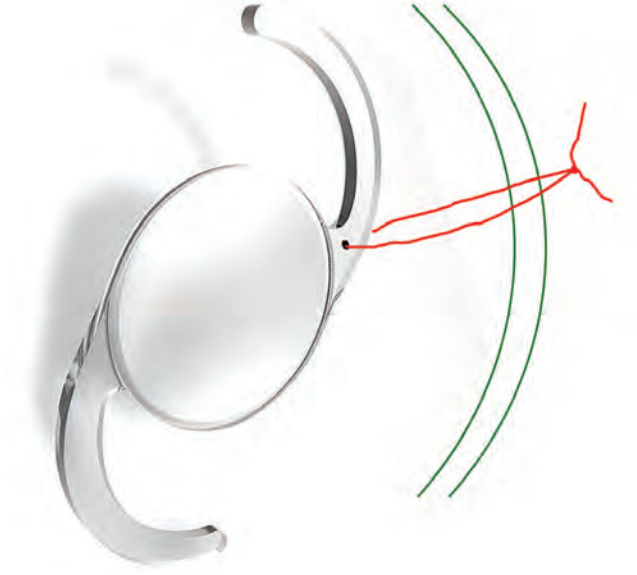

Image courtesy of HumanOptics

Figure 5. To reposition the Aspira IOL (HumanOptics)—which has no holes and has a tapered haptic—surgeons can use the piercing or impaling modification.

handshake maneuver pursued (Figure 5).

The Akreos IOL can be scleral fixated with a similar handshake maneuver but requires another modification to use the holes in all four haptics (Figure 6).[10] The polypropylene-containing 27-gauge needle is introduced through a partial-thickness radial scleral incision about 2 clock hours from the scleral flap, directed through one haptic hole, and grasped by the first intraocular forceps. The second forceps is introduced through the base of the usual scleral flap through the hole in the second haptic on that side, the handshake maneuver is used to take the suture from the first forceps, and the non-needled end is withdrawn from the eye. Then, the needled end of the suture is at the stab incision through the radial scleral incision; it is grasped with a needle driver

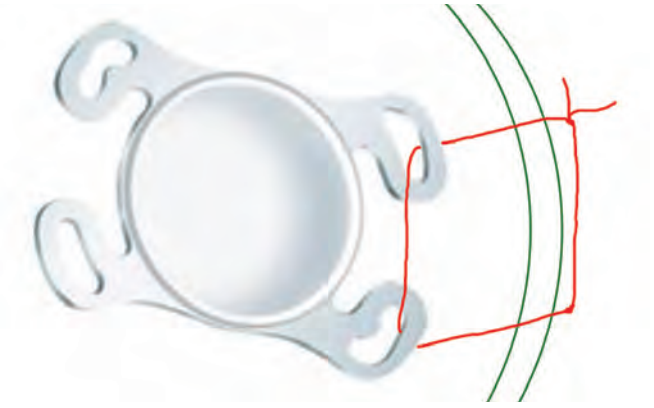

Image courtesy of Bausch + Lomb

Figure 6. When rescuing an Akreos lens with scleral fixation, surgeons can use a modified handshake technique to use the holes in each of the four haptics.

and passed intrasclerally to the partial-thickness scleral flap, where the ends are then tied (temporarily until the other side is tied to center the optic).

REPLACE OR RESCUE

IOL rescue is not ideal when there is a damaged or broken haptic or if the patient is on tamsulosine (Flomax, Sanofi), which carries a risk of subsequent uveitis-glaucoma-hyphema syndrome and could ultimately require IOL exchange.[11,12]

If you are rescuing a lens, almost all styles of dislocated IOLs can be repositioned with the same base scleral fixation technique, but with a few customized modifications. Master the classic approach and just a few tricks in the OR, and you can ensure a smooth IOL rescue, no matter the lens. ■

Author disclaimer: These techniques are considered off-label for these lenses.

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OXYGEN-ASSOCIATED RETINOPATHY AND ROP


These distinct clinical entities require tailored management strategies.

BY MARÍA ANA MARTÍNEZ-CASTELLANOS, MD, AND MANUEL JASSO, MD

Retinal vascular disorders in neonates, particularly oxygen-associated retinopathy (OAR) and retinopathy of prematurity (ROP), represent significant causes of preventable childhood blindness worldwide.[1] While these conditions share some pathological features, they differ fundamentally in their etiology, clinical presentation, and management approaches.[2] This article provides a comprehensive comparison of OAR and ROP based on current evidence, with particular emphasis on their distinctive clinical features and management strategies.

CLINICAL AND ANGIOGRAPHIC DIFFERENTIATION

OAR and ROP demonstrate distinct clinical presentations that enable differentiation through careful examination.[3] OAR typically manifests with dichotomous branching of the retinal vessels and prominent peripapillary involvement, reflecting its pathogenesis from oxygen toxicity in both preterm and full-term infants; in contrast, ROP exhibits the characteristic menorah pattern of vascular growth, consistent with its developmental origin in premature infants with incomplete retinal vascularization (Figure 1).[4,5]

Fluorescein angiography sheds light on further diagnostic differences between OAR and ROP.[6] OAR demonstrates delayed arterial filling and patchy choroidal perfusion patterns, while ROP shows a clear demarcation between the vascular and avascular retina.[7] These angiographic features not only aid in diagnosis, but also provide prognostic information regarding disease progression.[8]

DIVERGENT EARLY-STAGE MANAGEMENT

The most critical distinction between OAR and ROP lies in their differential response to early intervention.[9] In OAR cases identified during the vaso-obliteration phase, carefully titrated oxygen therapy at 88% to 95% FiO_2 concentration can induce disease regression (Figure 2).[10] This therapeutic window promotes vascular reperfusion and facilitates physiological growth of previously obliterated vessels.[11]

In contrast, early-stage ROP typically requires only careful observation, as oxygen modulation does not provide therapeutic benefit in this condition.[12] This fundamental difference underscores the importance of accurate differentiation between these entities.[13]

Figure 1. Vascular patterns in OAR and ROP. OAR shows dichotomous branching with peripapillary involvement, while ROP exhibits the classic menorah pattern of abnormal vascular growth.

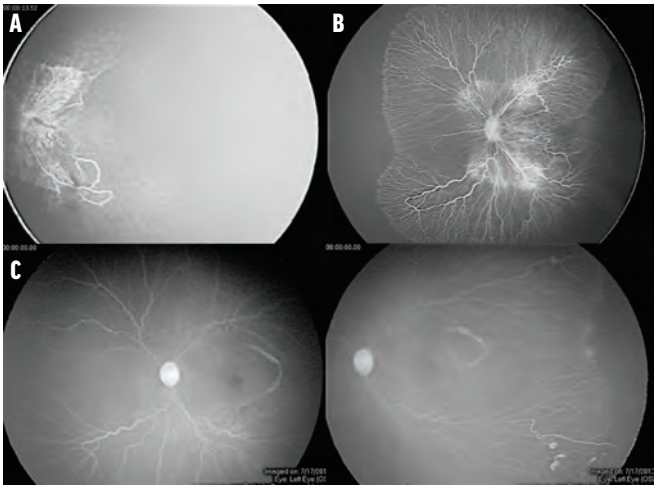

Figure 2. In OAR, carefully titrated oxygen therapy during the vaso-obliteration phase can promote regression and reperfusion of retinal vessels. A patient with aggressive vaso-obliteration before treatment (A) and 3 months (B) and 6 months (C) after regulated oxygen therapy has vascular reperfusion and physiological growth.

ADVANCED DISEASE MANAGEMENT

If either condition progresses to neovascularization, their management converges, requiring antiangiogenic therapy

ACCURATE DIFFERENTIATION BETWEEN OAR AND ROP IS ESSENTIAL FOR PROPER MANAGEMENT AND CARE.

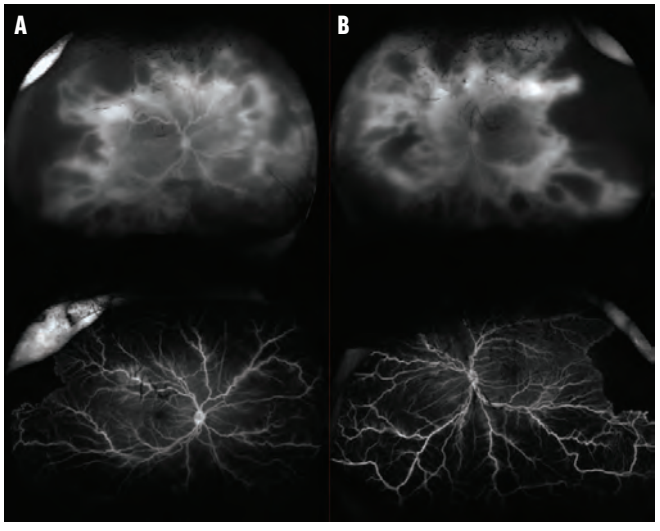

Figure 3. Before treatment with anti-VEGF therapy (A), capillary closure, ischemia, and aggressive neovascularization are obvious. Two weeks after anti-VEGF therapy (B), regression of neovascular changes is evident.

Figure 4. This child with stage 5 OAR is using a translucent prosthesis, which preserves residual light perception while supporting orbital growth during the postoperative rehabilitation.

with an anti-VEGF agent (Figure 3) or laser photocoagulation.[6] For retinal detachment (stages 4 and 5), vitrectomy becomes necessary regardless of etiology.[14] Stage 5 disease represents the most common indication for surgical intervention, although outcomes remain suboptimal.[15]

REHABILITATION AND GLOBAL HEALTH PERSPECTIVES

Postoperative rehabilitation is crucial for children with advanced disease.[16] Translucent prostheses offer particular benefits for OAR patients by preserving residual light perception while maintaining orbital growth (Figure 4).

The disproportionate burden of these conditions on children and families in low-income countries highlights health care disparities and the need for improved access to basic neonatal ophthalmic care.[17]

FIRST, DIFFERENTIATE

Accurate differentiation between OAR and ROP is essential for proper management and care.[18] The unique responsiveness of OAR to oxygen modulation represents a critical window for vision preservation, while advanced cases of both conditions require similar interventions. Global efforts should focus more on implementing preventive strategies and improving access to care. ■

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DR STABILITY WITH AUTOMATED INSULIN DELIVERY


Our study indicates the benefits of improved glycemic control outweigh the small potential risk of worsening diabetic eye disease.

BY FRANCESC MARCH DE RIBOT, MD, PHD, AND BEN WHEELER, MD, PHD

Automated insulin delivery (AID) devices integrate a continuous glucose monitor that automatically adjusts insulin delivery based on the readings. The goal is to maintain measurements within a target range, thus managing glucose levels more effectively in patients with diabetes.

AID systems are primarily used to treat patients with type 1 diabetes, especially for those who experience significant glycemic variability, frequent hypoglycemia, or difficulty with manual insulin dosing. Most systems are hybrid closed-loop systems, in which users manually input carbohydrate intake and bolus for meals, while the system adjusts background (basal) insulin delivery automatically.

AID systems have been shown to improve glycemic control, reduce hemoglobin A1c levels, minimize hypoglycemia, and improve quality of life for patients with diabetes.[1]

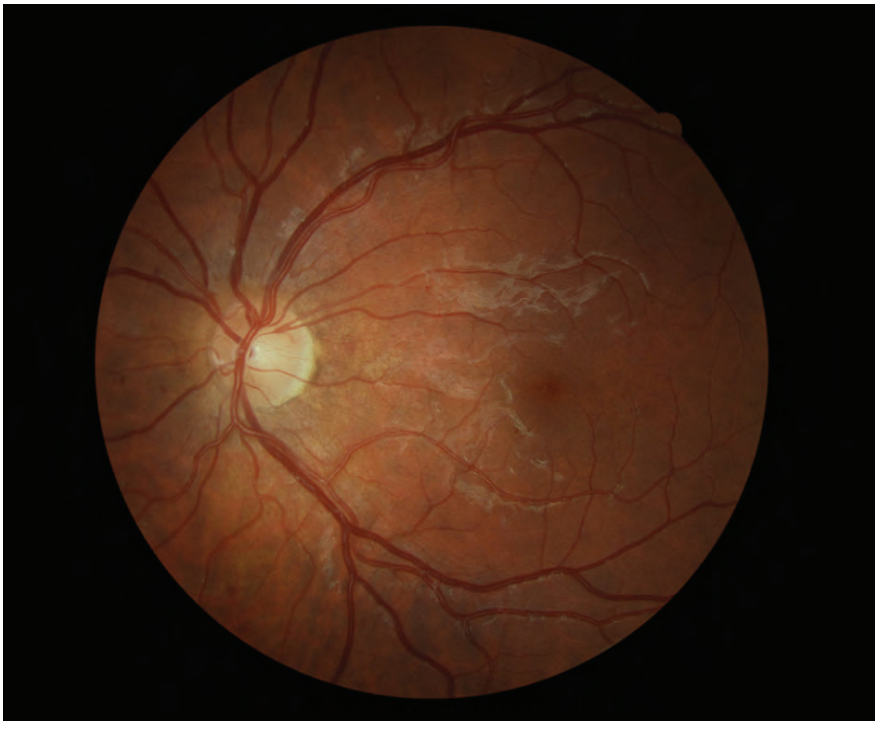

Figure. Patients with DR, such as this one, who start using an AID device can rest assured that their risk of EWDR is minimal (only 3% of patients developed clinically significant EWDR in our current study).

However, cost remains a major barrier, limiting access for many patients. AID technology also requires users to wear multiple devices, which may be uncomfortable and requires adaptation.

While the use of AID technology is beneficial for diabetes control, concern has been raised over rapid improvements in glucose control potentially leading to early worsening of diabetic retinopathy (EWDR; Figure). EWDR is a phenomenon in which tighter glucose control causes a temporary deterioration in DR,[2] underscoring the importance of close monitoring. Our team conducted a study to assess the progression of DR in patients commencing use of AID devices, and our results indicated that this technology is safe from a DR perspective.[3]

A LOOK AT THE DATA

Our retrospective observational study involved 165 pediatric patients older than 13 years of age with type 1 diabetes who had been using an AID device for at least 6 months. These criteria were chosen to align with the 6- to 12-month timeframe in which EWDR is most likely to occur.[2] DR was assessed using retinal photographs and recording a DR grading at baseline and following AID device initiation.

OUR STUDY SHOWED NO HIGHER RISK OF WORSENING IN DR GRADE BETWEEN THOSE WITH OR WITHOUT RAPID IMPROVEMENT IN THEIR HEMOGLOBIN A1C.

Demographic information was collected, including date of birth, date of diabetes diagnosis, sex, smoking status, body mass index, and hemoglobin A1c values. Data regarding other diabetes complications were also obtained, including presence of nephropathy, dyslipidemia, and formal diagnosis and/or treatment of hypertension.

The results showed that DR grading improved in 19% of individuals and remained stable in 60%, supporting the safety of AID technology in patients with type 1 diabetes; of the 21% whose DR worsened, only 3% developed clinically significant EWDR. Of these five patients, four experienced worsening from a nonproliferative stage to a proliferative stage, and one patient had new proliferation after previously being treated for proliferative disease.

Of note, being older than 18 years of age at AID initiation was the only statistically significant risk factor identified for EWDR on logistic regression. Risk factors in patients who required laser therapy included previous DR, diabetes diagnosis for more than 10 years, and coexistence of one or more diabetes complications.

No clinically important DR worsening occurred in patients with a diabetes diagnosis of less than 10 years and without preexisting DR, which suggests greater long-term benefits may be achieved by starting AID therapy immediately after a diabetes diagnosis.

CONSIDERATIONS WITH AID DEVICES

Our findings indicate that the risk of EWDR should not prevent AID use; still, for those at a higher risk of EWDR (ie, those with a longer history of diabetes and with associated complications), a closer follow-up and monitoring schedule may be warranted with the main goal of early detection of proliferative DR. The benefits of an AID device for patients with diabetes are clear, as improving glycemic levels reduces risk of diabetes complications, including DR (specifically, a 76% reduction in the risk for DR progression after 6.5 years of follow-up).[2]

There is no evidence that managing the magnitude of hemoglobin A1c change will lower the risk of DR progression in patients with diabetes. Our study showed no higher risk of worsening in DR grade between those with or without rapid improvement in their hemoglobin A1c. Given that those with severe diabetes may have the most to gain from using an AID device, this finding provides significant safety reassurance.

In addition, the fact that AID initiation in patients older than 18 years of age was the only statistically significant risk factor, and no clinically significant DR progression occurred in those with a diabetes diagnosis of less than 10 years and without preexisting DR, suggests children and adolescents with type 1 diabetes may generally experience low risk of EWDR following AID device initiation.

The progression of DR to proliferative disease in a small proportion of the participants (3%) is similar to previously published rates of natural history of DR progression (with or without changes in therapy). For example, the Diabetes Control and Complications Trial identified EWDR after conventional treatment in 7.6% of patients within the first 6 to 12 months.[2]

THE BENEFITS OUTWEIGH THE RISK

AID devices have proven to be safe and effective, as DR grades are mainly stable or improved with their use. Nevertheless, in a small minority of patients, DR progression may occur, and while most only progressed to minimal or mild grades, proliferative changes requiring laser treatment are possible in approximately 3% of cases. Clinicians should monitor for DR progression, particularly in patients with prior DR, a diabetes diagnosis for more than 10 years, and other known diabetes complications. Our data support that the benefits of AID technology on glycemia outweigh the potential short-term risk of DR progression. ■

1. Gilbert TR, Noar A, Blalock O, Polonsky WH. Change in hemoglobin A1c and quality of life with real-time continuous glucose monitoring use by people with insulin-treated diabetes in the Landmark Study. *Diabetes Technol Ther*. 2021;23(S1):S35-S39.
2. No authors listed. Early worsening of diabetic retinopathy in the Diabetes Control and Complications Trial. *Arch Ophthalmol*. 1998;116(7):874-886.
3. Johansson MME, March de Ribot F, Sime MJ, et al. Short-term diabetic retinopathy status in people with type 1 diabetes commencing automated insulin delivery. *Diabetes Technol Ther*. 2025;27(5):386-394.

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CODING ADVISOR
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WHAT, WHERE, AND WHY: CRUCIAL QUESTIONS GUIDING ACCURATE CODING

The details of the treatment approach matter when coding retinal injections and surgical procedures.

BY JOY WOODKE, COE, OCS, OCSR

Accurate coding for retina procedures requires careful consideration of key components of the patient encounter and management approach. From where the medication is delivered to what type of implanted material is removed, these crucial questions must be answered to submit a clean claim (Table 1). The clinical scenarios explored below can help you properly code your next patient visit.

WHERE WAS THE MEDICATION INJECTED?

The documentation and superbill note a Kenalog injection in the left eye. Although it is clear which medication was injected, to confirm the correct coding for this case, a crucial question remains: Where was the medication injected? The answer, which should be clearly documented in the medical record, will dictate the appropriate CPT code for the procedure (Table 2).

WHY WAS THE INJECTION PERFORMED?

For all intravitreal injections performed (CPT code 67028), the first question is what drug was used? Following that inquiry is why? The "why" is the indication, or diagnosis for the treatment, and will support the medical necessity. Each drug has FDA-approved indications, and

TABLE 1. INJECTION LOGISTICS AND BILLING CODES

What	Why	Where	CPT or Category III Code
Anti-VEGF, geographic atrophy and antibiotic drugs	Per FDA label and/or indication	Intravitreal, into the vitreous cavity, 3 mm to 4 mm posterior to the limbus	CPT code 67028, intravitreal injection of a pharmacological agent (separate procedure)
Triamcinolone acetonide (Xipere, Bausch + Lomb)	Macular edema associated with uveitis	Suprachoroidal space between the sclera and choroid	CPT code 67516, suprachoroidal space injection of a pharmacological agent (separate procedure)
Port delivery system (Susvimo, Genentech/Roche)	Wet AMD, diabetic macular edema, noninfectious uveitis	Sustained release intravitreal device into the vitreous cavity	CPT code 67027, implantation of intravitreal drug delivery system, including concomitant removal of vitreous
Voretigene neparvovec (Luxturna, Spark Therapeutics)	Gene therapy	Injection in the subretinal space	Category III code 0810T, subretinal injection of a pharmacologic agent, including vitrectomy and one or more retinotomies

TABLE 2. MEDICATION INJECTION LOCATION AND ASSOCIATED CPT CODE

Where	CPT Code
Intravitreal injection, into the vitreous cavity, 3 mm to 4 mm posterior to the limbus	67028, intravitreal injection of a pharmacological agent
Below the Tenon capsule or sub-Tenon injection	67515, injection of medication or other substance below Tenon capsule
Injection given between the conjunctiva and Tenon capsule	68200, subconjunctival injection

TABLE 3. SURGICAL REMOVAL/REPOSITIONING AND ASSOCIATED CPT CODES

Procedure	What	CPT Codes
Pars plana vitrectomy with IOL exchange	What was removed? IOL	66986, IOL exchange; 67036, pars plana vitrectomy
Pars plana vitrectomy with reposition of dislocated IOL	What was repositioned? IOL	67036, pars plana vitrectomy; 66825, reposition of IOL
Pars plana vitrectomy with removal of lens material by phaco or mechanical	What was removed? Cataract fragments, natural lens	67036, pars plana vitrectomy; 66850, removal of lens material

reporting these diagnoses will ensure claim approval, unless the payer has a policy with expanded coverage.

Pitfalls to avoid during chart documentation include unspecified indications. For example, do not report choroidal neovascularization, ICD-10 H31.8, or retinal neovascularization, unspecified, H350.052, when injecting faricimab-svoa (Vabysmo, Genentech/Roche). Instead, use the more specific diagnosis of exudative wet macular degeneration with active choroidal neovascularization, ICD-10 H35.3221.

WHAT WAS REMOVED?

When performing surgery to remove any implanted material, the first two questions are: 1) What is being removed, and 2) how?

Consider a procedure described as a removal of a dislocated lens. In this situation, be sure to confirm if this is a removal of a dislocated IOL or a removal of cataract fragments following surgery. The answer will guide the appropriate coding (Table 3).

WHY WAS THE PROCEDURE PERFORMED?

A frequent procedure in retina clinics, pneumatic retinopexy (injection of gas), is typically performed for retinal detachment. But that isn't the only indication—when the diagnosis is submacular hemorrhage, the coding is much different (Table 4).

TABLE 4. PROCEDURE AND ASSOCIATED CPT CODE

Procedure	Why	CPT Code
Pneumatic retinopexy	Retinal detachment	67110, repair of retinal detachment by injection of air or other gas
Pneumatic displacement	Submacular hemorrhage	67025, injection of vitreous substitute, pars plana, or limbal approach

TABLE 5. CODING FOR A SKILLED NURSING FACILITY (SNF)

Service	Bill to SNF	Bill to Medicare Part B
Testing	Technical component 9XXXX-TC	Professional component 9XXXX-26
Drugs	HCPCS code	Not paid by Medicare Part B while residing in the SNF
Facility fee	CPT or category III code	Not paid by Medicare Part B while residing in the SNF
Durable medical equipment	HCPCS code	Not paid by Medicare Part B while residing in the SNF

WHERE IS THE PATIENT RESIDING?

Is the patient living in a skilled nursing facility (SNF) following an injury and being rehabilitated? Due to consolidated billing for SNFs, there are specific services that are not covered by Medicare Part B when the beneficiary is residing in the facility.[1] These services would be paid for by the SNF from its consolidate payment. Prior arrangements with the SNF can streamline reimbursement (Table 5).

When a registered hospital inpatient is seen in the office, services provided are made under the physician fee schedule facility rate.[2] As a result, the physician providing the services must report the place of service 21, inpatient hospital, as this represents the setting where the patient is currently receiving care, not place of service 11, office. If not reported appropriately, Medicare will deny or recoup the reimbursement due to an incorrect claim submission. Additionally, reimbursement for the medications provided during inpatient status is often bundled with the facility and not separately payable. ■

1. Consolidated billing. CMS. Accessed September 2, 2025. bit.ly/4piFRoP
2. Medicare claims processing manual. CMS. Accessed September 2, 2025. bit.ly/3I3VYWx

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MAKING THE MOST OF A RETINA WET LAB

Here are some tips and tricks I learned after a recent wet lab experience.

BY FLAVIUS BECA, MD

For retina fellows, hands-on experience is everything. Wet labs offer an invaluable opportunity to practice surgical techniques in a low-stakes, high-yield environment—with cutting-edge tools, expert faculty, and collaborative learning. Having attended the 11th annual fellows Advanced Vitreous Surgery (fAVS) wet lab hosted at Duke University on May 15, 2025, I walked away from the experience with better technical skills and a better understanding of how to approach wet labs more intentionally. Here are a few takeaways and tips to maximize your time at a wet lab.

NO. 1: PLAN YOUR STATIONS STRATEGICALLY

Before the lab begins, review the agenda and identify the stations most relevant to your current learning curve. Whether it's membrane peeling, chandelier-assisted scleral buckling, or suprachoroidal drug delivery, prioritize the stations where you need the most repetition or have the least real-world exposure (Figure 1). Although the lab is often designed to allow you to reach every station, lines can form and backups happen, so being strategic is important to allow you to get to your desired stations. Create a rough schedule in your mind—if time runs short, you'll have hit your highest value targets.

NO. 2: INTERACT INTENTIONALLY WITH FACULTY AND INDUSTRY

One of the greatest assets of a wet lab is direct access to experienced retina surgeons. Don't hesitate to ask questions, whether technical or personal. Keep it conversational and specific. At some courses, industry representatives can also provide perspective and great insight in the design and application of devices and delivery

Image courtesy of Kevin Caldwell Photography

Figure 1. Wet labs are the ideal opportunity to practice surgical techniques with the help of world-renowned retina surgeons. This wet lab took place at the 15th annual Mass Eye and Ear Vitrectomy Course in Boston.

Image courtesy of Kevin Caldwell Photography

Figure 2. Industry representatives can be invaluable resources during a wet lab to help trainees as they try new vitrectomy platforms and surgical tools. This wet lab took place during the 13th annual Vit-Buckle Society meeting in Austin.

systems (Figure 2). Industry representatives can sometimes even report on various approaches different surgeons typically use or pearls to master a novel technique. These informal interactions can clarify your technique and expand your surgical perspective far beyond what the hands can feel.

NO. 3: LEARN WHILE YOU WAIT

Downtime at a wet lab is inevitable, whether waiting for a microscope or equipment turnover. Use this time to observe others, ask to scrub in beside a peer, or review recorded procedures, if available. Watching how others approach the same task—especially faculty—can give you a glimpse into alternate techniques or instrument handling you hadn't considered (Figure 3).

NO. 4: PRACTICE WITH PURPOSE

Once you're at a station, don't try to do everything. Focus your efforts. Have one or two specific goals in mind per station. Treat the lab like an OR case—you'll retain more, and the muscle memory will stick.

NO. 5: REFLECT AND REAPPLY

After the lab, jot down a few take-home pearls. At the Duke fAVS wet lab, I learned alternative ways to remove an IOL during a lens exchange and how adjusting the angle of my force vector during a membrane peel could improve the efficiency of my peel. Small adjustments like these can

Image courtesy of Kevin Caldwell Photography

Figure 3. While waiting for a turn at the stations, wet lab participants can watch and learn from each other. This is the wet lab from the 11th annual fAVS Course in Durham, North Carolina.

WET LABS ARE MORE THAN JUST A REHEARSAL SPACE—THEY ARE ACCELERATORS FOR SURGICAL DEVELOPMENT.

translate directly into improved performance in the OR. Bring these ideas back to your attendings, discuss them during cases, and apply them purposefully.

TAKE ADVANTAGE OF THE OPPORTUNITY

Wet labs are more than just a rehearsal space—they are accelerators for surgical development. Approach them with intention, humility, and curiosity. Faculty are there to teach, and your peers are there to grow alongside you. These sessions also offer valuable opportunities to connect with colleagues and industry leaders from around the country. With the right mindset, even a brief session at the microscope can spark lasting improvements in your surgical intuition. ■

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(Continued from page 38)

CLINICIANS SHOULD ALWAYS FOCUS ON MINIMALISM AND PRECISION, AND IOCT CAN ALLOW THESE PRINCIPLES TO FLOURISH IN THE OR.

who are understandably nervous. Having this information allows for incremental discussions to manage parent (and patient) expectations for vision, as well as any intervention that may be needed to correct vision deprivation such as patching or glasses/contact lens wear.

IMAGING AS A SURGICAL AND DIAGNOSTIC REVOLUTION

As highlighted by these cases, iOCT can be an instructive tool to help surgeons obtain the best outcomes for patients. Although new technology is tempting to use, surgeons should always be mindful of how and why the technology is being employed. Clinicians should always focus on minimalism and precision, and iOCT can allow these principles to flourish in the OR.

Hopefully with more time and investment, OCT will be easily deployable and used in most surgeries, perhaps even elucidating new pathophysiology of common retinal disease we only thought we knew and providing the means to intervene sooner and more efficiently to preserve and restore vision. ■

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INDEX OF ADVERTISERS

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

INDICATIONS AND USAGE

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

CONTRAINDICATIONS

Ocular or Periocular Infections
SYFOVRE is contraindicated in patients with ocular or periocular infections.
Active Intraocular Inflammation
SYFOVRE is contraindicated in patients with active intraocular inflammation.
Hypersensitivity
SYFOVRE is contraindicated in patients with hypersensitivity to pegcetacoplan or to any of the excipients in SYFOVRE. Systemic hypersensitivity reactions (e.g., anaphylaxis, rash, urticaria) have occurred.

WARNINGS AND PRECAUTIONS

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

ADVERSE REACTIONS

Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.
A total of 839 patients with GA in two Phase 3 studies (OAKS and DERBY) were treated with intravitreal SYFOVRE, 15 mg (0.1 mL of 150 mg/mL solution). Four hundred nineteen (419) of these patients were treated in the affected eye monthly and 420 were treated in the affected eye every other month. Four hundred seventeen (417) patients were assigned to sham.
The most common adverse reactions (≥5%) reported in patients receiving SYFOVRE were ocular discomfort, neovascular age-related macular degeneration, vitreous floaters, and conjunctival hemorrhage.
Table 1: Adverse Reactions in Study Eye Reported in ≥2% of Patients Treated with SYFOVRE Through Month 24 in Studies OAKS and DERBY

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

PM: SYFOVRE monthly; PEOM: SYFOVRE every other month

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

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

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

USE IN SPECIFIC POPULATIONS

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

PATIENT COUNSELING INFORMATION

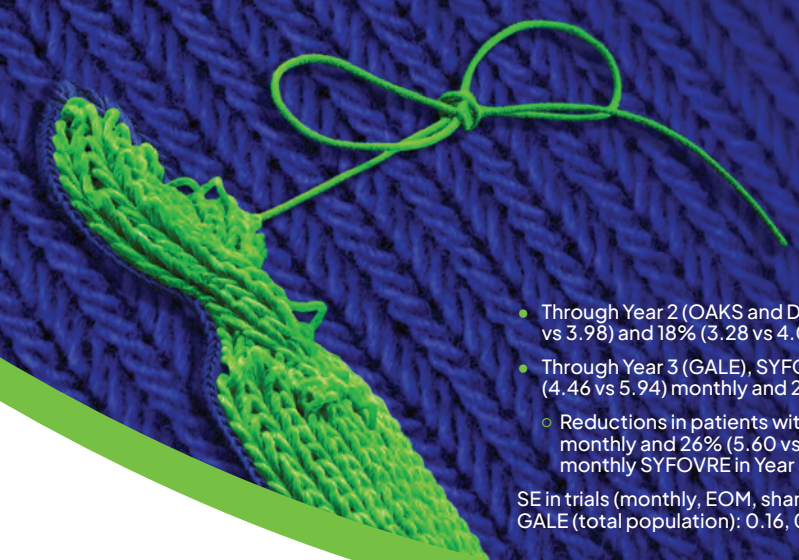
Advise patients that following SYFOVRE administration, patients are at risk of developing endophthalmitis, retinal detachments, retinal vasculitis with or without retinal vascular occlusion and neovascular AMD. If the eye becomes red, sensitive to light, painful, or if a patient develops any change in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

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

SYF-PI-20Dec2024-3.0

12/24 US-PEGGA-2400436 v1.0

SYFOVRE®
(pegcetacoplan injection)
15 mg / 0.1 mL



Save more retinal tissue

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

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

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

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

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

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

Discover more at SyfovreECP.com

INDICATION

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

IMPORTANT SAFETY INFORMATION

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- SYFOVRE is contraindicated in patients with ocular or periocular infections, in patients with active intraocular inflammation, and in patients with hypersensitivity to pegcetacoplan or any of the excipients in SYFOVRE. Systemic hypersensitivity reactions (e.g., anaphylaxis, rash, urticaria) have occurred.

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

ADVERSE REACTIONS

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

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

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

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

References: 1. SYFOVRE (pegcetacoplan injection) [package insert]. Waltham, MA: Apellis Pharmaceuticals, Inc.; 2024. **2.** Data on file. Apellis Pharmaceuticals, Inc. **3.** Sunness JS, Margalit E, Srikumaran D, et al. The long-term natural history of geographic atrophy from age-related macular degeneration: enlargement of atrophy and implications for interventional clinical trials. *Ophthalmology*. 2007;114(2):271–277. doi:10.1016/j.ophtha.2006.09.016.

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