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Retina Today

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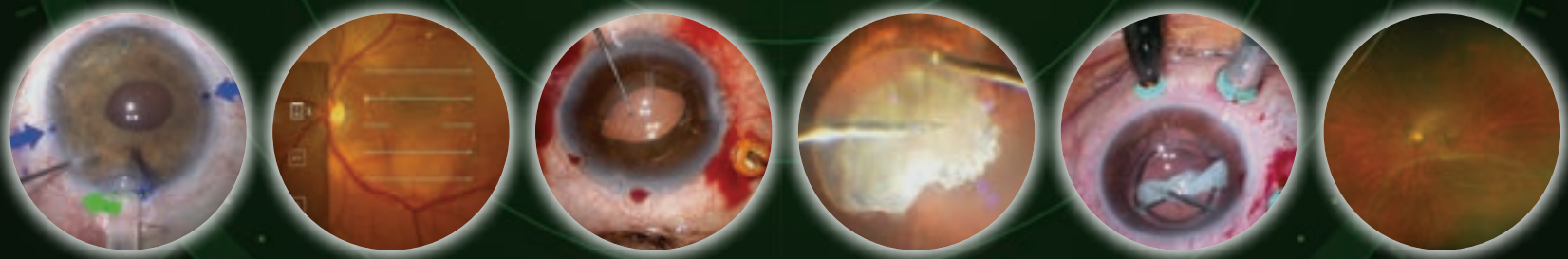
eyetube

SURGICAL TECHNIQUES AND TECHNOLOGIES



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INDICATION

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

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

Endophthalmitis and Retinal Detachments

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

A moment worth protecting

Every moment is precious for your patients with geographic atrophy. Help protect their moments from the start with IZERVAY™.

Learn more at
IZERVAYecp.com

iZervay™
(avacincaptad pegol intravitreal solution) 2 mg

Neovascular AMD

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

Increase in Intraocular Pressure

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

ADVERSE REACTIONS

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

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

astellas

IZERVAY™ (avacincaptad pegol intravitreal solution)
Rx only

Brief Summary: This information is not comprehensive. Visit IZERVAYecp.com to obtain the FDA-approved product labeling or call 609-474-6755.

1 INDICATIONS AND USAGE

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

2 DOSAGE AND ADMINISTRATION

2.1 General Dosing Information

IZERVAY must be administered by a qualified physician.

2.2 Recommended Dosage

The recommended dose for IZERVAY is 2 mg (0.1 mL of 20 mg/mL solution) administered by intravitreal injection to each affected eye once monthly (approximately every 28 ± 7 days) for up to 12 months.

2.4 Injection Procedure

Only 0.1 mL (2 mg) should be administered to deliver a single dose. Any excess volume should be disposed.

Prior to the intravitreal injection, patients should be monitored for elevated intraocular pressure (IOP) using tonometry. If necessary, ocular hypotensive medication can be given to lower the IOP.

The intravitreal injection procedure must be carried out under controlled aseptic conditions, which includes the use of surgical hand disinfection, sterile gloves, a sterile drape, and a sterile eyelid speculum (or equivalent). Adequate anesthesia and a broad-spectrum topical microbicide should be given prior to the injection.

Inject slowly until the rubber stopper reaches the end of the syringe to deliver the volume of 0.1 mL. Confirm delivery of the full dose by checking that the rubber stopper has reached the end of the syringe barrel.

Immediately following the intravitreal injection, patients should be monitored for elevation in intraocular pressure (IOP). Appropriate monitoring may consist of a check for perfusion of the optic nerve head or tonometry.

Following intravitreal injection, patients should be instructed to report any symptoms suggestive of endophthalmitis (e.g., eye pain, redness of the eye, photophobia, blurring of vision) without delay.

Each vial and syringe should only be used for the treatment of a single eye. If the contralateral eye requires treatment, a new vial and syringe should be used and the sterile field, syringe, gloves, drapes, eyelid speculum, filter needle, and injection needle should be changed before IZERVAY is administered to the other eye. Repeat the same procedure steps as above.

Any unused medicinal product or waste material should be disposed of in accordance with local regulations.

3 DOSAGE FORMS AND STRENGTHS

Intravitreal solution: 20 mg/mL clear to slightly opalescent, colorless to slightly yellow solution in a single-dose vial.

4 CONTRAINDICATIONS

4.1 Ocular or Periocular Infections

IZERVAY is contraindicated in patients with ocular or periocular infections.

4.2 Active Intraocular Inflammation

IZERVAY is contraindicated in patients with active intraocular inflammation.

5 WARNINGS AND PRECAUTIONS

5.1 Endophthalmitis and Retinal Detachments

Intravitreal injections may be associated with endophthalmitis and retinal detachments. Proper aseptic injection techniques must always be used when administering IZERVAY in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay, to permit prompt and appropriate management.

5.2 Neovascular AMD

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

5.3 Increase in Intraocular Pressure

Transient increases in intraocular pressure (IOP) have been observed after an intravitreal injection, including with IZERVAY. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

6 ADVERSE REACTIONS

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

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

6.1 Clinical Trials Experience

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

The safety of avacincaptad pegol was evaluated in 733 patients with AMD in two sham-controlled studies (GATHER1 and GATHER2). Of these patients, 292 were treated with intravitreal IZERVAY 2 mg (0.1 mL of 20 mg/mL solution). Three hundred thirty-two (332) patients were assigned to sham.

Adverse reactions reported in ≥2% of patients who received treatment with IZERVAY pooled across GATHER1 and GATHER2, are listed below in Table 1.

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

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

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

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies of IZERVAY administration in pregnant women. The use of IZERVAY may be considered following an assessment of the risks and benefits.

Administration of avacincaptad pegol to pregnant rats and rabbits throughout the period of organogenesis resulted in no evidence of adverse effects to the fetus or pregnant female at intravenous (IV) doses 5.1 times and 3.2 times the human exposure (based on AUC) at the maximum recommended human dose (MRHD) of 2 mg once monthly, respectively.

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

Animal Data

An embryo fetal developmental toxicity study was conducted with pregnant rats. Pregnant rats received daily intravenous (IV) injections of avacincaptad pegol from day 6 to day 17 of gestation at 0.1, 0.4, 1.2 mg/kg/day. No maternal or embryofetal adverse effects were observed at any dose evaluated. An increase in the incidence of a non-adverse skeletal variation, described as short thoracolumbar (ossification site without distal cartilage) supernumerary ribs, was observed at all doses evaluated. The clinical relevance of this finding is unknown. Plasma exposures at the high dose were 5.1 times the MRHD, based on Area Under the Curve (AUC).

An embryo fetal developmental toxicity study was conducted with pregnant rabbits. Pregnant rabbits received daily IV injections of avacincaptad pegol from day 7 to day 19 of gestation at 0.12, 0.4, 1.2 mg/kg/day. No maternal or embryofetal adverse effects were observed at any dose evaluated. Plasma exposure in pregnant rabbits at the highest dose of 1.2 mg/kg/day was 3.2 times the human exposure at the MRHD, based on AUC.

8.2 Lactation

There is no information regarding the presence of avacincaptad pegol in human milk, the effects of the drug on the breastfed infant or on milk production.

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

8.4 Pediatric Use

Safety and effectiveness of IZERVAY in pediatric patients have not been established.

8.5 Geriatric Use

Of the total number of patients who received IZERVAY in the two clinical trials, 90% (263/292) were ≥65 years and 61% (178/292) were ≥75 years of age. No significant differences in efficacy or safety of avacincaptad pegol were seen with increasing age in these studies. No dose adjustment is required in patients 65 years and above.

17 PATIENT COUNSELING INFORMATION

Advise patients that following IZERVAY administration, patients are at risk of developing neovascular AMD, endophthalmitis, elevated intraocular pressure and retinal detachments. If the eye becomes red, sensitive to light, painful, or if a patient develops a change in vision, instruct the patient to seek immediate care from an ophthalmologist.

Patients may experience temporary visual disturbances and blurring after an intravitreal injection with IZERVAY and the associated eye examinations. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

Manufactured by:
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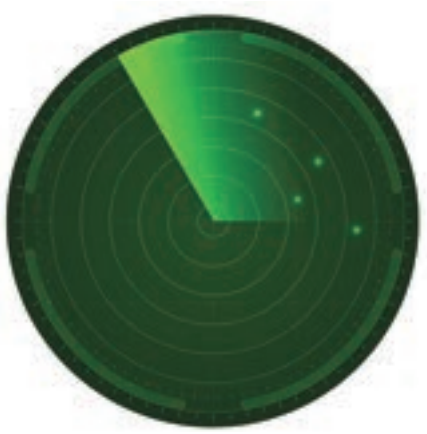

SEMAGLUTIDE INCREASES RISK OF NAION IN DIABETES

The use of semaglutide, a glucagon-like peptide-1 receptor agonist designed to improve glycemic control and reduce cardiovascular outcomes in patients with type 2 diabetes (and used off-label as a weight loss drug[1]), has recently been implicated in the increased risk of ocular diseases.[2] A recent study evaluated the potential relationship between the use of semaglutide and the development of nonarteritic anterior ischemic optic neuropathy (NAION); during 5 years of observation, the researchers found that once-weekly semaglutide more than doubled the risk of NAION in patients with type 2 diabetes.[3]

The longitudinal cohort study included 424,152 participants with type 2 diabetes who were stratified according to exposure (n = 106,454) or nonexposure (n = 317,698) to once-weekly treatment with semaglutide.[3]

During the 5-year observation period, 218 people developed NAION. Semaglutide exposure was associated with a higher incidence rate (0.228 vs 0.093 per 1,000 person-years, $P < .001$) and independently predicted a higher risk of NAION (hazard ratio: 2.19). Overall, 67 patients exposed to semaglutide developed NAION, with a median time of 22.2 months from first prescription to NAION occurrence.[3]

"Given the irreversible nature of NAION, it is important to acknowledge this risk, and upcoming studies should aim to identify high-risk subgroups," the study authors concluded in their paper.[3]

1. FDA's concerns with unapproved GLP-1 drugs used for weight loss. Food and Drug Administration. December 18, 2024. Accessed January 7, 2025. www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/fdas-concerns-unapproved-glp-1-drugs-used-weight-loss
2. Yoshida Y, Joshi P, Barri S, et al. Progression of retinopathy with glucagon-like peptide-1 receptor agonists with cardiovascular benefits in type 2 diabetes - A systematic review and meta-analysis. *J Diabetes Complications*. 2022;36(8):108255.
3. Grauslund J, Taha AA, Molander LD, Kawasaki R, Möller S, Højlund K, Stokholm L. Once-weekly semaglutide doubles the five-year risk of nonarteritic anterior ischemic optic neuropathy in a Danish cohort of 424,152 persons with type 2 diabetes. *Int J Retina Vitreous*. 2024;10(1):97.

MARKER OF CELL DEATH MAY ALSO BIND TO IMMUNE CELLS

Annexin-V has long been used as a marker of retinal ganglion cell apoptosis, which causes vision loss in glaucoma. New findings from the National Eye Institute, published in the *International Journal of Biological Sciences*, report that annexin-V also binds to immune cells.[1]

Annexin-V became a widely used marker of cell death because it binds to phosphatidyl serine, a lipid that moves to the surface of a cell in the early stages of apoptosis. It can be fluorescently labeled, which enables researchers to noninvasively visualize and track apoptosis of retinal ganglion cells in animal and human models using an imaging technique known as DARC (detection of apoptosing retinal cells), now common in the investigation of various eye diseases.[2]

Unexpectedly, the researchers found that annexin-V labeling appears at the optic nerve head, prompting them to investigate further.[2]

The team used an optic nerve crush model in mice to validate DARC imaging of apoptosis. They found that, in addition to apoptotic retinal ganglion cells, annexin-V also binds to immune cells and a subset of microglial cells in the retina, suggesting it plays a role in detecting early inflammatory responses.[2]

This provides an opportunity to monitor potential therapeutics that target microglial activation and neuroinflammation in the retina, which could be of value for neurodegenerative diseases such as AMD, glaucoma, and retinitis pigmentosa.[2]

1. Miyagishima KJ, Nadal-Nicolás FM, Ma W, Li W. Annexin-V binds subpopulation of immune cells altering its interpretation as an in vivo biomarker for apoptosis in the retina. *Int J Biol Sci*. 2024;20(15):6073-6089.
2. NEI study: new take on old marker of cell death. National Eye Institute. December 16, 2024. Accessed January 6, 2025. www.nei.nih.gov/about/news-and-events/news/nei-study-new-take-old-marker-cell-death

DNA DAMAGE IS A KEY CONTRIBUTOR TO AMD DEVELOPMENT

A research team recently reported that DNA damage compromises the retina's function and accelerates vision loss, playing a significant role in AMD development. They noted in their study, published in *Aging Cell*, that targeting specific retinal cell types may lead to treatments that slow or stop progression.[1,2]

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*Based on bench testing.

Reference: 1. Alcon data on file, 2024.

Alcon

The researchers compared a mouse model with reduced levels of ERCC1-XPF, a DNA repair enzyme, with both young, healthy mice and naturally aging mice. By 3 months, the model showed signs of visual impairment, structural alterations in the retina, abnormal blood vessel formation, shifts in gene expression and metabolism, and mitochondrial dysfunction in the retinal pigment epithelium. All these changes mirror those seen in natural human eye aging.[3]

"Our findings highlight the critical role DNA damage repair plays in maintaining retina health for good vision," author Dorota Skowronska-Krawczyk, University of California, Irvine, associate professor of physiology and biophysics, said in a news release. "Because age is the strongest risk factor for AMD, gaining deeper insights into the underlying biology of aging in the eye is essential for developing effective therapies."[3]

1. Narasimhan A, Min SH, Johnson LL, et al. The Ercc1-/Δ mouse model of XFE progeroid syndrome undergoes accelerated retinal degeneration [published online ahead of print November 27, 2024]. *Aging Cell*.
2. UC Irvine-co-led study finds DNA damage is key factor in age-related macular degeneration. UC Irvine. December 3, 2024. Accessed January 6, 2025. news.uci.edu/2024/12/03/uc-irvine-co-led-study-finds-dna-damage-is-key-factor-in-age-related-macular-degeneration
3. UC Irvine scientists find DNA damage is key factor in AMD. Eyewire+. December 6, 2024. Accessed January 6, 2025. eyewire.news/news/uc-irvine-scientists-find-dna-damage-is-key-factor-in-amd

CHATGPT-4o OUTPERFORMS GEMINI ADVANCED IN OCT INTERPRETATION

A study recently published online in *Retina* assessing the diagnostic capabilities of chatbots found that ChatGPT-4o outperformed Gemini Advanced in terms of the diagnostic accuracy of OCT and OCT angiography (OCTA) interpretation. The study included 50 cases with different surgical (n = 27) and medical (n = 23) retinal pathologies.[1] To test the diagnostic accuracy of these platforms, the researchers dragged OCT and OCTA images into the interfaces and asked the AI algorithms to "describe the image." The answers were categorized as correct, partially correct, wrong, unable to assess examination type, or diagnosis not given.

ChatGPT indicated the correct diagnosis in 31 cases (62%), significantly higher than Gemini, 16 cases (32%). In 24% of the cases, Gemini was not able to produce any answer, stating, "That's not something I'm able to do yet." For both, the primary misdiagnosis was macular edema, given erroneously in 16% and 14% of cases, respectively. Compared with Gemini, ChatGPT showed higher rates of correct diagnoses, both in the surgical (52% vs 30%) and medical retina cases (78% vs 43%). Notably, when presented without the corresponding structural image, Gemini confused images for artwork.[1]

1. Carlà MM, Crincoli E, Rizzo S. Retinal imaging analysis performed by ChatGPT-4o and Gemini Advanced: the turning point of the revolution? [published online ahead of print December 11, 2024]. *Retina*.

(Continued on page 16)

NEW YEAR, NEW OR


It's that time of year again when everyone is struggling to keep up with their New Year's resolutions to get back into shape, improve their diet, or pick up a neglected hobby. One survey found that only 13% of Americans make it to month 4 with their resolutions![1] Why so low, you ask? Experts have suggested that failed resolutions are often due to unrealistic expectations.

To do better, one Harvard-trained clinical psychologist recommends that people link their New Year's resolutions to their personal values to improve their chances of sticking with them.[1] As retina specialists, we all want to save our patients' vision—but what specific outcomes should we aim to achieve? Maybe your goal this year is to *learn a new approach to macular hole repair*, *discover a new OCT biomarker* (anyone else identifying SMACH, DRIL, DRAMA, or RIPLs on OCT?),[2-5] or *attend more retina conferences* (check out retinatoday.com/calendar for this one). However big or small your goals may be, realizing them will benefit your patients, which will also lead to a happier, healthier, and better-informed physician.[6,7]

So, let's start 2025 off right by setting attainable goals for ourselves. If one of your resolutions is to enhance your surgical skills, this issue of *Retina Today* is a great place to start. Here, experts share tips and tricks for optimizing their favorite secondary IOL techniques, while others explain why you need to dust off those scleral buckling maneuvers or practice handling human amniotic membrane grafts. Several novel surgeries are poised to shake up your OR routine, such as implanting the port delivery system (Susvimo, Genentech/Roche) or performing subretinal drug delivery, and you will find a step-by-step guide to these procedures at your fingertips.

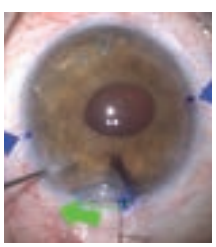
If you are feeling particularly ambitious this year, contemplate the feasibility of office-based vitrectomy and learn from international surgeons who have found success with this unorthodox model. On the lighter side, we also have a fun Q&A in which leaders in retina discuss their approaches to tough surgical scenarios (think symptomatic vitreous opacities in younger patients) and controversial topics (is music in the OR a yay or a nay?).

This issue is a celebration of innovation made possible by surgeons and researchers who never consider failing at their resolutions to improve clinic flow, OR efficiency, and patient outcomes. Try some of the surgical tips and tricks outlined in this issue, and you will be well on your way to a year of growth and prosperity as a vitreoretinal surgeon. Happy 2025, everyone! ■

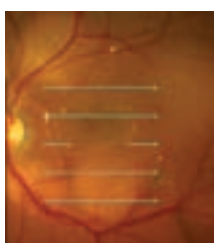
– Christina Y. Weng, MD, MBA, and Ashkan M. Abbey, MD

1. Lloyd M. 2024 New year's resolutions: nearly half cite fitness as their top priority. *Forbes*. January 12, 2024. Accessed January 3, 2025. www.forbes.com/health/mind/new-year-resolutions-survey-2024
2. Ramtohul P, Pellegrini M, Pichi F, et al. Stellate multiform amelanotic choroidopathy (SMACH). Clinical and multimodal imaging features [published online ahead of print May 1, 2023]. *Retina*.
3. Midena E, Torresin T, Schiavon S, et al. The disorganization of retinal inner layers is correlated to müller cells impairment in diabetic macular edema: an imaging and omics study. *Int J Mol Sci*. 2023;24(11):9607.
4. Madala S, Adabifirouzjaei F, Lando L, et al. Retinal ischemic perivascular lesions, a biomarker of cardiovascular disease. *Ophthalmol Retina*. 2022;6(9):865-867.
5. Cabral D, Ramtohul P, Fradinho AC, Freund KB. Volume rendering of deep retinal age-related microvascular anomalies. *Ophthalmol Retina*. 2022;6(12):1185-1193.
6. Woodward R, Cheng T, Fromewick J, Galvin SL, Latessa R. What happy physicians have in common: A qualitative study of workplace perceptions of physicians with low burnout scores. *SAGE Open Med*. 2022;10:20503121221085841.
7. Windover AK, Martinez K, Mercer MB, Neuendorf K, Boissy A, Rothberg MB. Correlates and outcomes of physician burnout within a large academic medical center. *JAMA Intern Med*. 2018;178(6):856-858.

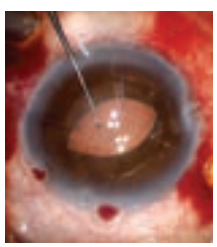
ON THE COVER



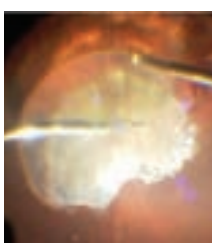
During the classic Yamane technique, place limbal marks 180° apart (blue arrows), and shift the main incision toward the surgeon's left (green arrow).
In: *Your Favorite Secondary IOL Technique*.



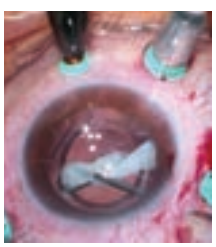
Surgeons can use intraoperative OCT to help ensure proper bleb placement during subretinal gene therapy procedures.
In: *Novel Surgical Techniques to Master*.



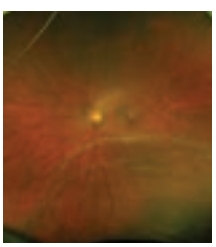
Suturing to the iris using McCannel sutures is an excellent surgical approach for a subluxed three-piece IOL in a patient with a thin sclera or conjunctiva.
In: *Your Favorite Secondary IOL Technique*.



Office-based retinal surgery in Japan is indicated for any adult vitreoretinal diseases, including the removal of retained lens fragments.
In: *The Feasibility of Vitrectomy in the Office-Based OR*.



Use ILM forceps to insert the human amniotic membrane graft into the eye and place it basement membrane-side down onto the macula.
In: *Surgical Case Spotlight: Amniotic Membrane Graft and PFO*.



Widefield fundus imaging shows that, 1 year after primary scleral buckling surgery, the retina remains attached in the right eye of a patient with high myopia.
In: *An Old Technique Made New: Scleral Buckling*.

SURGICAL TECHNIQUES AND TECHNOLOGIES

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FEATURED ARTICLES

ONLINE FEATURE

Integrating New Tech Into the OR
By Asheesh Tewari, MD; S.K. Steven Houston III, MD; and Emmanuel Y. Chang, MD, PhD

DEPARTMENTS

ONLINE EXCLUSIVE

Highlights From APVRS and fAVS 2024
By Zehua Jiang, PhD; Stanley Poh, MBBS, MMed (Ophth), FRCOphth, FAMS; and Gemmy Cheung, MBBS, FRCOphth, FAMS, MCI

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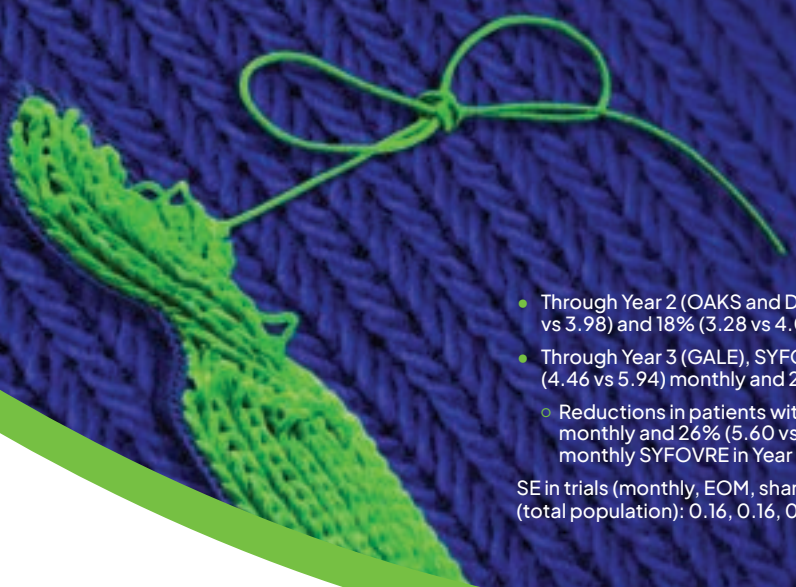


Save more retinal tissue

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

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

- **Endophthalmitis and Retinal Detachments**
  - Intravitreal injections, including those with SYFOVRE, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering SYFOVRE to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.
- **Retinal Vasculitis and/or Retinal Vascular Occlusion**
  - Retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation, have been reported with the use of SYFOVRE. Cases may occur with the first dose of SYFOVRE and may result in severe vision loss. Discontinue treatment with SYFOVRE in patients who develop these events. Patients should be instructed to report any change in vision without delay.
- **Neovascular AMD**
  - In clinical trials, use of SYFOVRE was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (12% when administered monthly, 7% when administered every other month and 3% in the control group) by Month 24. Patients receiving SYFOVRE should be monitored for signs of neovascular AMD. In case anti-Vascular Endothelial Growth Factor (anti-VEGF) is required, it should be given separately from SYFOVRE administration.
- **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.; 2023. **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.

Apellis

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

INDICATIONS AND USAGE

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

CONTRAINDICATIONS

Ocular or Periocular Infections
SYFOVRE is contraindicated in patients with ocular or periocular infections.
Active Intraocular Inflammation
SYFOVRE is contraindicated in patients with active intraocular inflammation.

WARNINGS AND PRECAUTIONS

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

ADVERSE REACTIONS

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

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

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

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

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

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

USE IN SPECIFIC POPULATIONS

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

PATIENT COUNSELING INFORMATION

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

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

SYF-PI-30NOV2023-2.0

12/23 US-PEGGA-2200163 v4.0

SUBTHRESHOLD LASER THERAPY FOR CSCR

Two cases demonstrate the effectiveness of this treatment approach.

BY RAMI MADANI, BS; ADAM AYOUB, BS; AND TAREK ALASIL, MD

Central serous chorioretinopathy (CSCR) is characterized by decompensation of the retinal pigment epithelium (RPE) and alterations of the choroidal vasculature, leading to the accumulation of fluid under the macula and, ultimately, serous detachment of the macula.[1] The exact mechanism of CSCR involves increased hydrostatic pressure in the choroid and reduced efficacy of the RPE pump.

Increased endogenous cortisol production caused by factors such as psychological stress, depression, and pregnancy can predispose patients to CSCR.[2] Additionally, type A personality traits and exogenous corticosteroid use have demonstrated strong associations with the pathogenesis of CSCR due to catecholamine-induced alterations in choroidal blood flow and permeability.[3] Research has also identified genetic predispositions and systemic risk factors of CSCR.[4]

While some cases of CSCR resolve spontaneously, others are nonresolving and require treatment. Such chronic cases, if left untreated, can lead to severe visual decline and even permanent loss of vision.[4] Because of the condition's variable prognosis and complex etiology, CSCR management presents a significant challenge. Current treatment options include laser photocoagulation, photodynamic therapy (PDT), anti-VEGF therapy, and eplerenone; however, concerns have been raised regarding cost, safety, and availability of these therapeutic modalities.[5] Subthreshold laser therapy, which uses micropulses to stimulate the RPE without visible retinal damage, offers a potentially safer alternative with quick visual recovery.[6] Here, we discuss two cases of CSCR treated with 577 nm subthreshold laser therapy using the TruScan Pro Laser 577 (LIGHTMED) and compare this approach with traditional treatment options.

CASE PRESENTATIONS

Patient No. 1

A 43-year-old woman presented with a diagnosis of CSCR in her right eye and a VA of 20/60 OD. Fluorescein angiography (FA) revealed an expansile dot consistent with CSCR, indicating leakage in the macular area (Figure 1). Given the localization of the leakage and the patient's visual acuity, the decision was made to proceed with subthreshold laser therapy using a 577 nm wavelength. The patient exhibited significant improvement in VA to 20/30+2 OD 1 month after treatment. She experienced no adverse events, and the fundus autofluorescence performed post-treatment demonstrated no signs of damage (Figure 2).

Patient No. 2

A 55-year-old man sought evaluation for blurry vision in his left eye and presented with a VA of 20/50 OS. FA and ICG angiography demonstrated an expansile dot along the superior arcade with inferior guttering toward the central macula, indicative of CSCR (Figure 3). The decision was made to employ both focal laser therapy at the superior leaking spot, due to its off-center location, and a single session of subthreshold laser within the macula. One month after treatment, a slight improvement in his VA to 20/50+2 OS was noted. This early indication of a positive response to treatment suggested the focal laser successfully targeted the leakage point, while the subthreshold laser stimulated the processes of stabilizing the RPE and reducing subretinal fluid.

After 2 months, the patient's VA showed a pronounced improvement to 20/30 OS with ongoing resolution of subretinal fluid and restoration of the macular architecture; after 6 months, the patient's VA improved to 20/25-1 OS (Figure 4). This improvement suggests subthreshold laser therapy not only addressed the immediate leakage causing the CSCR, but also promoted longterm retinal health and stability without causing additional damage.

COMPARISON WITH TRADITIONAL APPROACHES

Conventional laser photocoagulation, while a proven therapy in the management of CSCR cases exhibiting clear extrafoveal leakage, works by accelerating the resolution of subretinal fluid and sealing the leakage points; however, this process inflicts irreversible tissue damage and is associated

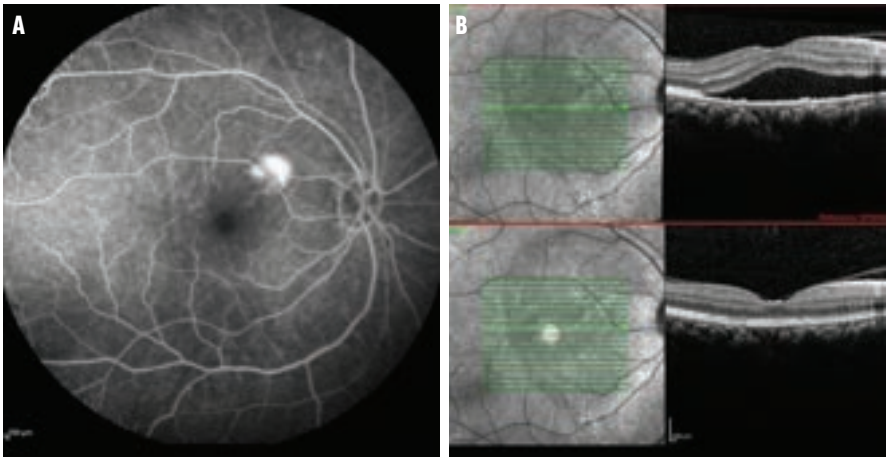


Figure 1. FA of the first patient's right eye demonstrated an expansile dot consistent with CSCR (A). Comparative spectral-domain OCT imaging revealed a serous retinal detachment in her right eye (B).

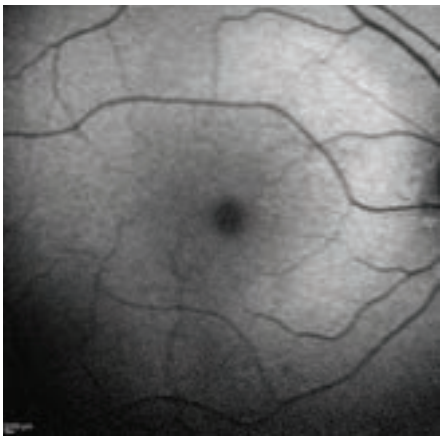


Figure 2. One month post-subthreshold laser treatment, the fundus autofluorescence showed resolution of her retinal detachment and revealed no retinal damage.

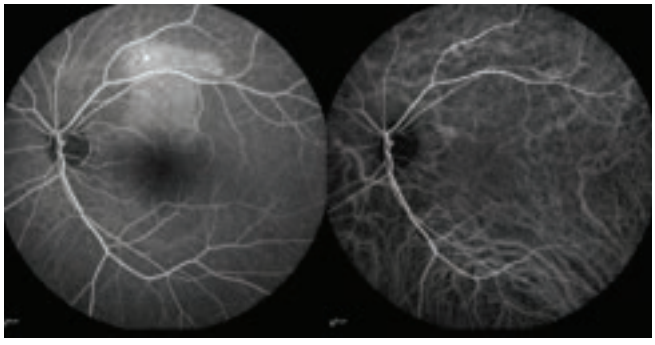


Figure 3. FA (left) and ICG angiography (right) performed for the second patient demonstrated an expansile dot along the superior arcade with inferior guttering toward the central macula, consistent with CSCR.

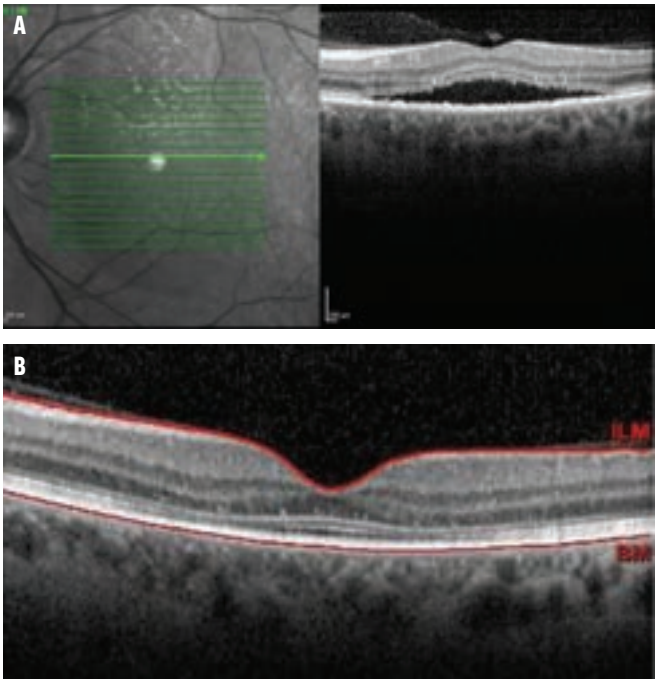


Figure 4. Spectral-domain OCT images of this patient showed evident subretinal fluid in his left eye (A). Six months post-treatment, there was a remarkable improvement in retinal architecture and resolution of fluid (B).

with complications such as scotoma, choroidal neovascularization, and enlargement of the burn-treated area over time.[7] Use of 577 nm subthreshold laser therapy would avoid these potential adverse events.

PDT is another established treatment modality, specifically in CSCR cases with subfoveal or juxtafoveal leakage, multiple leaks, or chronic, diffuse RPE decompensation. PDT facilitates choroidal vascular remodeling and induces choroidal hypoperfusion. This approach involves initial intravenous administration of verteporfin, which accumulates in the ocular tissue and is activated by laser irradiation at the leakage points, thereby sealing the RPE defects and potentially mitigating the risk of recurrence in certain cases.[8] While the efficacy and reliable safety profile of PDT cannot be overstated, the unavailability of PDT in most outpatient retina clinics, especially in underserved areas, limits its practicality as a therapeutic option.

Eplerenone, a selective aldosterone-receptor antagonist and potassium-sparing diuretic, has also emerged as an alternative therapeutic strategy for CSCR. It is administered orally and, therefore, offers a noninvasive treatment pathway. However, current literature highlights limitations in its effectiveness mainly for certain chronic cases of CSCR.[9]

Subthreshold yellow laser therapy distinguishes itself by its mechanism of gently heating the RPE without surpassing the threshold for protein denaturation. Its mechanism of action employs a train of short, repetitive pulses ranging from 0.1 to 0.5 seconds, with a brief period between successive micropulses. The time between pulses allows for heat dissipation, limiting the side effects of traditional photocoagulation and targeting the RPE specifically. Practical observations have shown that when a short pulse duration is applied to the retina, only the RPE is affected, with no harm

RT Retina Today ONE TO Watch

PETER TANG, MD, PHD

WHERE IT ALL BEGAN

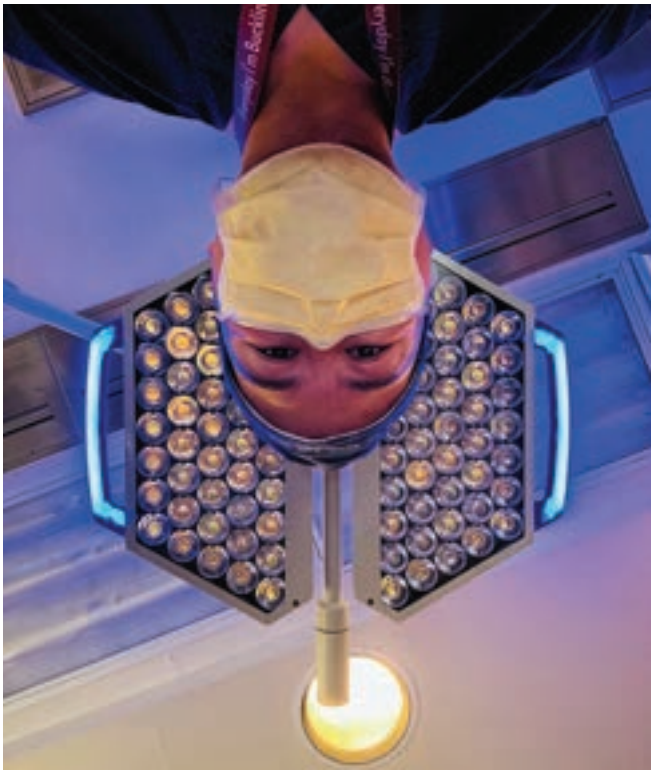
I was born in Changsha, China, immigrated to Los Angeles with my parents at age 5, and then moved to suburban Philadelphia, where I grew up. We didn't have much money to buy toys when I was young, so I crafted my own with imagination, a pair of scissors, tape, and empty cereal boxes. My homemade toys gradually became bigger, more colorful, and more elaborate. I became so skilled at making them that my friends began asking me to make them toys as well. Sometimes they would even trade their store-bought toys for my homemade toys. Before I knew it, I was running my first business—and I realized I loved working with my hands.

MY PATH TO RETINA

During my undergraduate studies, I initially matriculated into the Wharton School of Business at the University of Pennsylvania before switching over to Biology. As part of the curriculum, I had to complete mandatory laboratory rotations. By chance I was assigned to Jean Bennett, MD, PhD, at the Scheie Eye Institute. It was an exciting time to be in the Bennett lab in the early 2000s, as they were developing gene therapy to treat congenital retinal dystrophies. This opened my eyes to the MD/PhD pathway, translational medicine, and vitreoretinal surgery. I was set on becoming a retina specialist, and every step since then reinforced my conviction.

SUPPORT ALONG THE WAY

One of my most impactful mentors and friends is Prithvi Mruthyunjaya, MD, MHS, at the Byers Eye Institute at Stanford University. His thoughtfulness for his patients, dedication to his trainees, and unwaivering pursuit of elevating his craft are characteristics I try to emulate in my own career. To this day, he is only a phone call or text message away.



Dr. Tang's advice: Be so good that they can't ignore you. Never be too good to say please and thank you.

AN EXPERIENCE TO REMEMBER

It is not one experience, per se, but a shared moment that I strive for each day. This moment is when something *clicks* in the mind of my trainee, whether that be a resident physician or a medical student. After seeing multiple patients, staffing numerous surgeries, or talking through endless scenarios, the moment that my trainee *gets it* is a very special one for me. I am fortunate to be in academic medicine and work toward many more of those moments every day. ■

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To read about our other Ones to Watch, scan the QR code or visit ***Retina Today*** at retinatoday.com/resource/one-to-watch

to the inner retinal layers.[10] Thus, this innovative approach minimizes collateral tissue damage, a notable disadvantage of laser photocoagulation, by preventing the transfer of excessive thermal energy to the neurosensory retina and avoiding visible burns. Subthreshold yellow laser also is thought to enhance RPE function through the induction of heat shock proteins.[11]

A WORTHWHILE ADDITION TO YOUR ARMAMENTARIUM

The 577 nm subthreshold laser therapy is a viable option for treating cases of CSCR recalcitrant to standard laser photocoagulation therapy. It can also be done in most outpatient retina clinics, which typically lack the resources and equipment to perform PDT. Large-scale studies should focus on expanding the use of the 577 nm subthreshold laser in the management of CSCR; specifically, there is a need for clinical trials to directly compare its safety and efficacy with that of laser photocoagulation to firmly establish its position within the spectrum of available treatments for CSCR.[12] ■

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(Continued from page 8)

MUSEUM EXHIBIT IMPROVES ACCESSIBILITY FOR VISUALLY IMPAIRED

The Truhlesen-Marmor Museum of the Eye, located on the ground floor of the American Academy of Ophthalmology in San Francisco, opened a new exhibit in December to enhance the museum experience for guests who are blind or visually impaired.[1]

Features of the exhibit use 3D, tactile renderings of images, braille, and sound to deliver information about the artwork. The exhibit honors the legacy of noted ophthalmologist and ophthalmic historian, Jay M. Galst, MD, who passed away in 2020. It is now free and open to the public.[1] ■

1. New Museum of the Eye exhibit brings images to life for the visually impaired and blind. Eyewire+. December 31, 2024. Accessed January 7, 2025. bit.ly/3DZWpPm

Eyewire+ Pharma Update

- **Galimedix Therapeutics** announced the initiation of a phase 2 trial for its GAL-101 eye drops for the treatment of geographic atrophy (GA). The trial is enrolling up to 110 participants with a primary endpoint of reduction in the rate of change of the GA lesion size.
- **Opus Genetics** reached an agreement with the FDA on a special protocol assessment for a phase 3 clinical trial evaluating oral APX3330 for the treatment of moderate to severe nonproliferative diabetic retinopathy.
- **Celltrion** announced that the Committee for Medicinal Products for Human Use of the European Medicines Agency (EMA) recommended marketing authorizations for three biosimilar candidates, including CT-P42 (Eydenzelt), an aflibercept biosimilar.
- The FDA cleared the investigational new drug application for the phase 1/2 trial of **VG801 (ViGeneron)**, a gene therapy candidate for the treatment of Stargardt disease, among other retinal dystrophies caused by mutations in the *ABCA4* gene.
- The phase 3 QUASAR trial of **8 mg aflibercept (Eylea HD, Regeneron)** for the treatment of patients with macular edema following central, branch, and hemiretinal vein occlusions met its primary endpoint.
- The EMA approved the **6 mg faricimab (Vabysmo, Genentech/Roche)** single-dose prefilled syringe for the treatment of wet AMD, diabetic macular edema, and macular edema following retinal vein occlusion.
- **Regeneron** recently acquired Oxular, whose lead drug candidate is OXU-001, a dexamethasone formulation delivered to the suprachoroidal space via a proprietary illuminated microcatheter.
- **OPL-0401 (Valo Health)** did not meet its primary or secondary endpoints in the phase 2 SPECTRA study of patients with diabetic retinopathy. Valo has suspend development and is seeking a partner to further develop the program.

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YOUR FAVORITE SECONDARY IOL TECHNIQUE

Surgeons share their go-to approaches for managing dislocated IOLs and pearls for surgical success.

By Ninel Z. Gregori, MD; Allison J. Chen, MD, MPH; Omesh P. Gupta, MD, MBA; María H. Berrocal, MD; and Jeremy D. Wolfe, MD, MS

When a patient walks into the clinic with a dislocated IOL, we have myriad surgical approaches to manage the case, depending on the patient's need. Which technique you choose is often a blend of the particulars of the case itself and surgeon preference. Here, we share our favorite approaches to secondary IOLs and our tips for optimizing the surgery.

IRIS FIXATION

By Ninel Z. Gregori, MD

Suturing to the iris is an excellent approach for a subluxed three-piece IOL in a patient with a thin sclera or conjunctiva. All sutures are contained within the eye, and there is no conduit for infectious organisms. I have used the MA60AC lens (Alcon) for years, but other three-piece IOLs should also work well.

For this technique, surgeons can use either McCannel sutures (throw and tie the sutures outside the eye) or Siepser knots (throw the sutures outside but tie them inside the eye) to secure the IOL to the iris. I prefer to use the McCannel suture with 9-0 or 10-0 prolene suture and a CIF-4 long-curved needle because it does not tear the iris (Video 1). The technique has three major steps to master:

1. Prolapse the optic over the iris and visualize the haptic, then pass the suture through the cornea, down to the iris, under the IOL haptic, back up through the iris, and out of the cornea.
2. Externalize the free ends of the suture through a paracentesis positioned over the haptic.
3. Tie the externalized ends with a square knot. I prefer to use 3-1-1-1 square knots—I add an extra throw to ensure the knot is stable.

I like to put two McCannel sutures around each haptic because doing so has led to zero dislocations. Consider passing the needle and suture close to the periphery of the iris to reduce the risk of creating the cat-eye look. When done correctly, this technique can provide stable optics with little risk of dislocation and an aesthetically round pupil.

AT A GLANCE

- Suturing to the iris is an excellent approach for a patient with a thin sclera or conjunctiva.
- Double-needle scleral fixation is useful for patients with healthy conjunctiva superiorly and inferiorly.
- Gore-Tex IOL fixation is ideal for dislocated IOLs or aphakia cases with a healthy and mobile conjunctiva.
- The modified Yamane technique is a good approach for eyes without capsular support that are aphakic or eyes that have a dislocated one-piece IOL.

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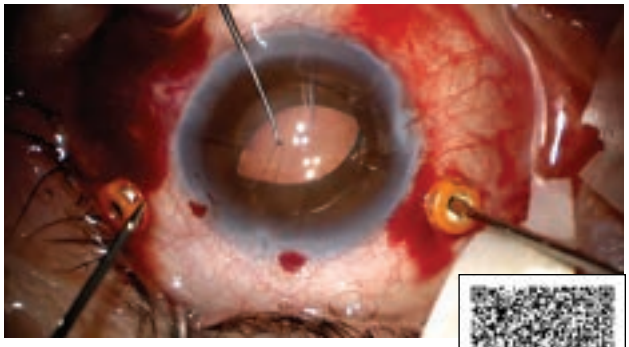

Video 1. Iris Fixation of an IOL With McCannel Sutures.
By Ninel Z. Gregori, MD

THE YAMANE TECHNIQUE

By Allison J. Chen, MD, MPH

Double-needle scleral fixation is an elegant surgery that requires less tissue manipulation than IOL suturing. Scleral maneuvering is minimized with only two tunneled sclerotomies; with a 30-gauge TSK needle, the tunneled sclerotomies automatically seal upon needle externalization.

I prefer to use this approach for any patient who has healthy conjunctiva superiorly and inferiorly so that there is adequate conjunctival coverage over the flanged terminal bulbs—this decreases the risk of haptic exposure and infection. I also look at the patient's white-to-white corneal diameter to ensure it is less than 15 mm to decrease the risk of high torque at the optic-haptic junction.

I would like to share these surgical pearls:

- The optimal three-piece IOLs to thread (due to the angles at the optic-haptic junction) include the Sensar AR40 series (polymethylmethacrylate [PMMA] haptics, Johnson & Johnson Vision), Tecnis ZA9003 (PMMA haptics, Johnson & Johnson Vision), and CT Lucia 602 (polyvinylidene fluoride haptic, Carl Zeiss Meditec). PMMA haptics tend to be more brittle and prone to damage if too much force is applied, but these IOLs are reliable. Watch for occasional dislocation or rotation of the optic-haptic junction with the CT Lucia 602 lens.
- The optimal tunneling needle for this technique is the TSK 30-gauge x 1/2" because it has a larger internal lumen than a usual 30-gauge needle, so there is more space for haptics to pass through. If the fit is quite snug (especially with the AR40 series), I occasionally switch to a 27-gauge needle with a larger lumen.
- My preference is to sit temporally and tunnel superiorly and inferiorly because the vertical diameter of the cornea is smaller than the horizontal diameter, and this position minimizes the torque on the haptics.

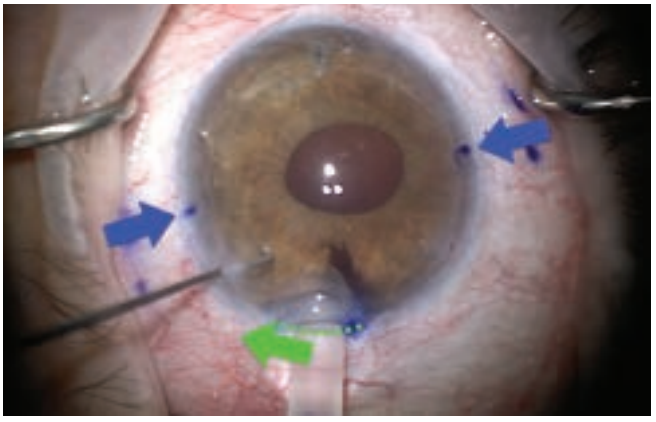

Figure 1. During the classic Yamane technique, place limbal marks 180° apart (blue arrows), and shift the main incision toward the surgeon's left (green arrow).

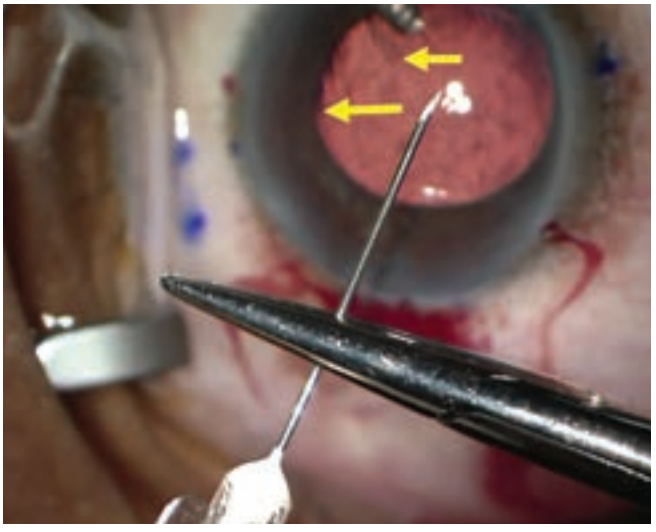

Figure 2. Turn the needle bevel toward the left (arrows) before bending the needle 45° to facilitate haptic docking.

- I shift the main incision to the left (clockwise) to facilitate docking of the trailing haptic (Figure 1).
- I turn the needle bevel toward the left before bending the needle upwards approximately 45° (Figure 2). This facilitates intraocular docking of the haptics because the needle bevel acts as a platform and provides countertraction against the haptic during docking.
- Balanced salt solution is placed in the syringe attached to the needle to prevent air bubbles from entering the anterior chamber during haptic threading. During scleral tunneling, the needle should enter the globe planar (or at a slightly more posterior angle) to the iris; try not to enter too anteriorly to avoid IOL-iris touch and future uveitis-glaucoma-hyphema syndrome. Tunnel symmetrically on both sides.
- I place a peripheral iridotomy (PI) as insurance against pupillary block in the setting of potential reverse iris capture in the future.

TIPS FOR TACKLING NEOCORTEX


By Steve Charles, MD, and Adam Pflugrath, MD

Dislocated IOLs are often accompanied by a large amount of neocortex (Sommering ring), making forceps purchase of the IOL difficult and requiring a larger incision, thereby increasing the risk of corneal endothelial damage during removal. Removal of neocortex from the haptics with a vitreous cutter is challenging, time consuming, and can result in IOL drops, increasing the risk of retinal damage. Often, it is not possible to remove any or all the neocortex with the vitreous cutter. We have found it useful to use the fragmenter to remove neocortex from the haptics. We perform a careful and complete pars plana vitrectomy with wide-angle visualization. We grasp the IOL haptic with textured end-grasping forceps and move the IOL to just posterior to the iris plane. We then remove the endoilluminator and enlarge the sclerotomy to accommodate the fragmenter; you could also create an additional sclerotomy with a 20-gauge MVR blade. We remove all neocortex and capsule from the haptics before moving the IOL through the pupil to the anterior chamber for explantation. ■

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SUTURED GORE-TEX IOL FIXATION

By Omesh P. Gupta, MD, MBA

Scleral fixation of a secondary IOL with polytetrafluoroethylene (Gore-Tex, W.L. Gore) uses a lens that is foldable through a small clear corneal incision (Video 2). The suture has a high tensile strength and, due its porous nature, promotes cellular ingrowth within 6 to 12 months. There is no permanent foreign body left underneath the conjunctiva.

The EnVista MX60 (Bausch + Lomb) is one of my favorite IOLs for this technique due to the hydrophilic material; it does not opacify with air or gas tamponade and has predictable refractive outcomes. In one study, eyes with Gore-Tex sutures were statistically closer to the refractive target compared with eyes treated with the Yamane technique.[1]

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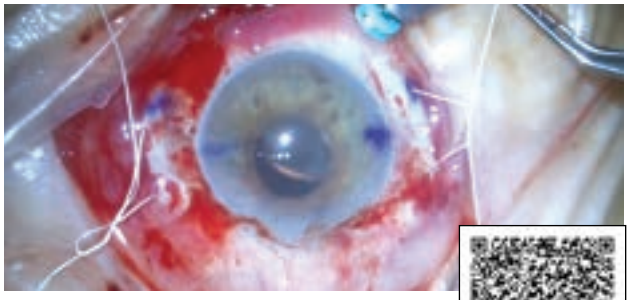

Video 2. Scleral Fixation of an IOL With Gore-Tex. By Omesh P. Gupta, MD, MBA

The procedure is ideal for any dislocated IOL or aphakia case with a healthy and mobile conjunctiva. I avoid eyes with atopic or cicatricial conjunctival disease. Relative contraindications include patients with significant conjunctival scarring secondary to trauma or previous ocular surgery. Patients with a history of a trabeculectomy, tube shunt, scleral buckle, or ruptured globe are all potential candidates.

The refractive outcome depends on fixating precisely 3 mm posterior to the limbus for an in-the-bag calculation. To improve efficiency, I try to perform these procedures from the same orientation. I sit superiorly and scleral fixate at the 3 and 9 clock hours. Meticulous hemostasis is crucial. Spending extra seconds cauterizing the scleral beds saves minutes during the case. Try to eliminate suture slack when threading the Gore-Tex in the eye to minimize the possibility of tangling the suture and twisting the IOL. Do not place any instruments through the eyelet of the lens and refrain from overtightening the suture—these missteps can affect the integrity of the eyelet, leading to fracture and dislocation. When reapproximating the conjunctiva, place the suture and scleral anchor away from the Gore-Tex. I prefer to close the conjunctiva inferotemporal and inferonasal, which ensures only intact conjunctiva is over the Gore-Tex without any conjunctival edges. Lastly, advising patients on the recovery time can help manage postoperative expectations. While these patients can recover significant vision within the first 1 to 2 weeks, most patients reach the ultimate vision approximately 4 to 6 weeks postoperatively. In addition, patients should also be advised that a refraction may be necessary.

TROCAR-ASSISTED MODIFIED YAMANE

By María H. Berrocal, MD

My go-to technique for secondary IOLs without capsular support is the trocar-assisted modified Yamane using the three trocars available in the vitrectomy pack (Video 3). This approach has two main advantages over the classic Yamane technique. First, the length and angle of the scleral tunnels are more

reproducible when performed with the 27-gauge trocar cannulas than with the 30-gauge needles, thus reducing the possibility of tilt. Second, grasping the tip of the haptic with forceps is easier than feeding them into the needle hub. I use only three trocars and change the infusion as needed. This streamlines the procedure because it does not require extra trocars and does not add cost.

I use this approach for eyes without capsular support that are aphakic or eyes that have a dislocated one-piece IOL that needs exchange. I use the CT Lucia 602 lens because the polyvinylidene fluoride haptics are sturdier than prolene haptics. I do not use this technique in highly myopic eyes with thin sclera because it is difficult to create a good tunnel. In those cases, my go-to technique is Gore-Tex fixation of an EnVista MX60 lens. There are several surgical pearls to keep in mind with the modified Yamane technique, including:

- Measure and mark 180° apart for the placement of the cannulas 2.5 mm to 3 mm from the limbus.
- Choose the areas of sclera that have no calcifications.
- Displace the conjunctiva as you enter the trocars, and enter in opposing directions.
- Grab the tip of the haptic and withdraw the cannula; as the forceps grasping the haptic moves out of the eye, cauterize the tip of the haptic to prevent migration into the eye when the second haptic is grasped.
- Reintroduce the removed cannula in another location.
- Move the infusion to another cannula if the initial infusion cannula will be used to remove the second haptic
- Pull on both haptics to ensure proper centration, and trim and cauterize if needed.
- Bury the cauterized tip into the sclera and perform a PI.

LASER-LOCK

By Jeremy D. Wolfe, MD, MS

The laser-lock technique is my go-to approach for cases in which the haptics are properly fixated in the sclera but the lens is tilted as a result of rotation at the optic-haptic junction. It is especially useful in eyes where an IOL exchange would be challenging due to scarring or other abnormalities of the cornea, sclera, or conjunctiva.

To optimize this new approach, visualization is key. Thus, I do not hesitate to use iris hooks to mechanically dilate the iris and improve visualization of the target. I prefer to use a curved laser probe to more effectively target the optic-haptic junction. In addition, I find longer laser duration to be most effective in this scenario.

SO MANY OPTIONS, SO LITTLE TIME

With myriad techniques at your fingertips for managing dislocated lenses, the true key to success is confidence in the approach. While it is useful to be proficient with several secondary IOL techniques, consider finding one that works best for you and mastering that approach. Just remember to be flexible when a patient requires a different technique to ensure lens stability and optimal visual outcomes. ■

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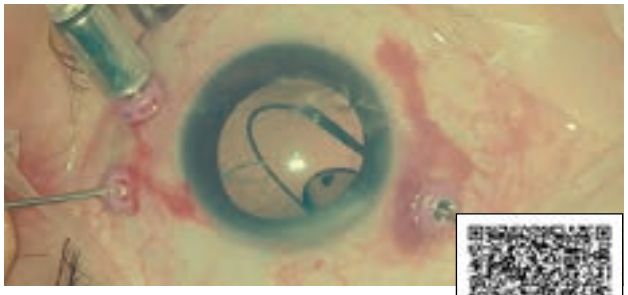

Video 3. Modified Yamane for Dislocated Three-Piece PMMA IOL. By María H. Berrocal, MD

1. Oh G, et al. Surgical outcomes of combined pars plana vitrectomy and scleral fixation of intraocular lenses: comparison of Gore-tex suture vs intrascleral haptic fixation. In Press.

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GEOGRAPHIC ATROPHY: Options in Clinical Therapy

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VOLUME 2

WANT TO READ THE FIRST ROUNDTABLE IN THIS SERIES? SCAN THE QR CODE.

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Complement Inhibition: The End of the Beginning, Not the Beginning of the End

JOHN W. KITCHENS, MD; MIGUEL BUSQUETS, MD; AND ESTHER KIM, MD

John W. Kitchens, MD: How does the approval of geographic atrophy (GA) treatments compare with the early treatments for wet age-related macular degeneration (AMD), which eventually advanced to the era of anti-VEGF therapy?

Miguel Busquets, MD: The FDA approval of complement mediators for the treatment of GA signaled a significant transformation in our capacity to practice medicine. Looking at the history of wet AMD, our field was thrilled to have access to photodynamic therapy (PDT) and pegaptanib sodium (Macugen) as the first treatments for this disease. Although these treatments didn't improve vision, they allowed us to begin controlling wet AMD and slowing its progression.

We face a similar dynamic in GA treatments today. Even if the efficacy and outcomes of GA treatments haven't reached their full potential, we still have an opportunity to treat patients who were previously untreatable.

Treating wet AMD patients with PDT and pegaptanib also led to deeper relationships with those patients who would eventually benefit from anti-VEGF treatment. We didn't give up on those patients, and that meant a lot to them. We can similarly set up GA patients for success by managing their disease with the treatments we currently have at our disposal.

Esther Kim, MD: I think of complement inhibitors for GA as signaling the end of the beginning, not the beginning of the end. We have somewhere to start, which is why the approval of these drugs is so exciting.

Dr. Kitchens: I'd like to hear about the patients in your clinic who you initially treated for GA.

Dr. Kim: Many of my earliest patients with GA who received treatment were patients with wet AMD who, despite complying with suggested anti-VEGF regimens, continued to lose vision due to concomitant GA.

Although these patients were frustrated that a new therapy would not restore sight in the way anti-VEGF agents could, they were comfortable with the concept of regular intravitreal injections, and were therefore easy to get on board.

Now I am seeing a second wave of patients: those who have been referred by comprehensive ophthalmologists and optometrists who have identified that referral to a retina specialist is warranted. This is a credit to our referring providers, as they have

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effectively educated themselves to spot nascent GA.

These patients present a new challenge, as we must build relationships with them and gain their trust before we tell them that, despite the likelihood of losing vision over time, the drugs that we have at our disposal are the best guard against progression of GA.

Dr. Kitchens: How do you use imaging to educate patients about their disease?

Dr. Kim: A picture says a thousand words. You can descriptively tell a patient with extrafoveal disease that future encroachment of their fovea will lead to vision loss, but they seem to instinctively understand the stakes and likely progression of GA when you show them an OCT or fundus autofluorescence image of their GA lesions. At that point, most of my patients opt for complement inhibition therapy.

We must stay positive with our patients once they understand the prognosis. Rather than bluntly stating that they will slowly lose vision, I frame the discussion around the fact that two FDA-approved therapies exist, and that they have been shown to slow the progression of disease. I always make it clear that they cannot expect to experience returned vision, but that these treatments are a significant improvement over non-intervention.

Which Patients Are Best Suited for Treatment?

JOHN W. KITCHENS, MD; SARADHA CHEXAL, MD; AND GEETA LALWANI, MD

John W. Kitchens, MD: We're all familiar with the data surrounding the two FDA-approved treatments for GA. But the art of medicine rests in figuring out how to apply those data to the real-world. With that in mind, which patients are best suited for complement inhibition therapy?

Geeta Lalwani, MD: Patient buy-in is key. Patients with functional vision in only one eye and GA in the contralateral eye are often highly motivated to initiate and comply with treatment. These patients understand the experience of lost vision and are eager to preserve whatever vision remains.

Patients who are likely to progress quickly based on imaging results—such as patients with multifocal lesions or fundus autofluorescenc patterns that forecast rapid growth—are great candidates for treatment. However, patients with extrafoveal disease who have not yet experienced significant disruption may be less interested in undergoing therapy than we would like them to be. This is where patient education comes in: it's on us to educate these patients about their disease and its likely consequences so that they can make a maximally informed treatment decision.

Saradha Chexal, MD: I find personal experience to be highly motivating for many GA patients. Even if they have not yet experienced vision loss due to GA, they often understand the stakes of disease progression if a family member, neighbor, or friend has struggled with vision loss. We still must educate these patients on the value of regular visits, but in these patients, some of the education regarding quality-of-life concerns is already done.

Dr. Kitchens: Convincing a motivated patient to come to the clinic for GA treatments is easy. But how do we motivate patients who fail to grasp the urgency of their disease?

Dr. Chexal: GA is a silent disease until it's not, so patients who aren't experiencing vision loss may be less interested in regular visits—and many only become interested after it's too late to effectively intervene.

In these patients, I find that longitudinal imaging results serve as an effective educational tool. If patients with extrafoveal disease can see how quickly their lesions have grown over a given period, they may be more likely to understand how treatment could benefit them.

Dr. Kitchens: What about patients who are just starting to experience symptoms? Is there any hope for them, or is it too late?

Dr. Lalwani: There is hope of buying them time. Patients sometimes best understand this concept via figurative language. I tell my patients to imagine that their two eyes are falling from the sky toward earth, and that using a complement inhibitor is akin to attaching a parachute to their eyes—and the higher up in the sky we deploy that parachute, the more time they will have until landing. Will it stop their eyes from landing on the ground? No. But will it slow the rate at which they fall through the atmosphere? Probably.

Incidentally, I find that this metaphor saves me chair time. Patients quickly understand the concept and are often interested in deploying a parachute after hearing their disease framed this way. ■

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NOVEL SURGICAL TECHNIQUES TO MASTER

An overview of ports, implants, and gene therapy making their way into your surgical toolkit.

By David A. Eichenbaum, MD, FASRS, and Albert J. Augustin, MD

Before the advent of anti-VEGF agents in 2006, most retina conditions were handled in the OR. Once anti-VEGF therapy proved efficacious for several retinal diseases, injection clinics quickly became packed with patients seeking medical treatment. However, recent advances in our therapeutic approaches may have some patients headed back to the OR for an ocular implant or subretinal drug delivery. Here, we share the latest surgical techniques you need to be familiar with and tips for mastering them in your OR.

IN THE OR NOW: PDS

By David A. Eichenbaum, MD, FASRS

With the reintroduction of the port delivery system (PDS) with ranibizumab (Susvimo, Genentech/Roche) in July 2024, physicians now have a surgical approach to consider for patients with wet AMD. PDS implantation can be performed by any retina surgeon, and the more technical aspects of the procedure are easily mastered with practice.

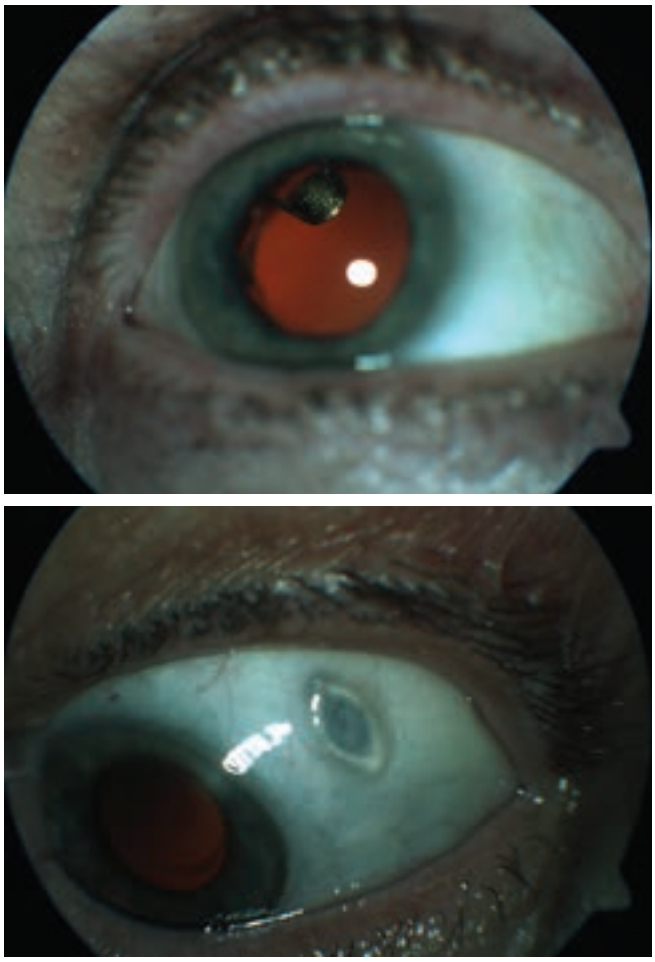
I start PDS cases by placing a 25- or 27-gauge infusion cannula in the far inferotemporal quadrant near the 5 clock hour and a traction suture through the cornea supero-temporally—approximately where I will place my port—to ensure good exposure.

Next, using nontraumatic forceps, I make a generous conjunctival flap (larger than the recommended 6 mm x 6 mm) and carefully and completely undermine the conjunctiva and Tenon's with blunt dissection, being careful to capture both layers of tissue. Surgeons should take care to position the entire flap inferiorly in the superotemporal quadrant because the implant is preferentially tucked superiorly and inset toward the corner of the flap. A slightly lower flap and implant position will facilitate refill-exchanges in the clinic. Surgeons should remember to keep the flap hydrated during the case to preserve its elasticity.

Once I have exposed and dried the sclera, often with wet-field eraser cautery, I make precise and discrete ink

AT A GLANCE

- Surgeons now have a surgical approach to wet AMD therapy with the port delivery system with ranibizumab (Susvimo, Genentech/Roche), which requires a careful implant procedure.
- Implanting the Smaller-Incision, New-Generation Implantable Miniature Telescope (Samsara Vision) requires a modified cataract surgery approach.
- When delivering gene therapy subretinally, inflate the finished bleb's borders to well outside the macula in the inferior periphery, and do not allow the bleb to touch the optic nerve.



Courtesy of David A. Eichenbaum, MD, FASRS

Figure 1. The PDS should be placed superiorly and inset toward the corner of the flap to facilitate refill-exchanges in the clinic.

marks with a 3.5 mm caliper using minimal pressure. One of the most important attributes to safe, long-term implant retention is an incision that is not too large; thus, an accurate measurement is worth the extra care and time. Because the implant will be refilled in the middle of the 3.5 mm marks, postoperative accessibility is important, so plan your 3.5 mm marks accordingly. The implant should be tucked deeper into the hinged base of the flap and not toward the edge of the radial wound to avoid positioning the flange near the radial incision.

After the sclera is marked, dissected, and the choroid at the pars plana is lasered with special attention to the wound edges, I use a 3.2 mm keratome blade slit knife to make the incision in one smooth motion, with the infusion off, incising past the diamond on the blade before withdrawing. I pause after withdrawing the blade to ensure there is no bleeding at the wound edges; if there is, I treat with taper-tip cautery, which I already have accessible but unopened in the OR.

I insert the implant with the supplied insertion device and turn the infusion on as soon as the implant is engaged in the wound for counter pressure. I clean any external vitreous with the cutter only after the implant is seated and ensure the implant flanges are aligned parallel to the limbus after placement (Figure 1).

The final step is to fully cover the implant with the conjunctiva-Tenon's flap. I typically use 8-0 Vicryl and close the distal corner first, targeting 1 mm to 2 mm of overlap onto the cornea because the tissue retracts posteriorly postoperatively. I ensure there is plenty of flap elasticity and undermine more now if needed to achieve traction-free closure over the flange. I am careful not to close the radial incision over the flange of the implant. If the implant's placement is too close to the radial incision and the conjunctiva is closing over the flange, I recommend generous conjunctival overlap along the radial edge.

IN CLINICAL TRIALS: IMPLANTS AND SUBRETINAL DELIVERY

Several surgical innovations curently under investigation may soon send certain AMD patients into the OR for novel treatment approaches.

Subretinal Gene Therapy

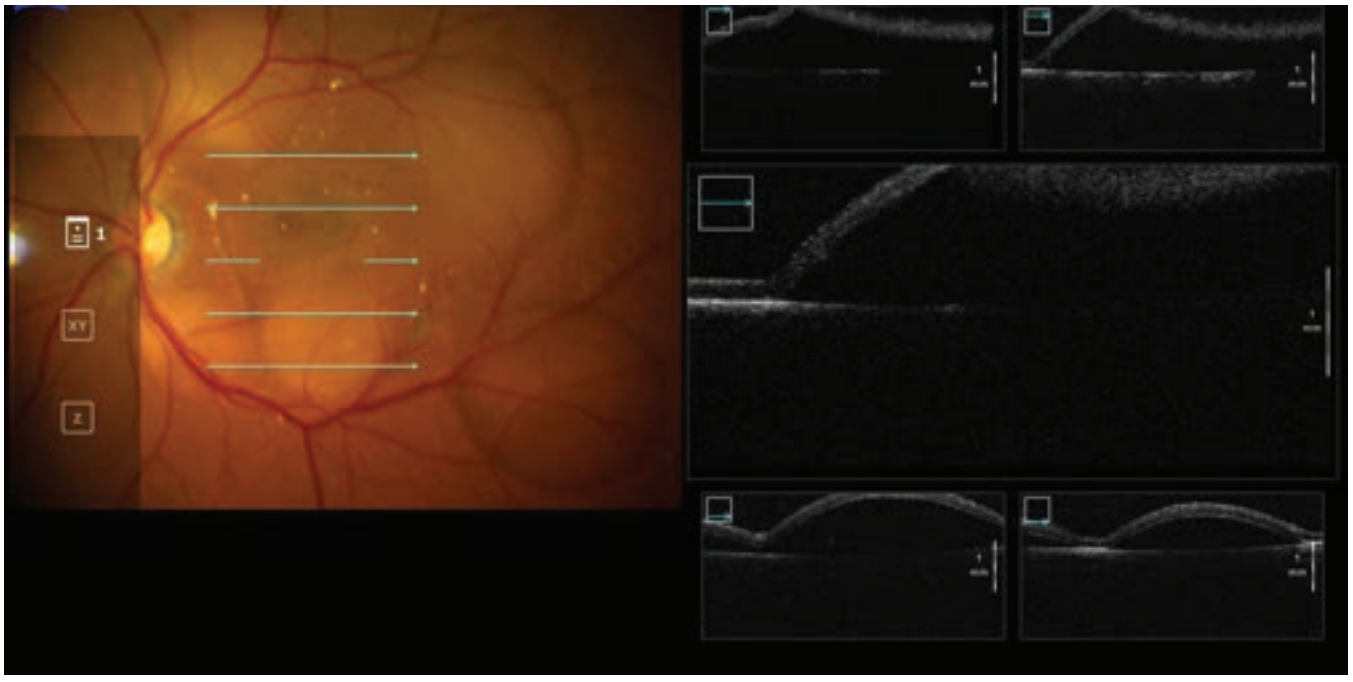
By David A. Eichenbaum, MD, FASRS

There are several technologies under investigation to mitigate frequent intravitreal anti-VEGF injections, including subretinal gene therapy with ABBV-RGX-314 (Regenexbio/Abbvie). This therapy requires vitrectomy followed by subretinal injection. The following tips and tricks can help make subretinal injection and bleb creation approachable and successful.

The first step is good visualization (Figure 2). In the ABBV-RGX-314 clinical trials, all subjects are pseudophakic, and, per protocol, we are using 23-gauge instrumentation with a retractable polyamide subretinal injection cannula. The same techniques can be applied to subretinal injection with 25-gauge nonretractable polyamide injectors. I perform the entire subretinal injection case under wide-angle visualization and do not use a high-magnification lens. I stain the vitreous with diluted triamcinolone to ensure that there is complete vitreous separation without vitreoschisis—even a thin sheet of posterior hyaloid will inhibit subretinal injection.

Next, the surgical protocol includes inflating the finished bleb's borders to well outside (at least 2 disc diameters) the macula in the inferior periphery and not allowing the bleb to touch the optic nerve. In my experience, subretinal blebs propagate posteriorly, and I place my bleb inferonasally; thus, I try to start my bleb as anteriorly as I can comfortably visualize. The 200 ul of gene therapy product injected generates a surprisingly large bleb, and, although I prefer one bleb, the trial allows for multiple blebs, if necessary.

It is vital to have a good spotter in the OR for accurate



Courtesy Charles C. Wykoff, MD, PhD

Figure 2. Intraoperative OCT can help surgeons ensure proper bleb placement during subretinal gene therapy procedures.

dosing. Before I begin my bleb, I turn my syringe with the gene product to my circulating nurse who then uses a penlight to illuminate the markings. I advance the bung to a visible marking with well more than 200 ul of fluid in the syringe. As soon as my bleb starts propagating, I voice "bleb," and the circulating nurse counts down 200 ul from that point. Filling a single bleb with a wide-open pedal takes about 60 seconds.

When initiating the bleb, I do not cut the tip of the polyamide subretinal cannula into an angle. I place my round cannula directly on the peripheral retina where I start my bleb, generating a very slight blanching of the retinal pigment epithelium-choroid, then pull back ever so slightly before hitting the pedal and starting the bleb. Surgeons can also start the flow of fluid before "touching down" and using the jet of fluid and the cannula tip to initiate the bleb.

To minimize efflux from the bleb, hold your cannula stable to keep from enlarging the tiny retinotomy, and plug the bleb for approximately 5 to 10 seconds after completing the injection. Upon withdrawing the cannula, some drug may flow out of the bleb, but this should be small with an atraumatic retinotomy and a few seconds of plugging. Scleral depression should be performed before bleb formation, not after.

To ensure that the subretinal drug stays in the inferior periphery, partially fill the eye with air and sit the patient up for several hours. I perform a 2/3 fluid-air exchange and instruct the patient to keep at least a 45° upright angle for 24 hours.

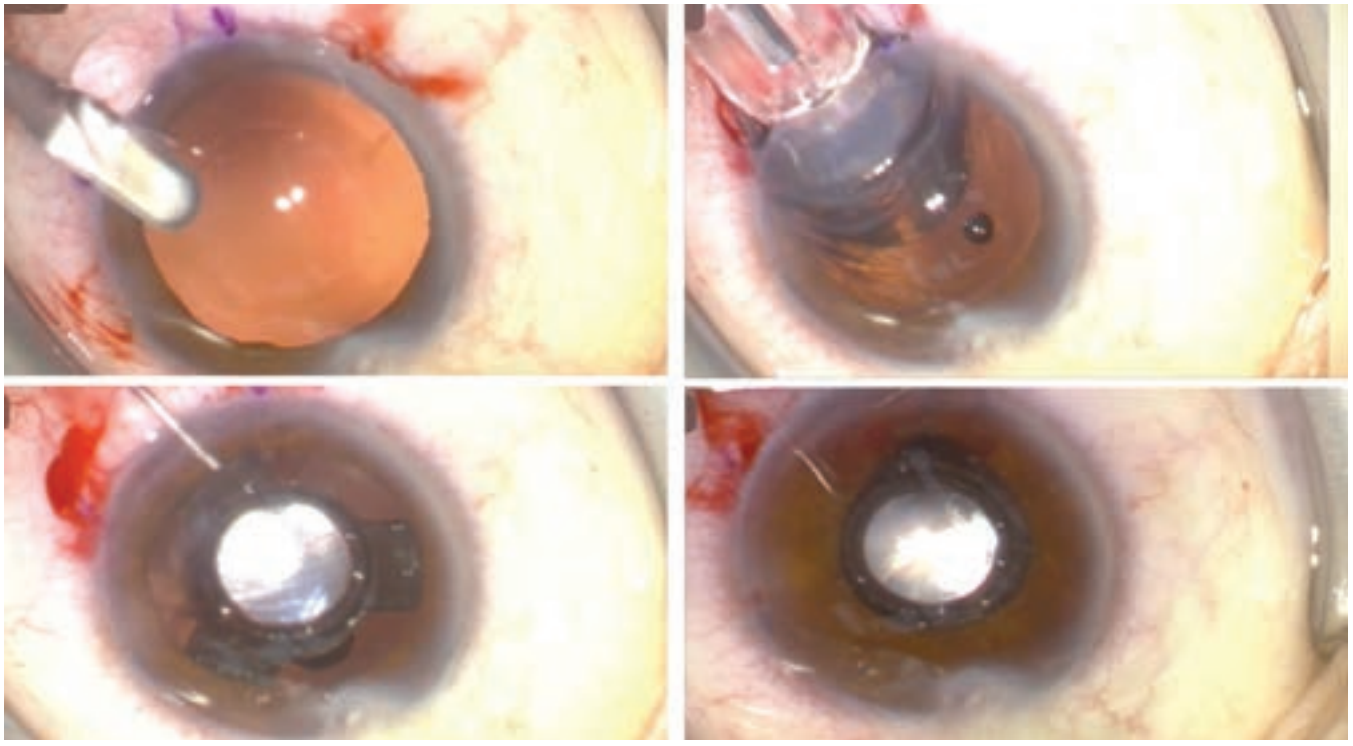
SING IMT: An Intraocular Telescopic Device for AMD

By Albert J. Augustin, MD

The Smaller-Incision, New-Generation Implantable Miniature Telescope (SING IMT, Samsara Vision; not yet FDA approved) offers a significant improvement over the original version for late-stage AMD patients, as it is smaller, less invasive, and capable of enhancing both distance and near visual acuity. Implanting the SING IMT requires a modified cataract surgery approach.

The SING IMT implantation begins with peribulbar anesthesia administered approximately 10 minutes before surgery. After adequate iris dilation, a conjunctival peritomy is performed at the 12 clock position, with scleral bleeding controlled using bipolar coagulation. A 2.75 mm sclerocorneal tunnel is created approximately 1 mm from the corneal limbus. Two side-service paracenteses are made at the 5 and 7 clock positions, and a dispersive OVD is injected into the anterior chamber to maintain stability. A continuous manual circular anterior capsulorhexis (5.5 mm to 6 mm) is completed, followed by standard cataract surgery procedures to prepare the eye for implantation.

The SING IMT is preloaded in the Tsert delivery system, including the cartridge and injector. Before implantation, the anterior chamber and capsular bag are filled with viscoadaptive OVD. The sclerocorneal incision is enlarged to 7.5 mm to 8 mm to accommodate the device, with the injector tip positioned at a 45° angle to the corneolimbal incision. As the tip reaches the capsulorhexis plane, the SING IMT is carefully inserted into the capsular bag (Figure 3). The two inferior



Courtesy of Albert J. Augustin, MD

Figure 3. Implantation of the SING IMT involves a modified cataract surgery followed by implantation of the device using the company's Tsert delivery system.

haptics and one superior haptic are secured within the capsular bag. Two or three nylon sutures (10-0) are applied to securely close the sclerocorneal incision.

After removing the OVD, an iridectomy is performed at the 12 clock position to prevent a postoperative pupillary block. Finally, 0.1 mL of intracameral cefuroxime is injected and the conjunctiva is sutured to ensure stability and minimize the risk of dislocation. The procedure takes approximately 20 to 30 minutes, with no significant complications reported. A successful implantation depends on achieving a sufficiently wide anterior capsulorhexis to avoid injector misalignment and associated complications.[1,2]

Postoperative care is critical to optimize outcomes and prevent complications, such as infection, inflammation, and device dislocation. The postoperative regimen includes topical antibiotics and antiinflammatory agents, administered for up to 30 days. Additional medications, including NSAIDs and cycloplegic agents, may be prescribed based on individual patient needs. The most crucial aspect of postoperative care is visual rehabilitation, which begins approximately 4 weeks after surgery. Rehabilitation involves six to eight biweekly sessions, designed to help patients adapt to the SING IMT's magnified central vision for activities such as reading and writing, while relying on peripheral vision for navigation and spatial awareness. Although rehabilitation is gradual, significant improvements in daily activities, such as watching television and recognizing faces, can be observed even after a few weeks of consistent practice.[3]

NEW CHALLENGES IN THE OR

These new surgical implants and techniques might not challenge a surgeon's skillset, but success can be assured by attention to the nuances of the surgery and adherence to the surgical best practices. Hopefully, more surgical tools find their way out of the pipeline and into retina ORs to help patients with AMD and other retina diseases. ■

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THE FEASIBILITY OF VITRECTOMY IN THE OFFICE-BASED OR

Surgeons weight in on the pros and cons of moving this procedure out of the OR and into the clinic.

By Taku Wakabayashi, MD, PhD; Yusuke Oshima, MD, PhD; Brandon Fram, MD; Emmanuel Y. Chang, MD, PhD; and Prethy Rao, MD, MPH

Between an aging population, increasing rates of eye disease, and better access to eye care, there is an expected rise in the annual number of eye surgeries performed. However, by 2035, the number of ophthalmologists is projected to decline by 12% while the demand for ophthalmologists is projected to increase by 24%.[1] One approach to increase access to surgery is to provide office-based procedures, and several studies have recently evaluated the real-world practicality of office-based vitrectomy.[2-4]

Here, we present the benefits and feasibility of office-based vitrectomy, as well as the hurdles to adoption in the United States.

THE IN-OFFICE OR IN JAPAN


By Taku Wakabayashi, MD, PhD, and Yusuke Oshima, MD, PhD

In Japan, vitreoretinal surgeries are increasingly performed in office-based ORs at private practices.[5,6] This shift has been made possible by advances in vitreoretinal surgery, including a reduction in incision size from 20-gauge to 25- or 27-gauge, the adoption of transconjunctival sutureless approaches, the development of high-speed cutters and small-gauge instruments, improved illumination, and the use of wide-angle viewing systems.

The in-office OR is more than just a procedure room within the practice—it is a fully equipped OR that meets the same standards as a hospital or ambulatory surgical center (ASC) OR.

WHEN TO CONSIDER OFFICE-BASED SURGERY

We consider office-based vitreoretinal surgery for any adult patient with vitreoretinal disease, including epiretinal membrane, macular hole, vitreous hemorrhage, subretinal hemorrhage, retained lens fragment, IOL dislocation,

AT A GLANCE

- In Japan, surgical fees paid by patients and revenue received by the practice are consistent across all settings, including university hospitals, public hospitals, and private practices offering office-based surgery.
- After analyzing 3,362 cases of office-based vitreoretinal surgeries at an eye clinic in Japan, the authors found a single-surgery anatomic success rate of 97.3% for a consecutive series of 883 retinal detachment cases.
- In the United States, barriers to the adoption of office-based vitreoretinal surgery include safety concerns, reimbursement considerations, and space limitations.

rhegmatogenous retinal detachment (RRD) requiring scleral buckle or vitrectomy, proliferative vitreoretinopathy, diabetic tractional RD, and endophthalmitis. The office-based setting is especially effective when urgent same-day surgery for macula-threatening RRD and endophthalmitis is required.

Office-based vitrectomy is not indicated in pediatric patients or in cases with severe open-globe injuries that require general anesthesia managed by an anesthesiologist.

ANESTHESIA

We perform all office-based surgeries using local anesthesia, which is common in Japan, even in academic centers and hospitals. Typically, the patients undergo topical anesthesia with 4% lidocaine followed by posterior sub-Tenon's anesthesia with 2% lidocaine administered through a 27-gauge cannula. Supplemental posterior sub-Tenon's lidocaine is occasionally added before peripheral vitreous shaving under scleral depression. When necessary, we perform retrobulbar anesthesia for cases with scleral buckle. On occasion, patients with significant preoperative anxiety receive oral benzodiazepine anxiolytics prior to surgery. Oral anesthesia has demonstrated safety and efficacy in ocular surgery.[7]

As of 2022, an anesthesiologist must be available on office-based surgery days, but their physical presence is no longer required for office-based surgeries under local anesthesia.

SAFETY

To ensure safety, we employ several pre- and perioperative assessments. Prior to surgery, we review each patient's medical history and medications, maintain close collaboration with primary care physicians, and obtain medical clearance when necessary. In cases of systemic complications, we arrange hospital admission, inform patients, and obtain consent regarding the possibility of being transferred to another facility. However, no cases to date have required perioperative intervention or transfer to a general hospital. For patients with severe medical comorbidities (eg, hypertension exceeding 200 mm Hg or a hemoglobin A1c of 15%), their systemic condition is prioritized for treatment before medical clearance is granted. Patients requiring advanced monitoring by an anesthesiologist due to significant comorbidities, such as severe heart failure, are deemed unsuitable for office-based vitreoretinal surgery.

During the perioperative period, we monitor vital signs, including temperature, blood pressure, and heart rate. In diabetic patients who require longer surgical times, we occasionally monitor blood glucose levels. For patients presenting with hypertension on the day of surgery, oral antihypertensive medication is administered before surgery.

REIMBURSEMENT

In Japan, surgical fees paid by patients and revenue received by the practice are consistent across all settings, including university hospitals, public hospitals, and private practices offering office-based surgery. However, reimbursement systems vary by country, and some have lowered reimbursement for office-based surgery.[5,6] In addition, the practice can charge an additional fee for a short-term postoperative stay if the practice can provide a recovery room, a minimum nurse-to-patient ratio of 1:4, and 24-hour emergency coverage for 3 days postoperatively.

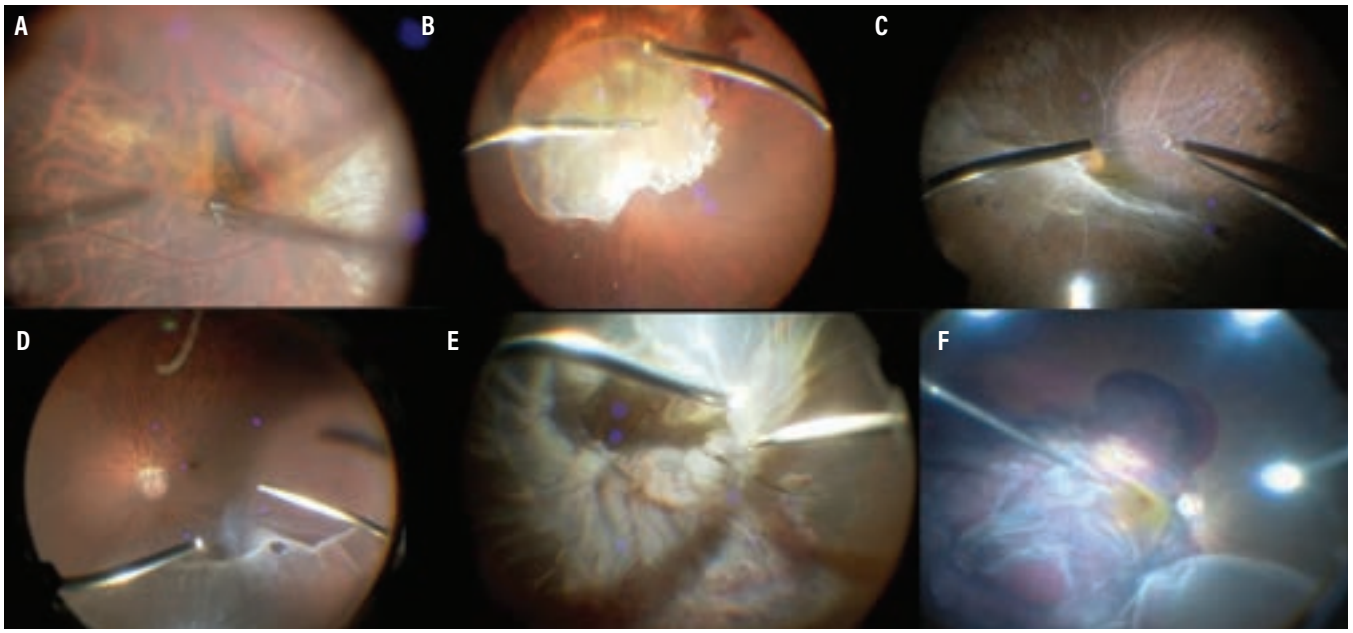

Figure 1. Office-based vitreoretinal surgery in Japan is indicated for any adult vitreoretinal diseases, including macular diseases (A), retained lens fragments (B), diabetic tractional RD (C), RRD (D), proliferative vitreoretinopathy (E), and subretinal hemorrhage (F).

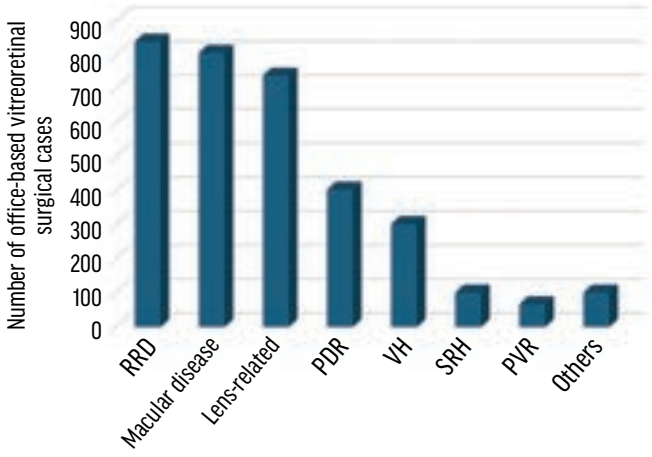

Figure 2. This chart shows the number of office-based vitreoretinal surgeries performed in an in-office OR at an eye clinic in Japan. Single-surgery anatomic success was achieved in 97.3% of eyes in a consecutive series of 883 RRD cases. Abbreviations: PDR, proliferative diabetic retinopathy; VH, vitreous hemorrhage; SRH, subretinal hemorrhage; PVR, proliferative vitreoretinopathy.

OUR DATA

We have performed 3,362 cases of office-based vitreoretinal surgery with 25- and 27-gauge systems for various vitreoretinal diseases (Figure 1). Our single-surgery anatomic success rate was 97.3% for a consecutive series of 883 RRD cases, and, to date, we have had no cases of postoperative endophthalmitis (Figure 2). Our anatomic and visual outcomes for office-based vitreoretinal surgery are comparable with those of academic hospitals. In the office, we can safely perform more surgeries per day due to the efficient setting and shorter turnover times.

WHY YOU SHOULD CONSIDER OFFICE-BASED SURGERY

Based on our favorable experiences, we predict that office-based vitreoretinal surgery will become more common in the next decades, at least in Japan (Figure 3). Providing in-office vitreoretinal surgery at clinics close to residential areas, combined with the larger surgical volumes possible, results in shorter wait times for patients and prompt treatment and recovery.

In Japan, office-based surgery is supported by the country's relatively robust health care and insurance systems, along with geographic accessibility to hospitals in the rare event of complications. The global adoption of in-office retinal surgery requires the development and understanding of various health care and reimbursement systems in different countries. Thus, reimbursement systems may either promote or hinder the office-based surgery trend.

Despite these hurdles, we believe that this trend will gain broader acceptance as a highly efficient and safe approach for the treatment of adult vitreoretinal diseases.

IN-OFFICE HURDLES IN THE UNITED STATES

By Brandon Fram, MD; Emmanuel Y. Chang, MD, PhD; and Prethy Rao, MD, MPH

While some literature shows promise in the possibility of office-based vitreoretinal surgery, the complex interplay of safety, feasibility, and differential reimbursements makes the current reality difficult in the United States from both a provider and a patient perspective.

SAFETY AND COMPLEXITY

Multiple studies demonstrate comparable complication rates of office-based cataract surgery and some vitreoretinal surgeries to those performed in ASCs and hospital surgery settings.[3,4,8,9] However, these studies were restrictive in the study criteria and may not represent the breadth of complexity in vitreoretinal surgery. For example, patients in the vitreoretinal surgery studies largely had procedures that are less time-intensive, more amenable to local anesthesia, and in healthier patients with low rates of serious comorbidities.[4,10]

However, vitreoretinal surgeons generally care for a sicker population of people who often need a mix of urgent, more complex, and longer surgeries. Vitreoretinal surgeons also care for pediatric patients with a history of prematurity or genetic conditions that require general anesthesia with a highly skilled anesthesiologist. Office-based surgery studies lack these cases. Even if topical anesthesia is feasible in the office, most studies focus on practices that have office-based ORs that were at or near a hospital or ASC. In the United States, this may not always be an option.

LOCATION AND REIMBURSEMENT

In addition to safety concerns, one of the biggest questions is cost. Conservative estimates to fully equip a retina OR are between $250,000 and $1,000,000, in addition to the costs to staff the OR, anesthesiology, and triage teams.[11] There is also a wide range of costly instrumentation that may be unexpectedly needed, such as chandeliers, lighted picks, perfluorocarbon, and silicone oil. New billing practices, equipment maintenance, and upkeep of OR materials would also fall to the physician/practice itself, rather than the facility.

In some countries, such as China and Japan, reimbursement for a vitrectomy is the same, irrespective of location. However, in the United States, hospital-based vitrectomy currently reimburses higher than ASCs.[11] Thus, in-office vitrectomy may result in even lower reimbursement for a highly complex surgery performed by surgeons with unique and extensive training. With direct costs of startup and maintenance falling on the physician or group and a lower reimbursement, in-office retina surgery may not be feasible for smaller, privately-owned practices and may skew toward larger hospital-based or private equity-based practices.

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While some companies assist with billing for office-based surgeries (eg, iOR Partners) and newer vitrectomy technology for in-office surgery, they are not widely used and require additional financial commitment.[12] These differential operating costs may ultimately fall to the patient and result in higher out-of-pocket costs if this is not balanced.

Another logistical consideration is the office space required. As a high-volume specialty, most modern ophthalmology offices are equipped and designed for patient throughput. The rooms are often narrower and shorter than what is needed for a comfortable vitreoretinal surgery setup with the necessary machinery and sterile areas. Large practices may have rooms that can be remodeled into an office OR or a room already designated for minor procedures, but for many, a lack of space may be prohibitive.

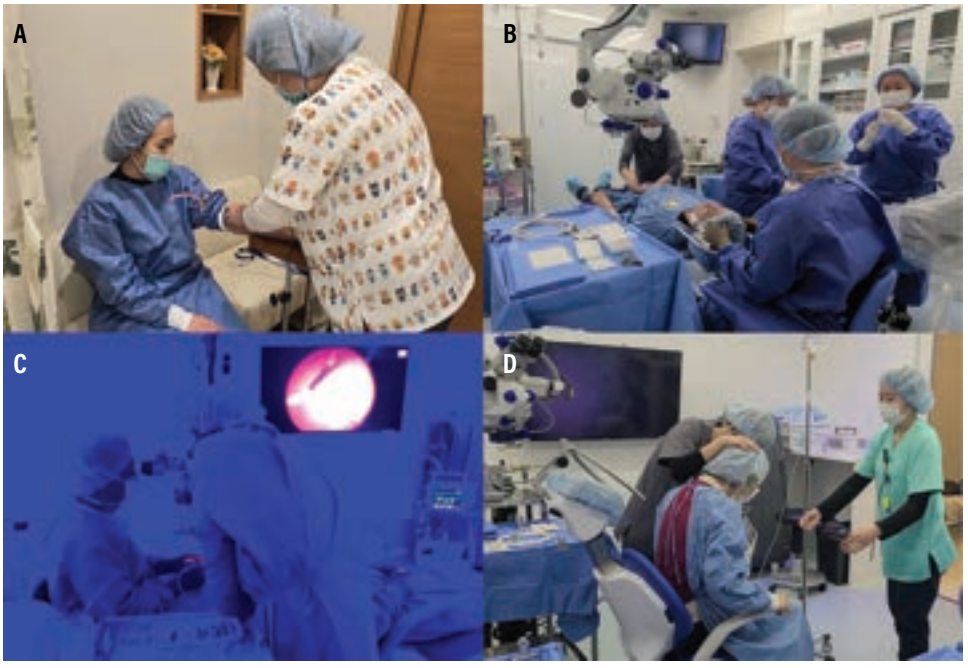

Figure 3. The flow of the day for an office-based vitrectomy. The patient changes into a gown and receives an intravenous line (A) before moving to the OR (B). Intraoperatively, the team monitors vital signs (C). If the patient is being seen for an RD repair, they assume face-down positioning immediately after surgery (D). After a brief rest in the recovery room, the patient returns home.

HURDLES TO ADOPTION

Many practices are developing an interest in office-based surgery worldwide because of the convenience and cost for patients and the inherent inefficiencies of hospital and ambulatory surgery. While many countries, including Japan, have addressed patient safety, space constraints, and differential operating costs to make office-based retina surgery a reality, the same cannot be said for the United States.

Still, in-office vitrectomy is an attractive option that may one day become preferred for some surgeries like cataract surgery; until then, it is likely to be limited to a select number of vitreoretinal surgeries. ■

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RETINA OR POTPOURRI: FIVE QUESTIONS FOR FIVE TOP SURGEONS

Experts discuss tough surgical scenarios and controversial topics.

By Steve Charles, MD; Charles C. Wykoff, MD, PhD; Audina M. Berrocal, MD; Şengül Özdek, MD; and Edward F. Hall, MD





The retina OR is one of the most dynamic surgical spaces. Each case is unique, no two surgeons are the same, and novel surgical techniques continue to push the envelope of what's possible. *Retina Today* asked five top retina surgeons—Steve Charles, MD; Charles C. Wykoff, MD, PhD; Audina M. Berrocal, MD; Şengül Özdek, MD; and Edward F. Hall, MD—to share their preferences in the OR. Here, they discuss everything from managing symptomatic vitreous opacities (SVOs) and challenging tractional retinal detachments (TRDs) to exciting new tools, their best efficiency tips, and even their music choices while operating.

HOW DO YOU MANAGE YOUNGER PATIENTS WITH SVOS?

Dr. Charles: I try not to operate vitreous opacities unless a posterior vitreous detachment (PVD) appears to be present. I do not make a PVD in these cases.

Dr. Wykoff: For most patient with SVOs, I recommend clinical observation because many experience improvement over weeks to months. If patients can document limitations in their activities of daily living, as well as lack of improvement over months of observation, I consider surgical intervention in some patients. Ideally, patients would be pseudophakic and have a complete PVD prior to surgical

AT A GLANCE

- If symptomatic vitreous opacities are visible and significantly affect the patient's life, surgeons often opt for clinical observation before scheduling a vitrectomy–although some surgeons won't offer surgery at all.
- Most surgeons are willing to leave some fibrovascular membranes if they can relieve the traction and reattach the retina.
- All surgeons agreed that having all possible disposables and tools immediately available in the OR will improve surgical efficiency.

intervention. If a patient is phakic and has an attached vitreous face, I am even more emphatic in discouraging surgical intervention.

Dr. Berrocal: It's surprising how little time some doctors spend evaluating, diagnosing, and validating patients' concerns regarding floaters. Many times, simply explaining the situation and, when appropriate, showing them imaging can alleviate their fears and worries. Recently, I developed a floater myself, and certain lighting conditions make it quite bothersome, which has deepened my empathy for my patients.

> **In instances where I do remove floaters, "less is more."**
> *– Audina M. Berrocal, MD*

That said, floaters can be tricky, as they sometimes manifest as symptoms of mental health issues or anxiety. In such cases, a referral to a counselor, psychiatrist, or psychologist may be necessary.

In instances where I do remove floaters, "less is more." Often, clearing the visual axis is sufficient, as removing a tight hyaloid can complicate matters unnecessarily.

Dr. Özdek: First, I listen to the patient's complaints to understand how much the SVOs affect their quality of life. Second, I perform a thorough ocular examination and document any SVOs with red-free OCT imaging. If the SVOs are visible and significantly affect the patient's life, I educate the patient on the condition and the possible treatment approach with vitrectomy, including the risks of cataract, retinal break, and RD (2.4%).[1] I send them home and call in 3 months; if they still insist, I schedule a vitrectomy. During the surgery, I induce a PVD up to the equator and trim the vitreous as much as possible without scleral indentation. Although inducing a PVD increases the risk of a retinal break and RD, I prefer to do it; if you don't, a spontaneous PVD soon follows, which may cause new floaters and a retinal break. To avoid complications, I laser the peripheral retina and trim the vitreous as much as possible.

> **I almost always leave some fibrovascular membranes in pediatric TRD cases.**
> *– Şengül Özdek, MD*

Dr. Hall: Managing younger patients with SVOs presents a unique challenge. First and foremost, a comprehensive discussion of the risks, benefits, and alternatives to vitrectomy is essential. Inducing a PVD in this population can be difficult and carries an increased risk of complications, especially if there is lattice degeneration or other concomitant peripheral pathology. I typically advise against vitrectomy for younger patients with an attached posterior hyaloid who present with SVO. I do not offer Nd:YAG vitreolysis.

If the patient experiences significant symptoms that align with clinical findings, I occasionally consider proceeding with vitrectomy. In such cases, I perform a core vitrectomy, followed by the application of diluted triamcinolone to visualize the cortical vitreous. Every effort is made to induce a PVD. A meticulous scleral-depressed examination at the conclusion of surgery is critical to identify and address any peripheral defects. Finally, I suture all sclerotomies and conjunctival incisions to further reduce the risk of complications. These cases carry significant potential liability, so it is important to be meticulous and document carefully.

ARE YOU WILLING TO LEAVE SOME FIBROVASCULAR MEMBRANES IN CHALLENGING TRD CASES?

Dr. Charles: Yes; I remove what is necessary to avoid retinal breaks but reattach the macula. I make every effort to avoid silicone oil by using scissors, not just the cutter, and avoiding peeling and aggressive PVD creation.

Dr. Wykoff: With TRD repair in the context of proliferative diabetic retinopathy (PDR), my surgical goal is to achieve an attached posterior pole without creating iatrogenic retinal breaks. I relieve as much traction and remove as much of the fibrovascular tissue as possible. I often leave fibrous stalks that are not causing residual retinal traction.

Dr. Berrocal: If the vitreous around the fibrovascular membranes is removed, I typically leave the membranes intact. With today's advanced vitrectors, we can get very close to the retina without causing damage, pulling, or creating holes or bleeding. As a result, these membranes may often be left in place.

Dr. Özdek: I almost always leave some fibrovascular membranes in pediatric TRD cases, such as retinopathy of prematurity, familial exudative vitreoretinopathy, and persistent fetal vasculature. I do not want to risk creating a retinal break by peeling more membranes; instead, I leave membranes that I feel are too risky to peel or if they are not crucial to relieve the traction. You can consider peeling the residual membranes in a second surgery, if needed.

For adults, I may leave some membranes in cases of significant PDR or vasculitis. Although a retinal break is less challenging in an adult, it necessitates use of gas or silicone oil tamponade. Additionally, peeling all membranes, especially in the major arcuate vessels, may cause uncontrollable bleeding, and cauterizing those vessels may lead to occlusion and irreversible damage. However, strongly adherent fibrovascular tissues left over the major vessels or the optic disc may be the reason for recurrent vitreous hemorrhage in adult PDR cases. Surgeons must evaluate each case carefully.

Dr. Hall: I perform a thorough core vitrectomy, trimming down to the fibrovascular plaque, and lyse all

anterior-posterior vitreous adhesion for 360°. Vitreoschisis is almost always present, so I use diluted triamcinolone to highlight residual vitreous. I perform as much segmentation and delamination as is safely possible. Most of the time, I can remove all membranes, but there are certainly cases in which there is strong vitreoretinal adhesion, particularly in the midperiphery and in highly ischemic eyes in which it may be nearly impossible to remove the hyaloid and/or membranes without creating iatrogenic breaks. In these cases, I trim as much as possible and may risk iatrogenic breaks if needed (particularly above the horizontal meridian). Judicious panretinal photocoagulation is important. Careful scleral depression at the end of surgery and proper wound closure are essential.

> I do look forward to a future where some type of augmented-reality visualization could be used to enhance surgical visualization.
> – Charles C. Wykoff, MD, PhD

WHAT EXCITES YOU THE MOST ABOUT THE FUTURE OF VITREORETINAL SURGERY?

Dr. Charles: The introduction of Alcon's new Unity Vitrectomy/Cataract System.

Dr. Wykoff: Our current vitrectomy platforms, instrumentation, and hardware for visualization are excellent. However, the field continues to move forward, and I look forward to improvements in all three. I currently use a microscope for visualization, and I'm very comfortable with my surgical setup. To date, I have not found the heads-up display options to be a necessity. That said, I do look forward to a future where some type of augmented-reality visualization could be used to enhance surgical visualization, as well as overlay key metrics related to fluidics and incorporate imaging such as OCT.

Dr. Berrocal: The integration of cutting-edge technology is essential for advancing our field. With tools like 3D surgery, OCT angiography, intraoperative OCT, microscope filters, and small-gauge surgery, a fully integrated system will reduce surgical time and significantly improve patient outcomes. Moreover, robotic surgery holds exciting potential, and it will be fascinating to see how these innovations are applied to our specialty.

As a fan of science fiction, I often imagine breakthroughs such as stimulating the vitreous instead of removing it (given that we likely haven't unlocked all its benefits), using glue for retinal tears, automatic laser, or even the potential for eye transplants one day.

Dr. Özdek: I am expecting better imaging systems that would allow us to see up to the pars plicata without indentation and too much effort. That would be exciting.

Dr. Hall: The future of vitreoretinal surgery is very exciting and will be marked by the continued advancement of intraoperative OCT, 3D visualization, and AI-assisted analysis to improve diagnostic accuracy, surgical planning, and enhanced OR efficiencies. Additionally, the continued evolution of drug delivery systems and gene therapy means that vitreoretinal surgeons may be busier than ever before. Meanwhile, advances in robotic surgery may help ameliorate surgeon fatigue, improve accuracy and precision, and even allow for more advanced technical maneuvers than are currently possible.

AS A BUSY, HIGH-VOLUME SURGEON, WHAT ARE YOUR TOP THREE TIPS FOR IMPROVING EFFICIENCY IN THE OR?

Dr. Charles: Pay your scrub techs, rehearse the case ahead of time, and ensure that you have all possible disposables and tools immediately available.

Dr. Wykoff: The most important aspect to maximize efficiency is a knowledgeable, team-oriented surgical assistant; I work with a fantastic scrub tech who often knows what I need before I do (Figure 1). Second, I always have a preoperative surgical plan and am aware of any unique situations for a given eye—for example, knowing where all the breaks and patches of lattice are in a rhegmatogenous RD. Finally, I ensure an efficient turnover and have ready access to all the potential instruments and surgical adjuncts in the OR itself to optimize flow and minimize interruptions.

Dr. Berrocal: Having the same well-trained staff is crucial. It's important to communicate all the instrumentation that might be needed ahead of time. Keeping a cart inside the room with the necessary instruments helps avoid delays.

> Pay your scrub techs, rehearse the case ahead of time, and ensure that you have all possible disposables and tools immediately available.
> – Steve Charles, MD

When training fellows, it's essential to know when to step in to keep the case moving forward. Ensuring that the next patient is in the holding area before you finish the current case is key to maintaining efficiency.

Pediatric cases tend to take longer, and working with a pediatric-trained anesthesiologist is a great asset, allowing us to handle a high volume of cases.

Dr. Özdek: I use two ORs at the same time with two fellows (Figure 2). I find this to be very efficient. While the fellows or residents do the initial steps to prepare the surgery for you, you can complete the crucial step of another surgery and then leave the closure of the entry sites to the fellow. I also do a lot of academic work between surgeries, if I have the time.

Figure 1. Dr. Wykoff and his powerhouse OR team celebrate after a successful subretinal gene therapy delivery case.

Figure 2. Dr. Özdek with her OR team, including (among others): Aylin Palandöken, RN; Olcay Salmanlı; Demet Coşkun, MD; H. Baran Özdemir, MD; Benay Karabulut, MD; and Ahmet Yiğiter, MD.

Figure 3. Dr. Hall (far left) with OR staff (left to right): Mary Wiersma, RN; Nataliya Nakonechnaya, RN; Kori Beck, RN; and Brian Volke, CST. We are fortunate to have such amazing staff at Brighton Surgery Center!

Dr. Hall: Efficiency is important, but never at the expense of outcomes. My three tips are:

1. Make sure you are comfortable and in an ergonomically sound position. Build from there. Don't worry about being a diva!
2. Worry about being a diva! You can greatly improve OR turnover by helping open supplies or even just informing staff what instrumentation you will need during the next case. Be friendly with your staff and assume positive intent (Figure 3).
3. Don't over-operate. For example, something as seemingly benign as clearing mild posterior capsule opacification can lead to difficulty with visualization, oil sticking to an IOL, etc. Don't open Pandora's box!

WHAT IS YOUR TAKE ON PLAYING MUSIC IN THE OR?

Dr. Charles: I never play music in the OR; I want to be able to talk to and hear the patient under the drape.

Dr. Wykoff: I do prefer to have music playing during surgery. My go-to is Journey Radio or similar. But I am flexible with this, and my operating team often sets the tunes.

Dr. Berrocal: I need to have music playing in the OR—it relaxes me and helps me focus. However, it must be music that I enjoy. My taste is eclectic, but I don't like jazz. On Fridays I play the favorite music of my scrub and circulator. It makes everyone enjoy the end of the week.

Efficiency is important, but never at the expense of outcomes.
– Edward F. Hall, MD

Dr. Özdek: I have playlists in my Spotify account labeled *OR*. Most of them are from Beethoven, Chopin, Vivaldi, Erik Satie, and Queen. My second list is Turkish nostalgic pop/rock from the 80s and 90s. I choose playlists depending on my mood.

Dr. Hall: Music in the OR is very important to me. The right music can help set the room at ease, including the patient, staff, and surgeon. The wrong music can be offensive, distracting, and increase tension in the OR. I usually choose the music, and I try to pick something with broad multigenerational appeal like Van Morrison or The Eagles. ■

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SURGICAL CASE SPOTLIGHT: AMNIOTIC MEMBRANE GRAFT AND PFO

With the right technique, this approach to refractory macular holes can lead to hole closure.

By Jennifer Adeghate, MD; Samantha R. Goldburg, MD; and Talia R. Kaden, MD



Refractory macular holes (MHs), for which standard techniques have failed, pose a unique challenge in vitreoretinal surgery. Reasons for nonclosure of MHs can include large size (> 500 µm), coexisting neurosensory retinal detachment (RD), high degree of myopia, and other causes of retinal pigment epithelial changes.[1-3] There is no consensus on how these MHs should be treated, and the strategy differs based on each case and the surgeon's experience. Techniques for addressing refractory holes include subretinal internal limiting membrane (ILM) patch with gas or oil, macular detachment, autologous retinal transplantation,[4] and human amniotic (hAM) graft placement.

Various techniques have been developed for repairing refractory MHs using amniotic membranes. Subretinal placement of a hAM graft has been shown to promote closure of refractory MHs.[5] Additionally, intraoperative PFO or 5,000 centistokes of silicone oil has been shown to improve graft adhesion to the macular surface and prevent graft dislocation.[6-8] In this article, we discuss a case in which we placed a large epiretinal hAM graft onto a giant MH (> 1,000 µm) using a combination of PFO to aid in macular adhesion, a Tano brush to mobilize the edges of the hole, and C_3F_8 gas for postoperative tamponade (Video).

THE TECHNIQUE

Our case involved a 50-year-old woman with a giant (> 1,000 µm) traumatic MH in the right eye. The patient

AT A GLANCE

- Placement of a human amniotic membrane graft has been shown to promote closure of refractory macular holes.
- In the case presented here, a greater than 1,600 µm macular hole was treated with a human amniotic membrane graft held in place during surgery with a PFO bubble.
- The authors postulate that waiting at least 2 minutes with the graft under PFO allows for displacement of fluid from underneath the graft and promotes adhesion to the macular surface.

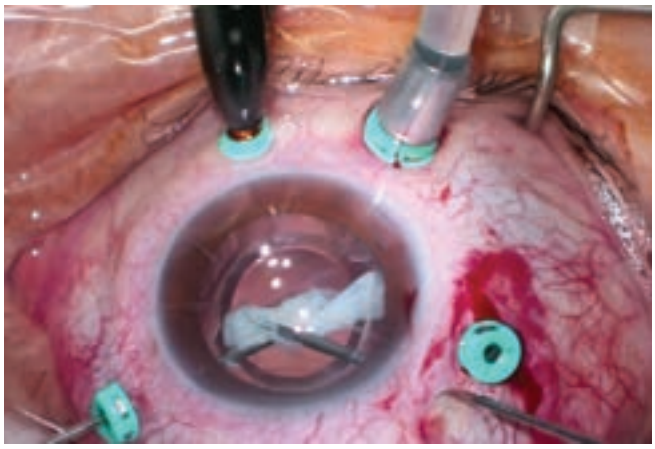
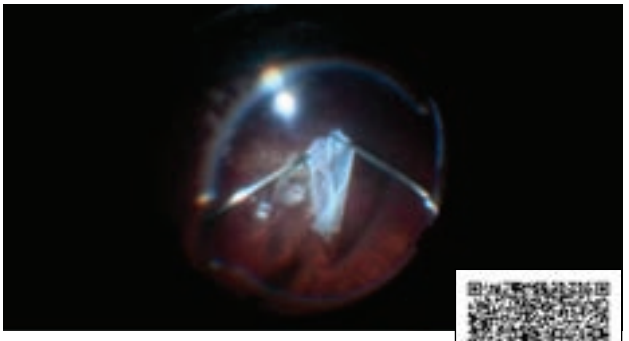


Figure. Use ILM forceps to insert the hAM graft into the eye and place it basement membrane-side down onto the macula.

WATCH IT NOW



Video. Addressing a Refractory Macular Hole With an Amniotic Membrane Graft and PFO.

endorsed a remote history of facial trauma that resulted in a decrease in vision. At that time, she presented to an outside physician who performed a vitrectomy with membrane peel and, per the operative note, an ILM flap. The surgeon lasered the peripheral lattice and a second full-thickness retinal defect in the superotemporal macula. She was left with 14% C_3F_8 gas. When she presented to our clinic 10 months later, she had a persistent MH and a VA of counting fingers.

After extensive discussion about her limited visual potential, the patient elected to proceed with a second vitrectomy, which was performed 14 months after the first. The residual ILM nasal to the hole was peeled, and gentle reapproximation of the edges of the hole was performed with a DDMS Tano diamond-dusted membrane scraper (Bausch + Lomb). The patient was again left with 14% C_3F_8 gas. Postoperatively, her VA improved to 20/300 with a residual scotoma that she found subjectively bothersome.

Over the course of the next year, she repeatedly requested additional intervention. The nasal retina began to elevate, and the hole enlarged to greater than 1,600 µm, leading to concern for possible RD. The decision was made to return to the OR for placement of a hAM graft.

We used a standard 25-gauge vitrectomy setup with a small superotemporal peritomy in anticipation of the placement of the hAM graft. A posterior capsulotomy was performed to improve visualization. The extent of the previous ILM peeling was confirmed using brilliant blue G, and scleral depression was performed to rule out peripheral pathology. A Tano brush was used to massage the edges of the MH to mobilize the hole and promote closure. A chandelier was placed inferiorly to allow for illumination of this bimanual technique, and a 20-gauge sclerotomy was made in the superotemporal quadrant. A 9 mm x 9 mm graft was measured and cut, and ILM forceps were used to insert the graft into the eye and place it basement membrane-side down onto the macula (Figure). At the outset, the edges of the graft curled inward, away from the retina. PFO was then placed over the graft to stabilize it.

At this time, small adjustments were made to the graft's position using the Tano brush. Given the intent to promote the egress of fluid from beneath the graft, the PFO bubble was enlarged to cover the entire graft. It was left in the eye while the additional sclerotomy was sutured, allowing the graft to settle under the PFO for approximately 5 minutes. A bimanual fluid-air exchange was then performed while holding the graft in place with the Tano brush. Once the PFO was removed from the eye, further curling and dislocation of the graft were no longer observed. An air-gas exchange with 14% C_3F_8 gas was then performed.

Postoperatively, the patient was placed in a supine position for 1 hour prior to assuming face-down positioning. At postoperative month 9, the graft remained in place, the hole was closed, VA had improved to 20/150 with refraction, and the patient was satisfied with the outcome.

DISCUSSION

Prior studies have shown closure of large refractory MHs using hAM, placed after fluid-air exchange with gas tamponade.[7] However, this technique does not always result in anatomic success.[9] In one systemic review of eight studies with 103 eyes that underwent hAM graft placement after failed vitrectomy and ILM peeling, the graft dislocation/contracture rate was 6%.[10] In studies using cryopreserved hAM grafts, the graft dislocation/contracture rate was lower, at 3%.[10]

There are reports of hAM for MHs with coexisting rhegmatogenous RD that used PFO to push the subretinal fluid through peripheral breaks and flatten the macula to facilitate hAM membrane insertion into the MH, with closure of all MHs seen at 6 months.[6] There are also data showing that hAM placed under PFO in the case of myopic MHs associated with RD resulted in MH closure in

(Continued on page 54)

REBECCA SOARES, MD, MPH

WHERE IT ALL BEGAN

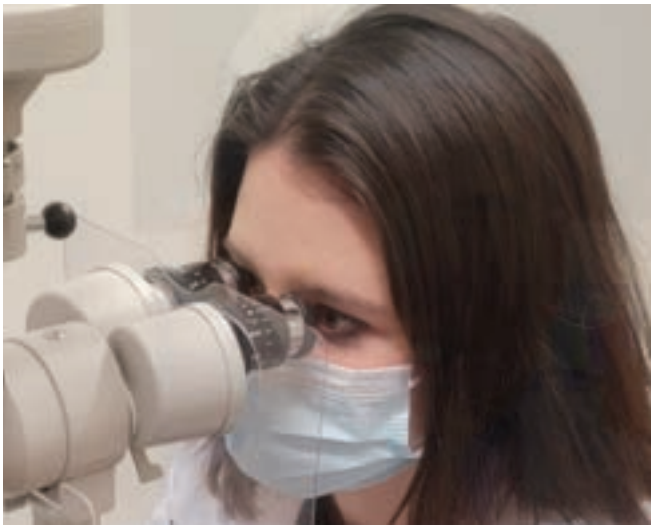
I grew up in the suburbs of Denver and went to Yale for undergraduate. At Emory University, I received a dual Doctor of Medicine and Master's in Public Health. Although I shadowed my uncle (a retired cataract surgeon) in the OR in high school, ophthalmology wasn't on my radar. I was more interested in chronic diseases, and I dreamed of working at the Centers for Disease Control (CDC) and Prevention. While studying at Emory, I had the opportunity to explore that side of health, considering the CDC is next to the medical school. However, after my first rotation in ophthalmology at Emory, I knew it was the field for me. I loved the individual clinical interaction and the opportunity to understand and expand public health within ophthalmology.

MY PATH TO RETINA

My first introduction to retina was at Emory, where I worked with a wonderful mentor, Timothy W. Olsen, MD, on a project evaluating the cost-effectiveness of retinopathy of prematurity treatment in different countries. I realized that, as a retina specialist, I would have the opportunity to interact with systemic diseases medically and surgically.

SUPPORT ALONG THE WAY

My desire to become a retina specialist grew when I was a resident at Wills Eye Hospital in Philadelphia. From a research perspective, Jason Hsu, MD; Yoshi Yonekawa, MD; and Sunir J. Garg, MD, taught me that retina is an ever-evolving field, and they helped me develop my investigative skills. All the attendings at Mid Atlantic Retina were supportive in my clinical and surgical development and my career. By the end of my fellowship, I could call on any of them as life-long mentors and colleagues. Post-training, I am grateful for the mentorship of David Reed, MD, and Chirag Shah, MD, MPH, who have helped me get on my feet as an attending. I am also grateful for the support of my partners at New England Retina—Andrew Lam, MD; Shilpa Gulati, MD; David R. Lally, MD; and Hari Mylvaganam, MD—for continuing to teach me clinically and help me develop my business acumen.



Dr. Soares' advice: Stay focused on what is going to be the most fulfilling option, holistically. After training, it is finally time to define your own priorities and needs, whether that is academic achievement, research development, building a practice, or focusing on family.

AN EXPERIENCE TO REMEMBER

I saw a patient who developed bilateral retinal detachments the same week his wife received a cancer diagnosis. It was a tumultuous time for his family, and my role was not only to be surgeon, but also to offer emotional encouragement. In the end, my patient maintained his vision and continued to drive his wife to her appointments. It was one of my first cases as an attending where I continuously followed a patient in need, and I'm glad I was able to support him through the experience. I am grateful to have a job where I can serve people at a critical moment in life and help them reach the other side. ■

Rebecca Soares, MD, MPH, is a vitreoretinal surgeon at New England Retina Consultants in Springfield, Massachussets. She sees a variety of medical and surgical pathology and participates in numerous clinical trials. Dr. Soares is a consultant for Abbvie and Regenxbio. She can be reached at **rebecca.russ.soares@gmail.com.**

AN OLD TECHNIQUE MADE NEW: SCLERAL BUCKLING

Why this approach remains integral to surgical success in the current era of vitreoretinal surgery.

By Omar M. Moinuddin, MD, and George A. Williams, MD


Although advances in the field of vitreoretinal surgery have significantly enhanced our understanding of rhegmatogenous retinal detachment (RRD), the core schema of RRD repair remains fundamentally unchanged: find, close, and seal the breaks.

Pars plana vitrectomy (PPV) and scleral buckling (SB) are the most frequently performed treatment options in the management of RD, with both conferring high rates of surgical success and postoperative visual improvement. While there exists general agreement on the approach for certain RDs, such as vitrectomy for eyes with significant media opacity, there is a lack of consensus on the preferred treatment for many cases of primary noncomplex RD.

Currently, there is a growing trend away from SB and toward PPV. Because the advent of wide-angle viewing systems, 3D heads-up display, and smaller-gauge instrumentation have enhanced the efficiency and safety of PPV, SB is becoming a forgotten art. This shift affects both new and experienced vitreoretinal surgeons alike, as SB is performed in less than 20% of RD repairs today.[1]

BUCKLE MECHANICS

Although PPV has become the dominant focus of modern vitreoretinal surgery, SB is not an obsolete surgical option. Rather, surgeons should recognize SB as a cornerstone in the framework of RD repair. To appreciate SB's value in the modern surgeon's toolkit, surgeons must have a robust understanding of the relationship between the pathophysiology of RRD and the biomechanics of SB, as well as the surgical implications on the eye and the outcomes data.

SB alters the forces leading to RD while concurrently augmenting forces that promote reattachment of the retina. RD is caused by a combination of vitreous traction and vitreous liquefaction, with ocular saccades enabling fluid passage into and propagation within the subretinal space. SB causes indentation of the eye wall to directly decrease the magnitude of this vitreous traction and indirectly change the direction of its exerted force. Encircling bands further compel the eye into a prolate geometric shape with a vitreous base that is reduced in diameter, thereby diminishing transvitreal traction.

AT A GLANCE

- Scleral buckling alters the forces leading to retinal detachment while concurrently augmenting forces that promote reattachment of the retina.
- Maintaining familiarity with scleral buckling is essential to maximize success for each patient.
- The authors prefer an encircling band for its multifaceted advantages: diffusely reducing transvitreal traction, addressing pathology in multiple quadrants, and maintaining adequate buckle height.

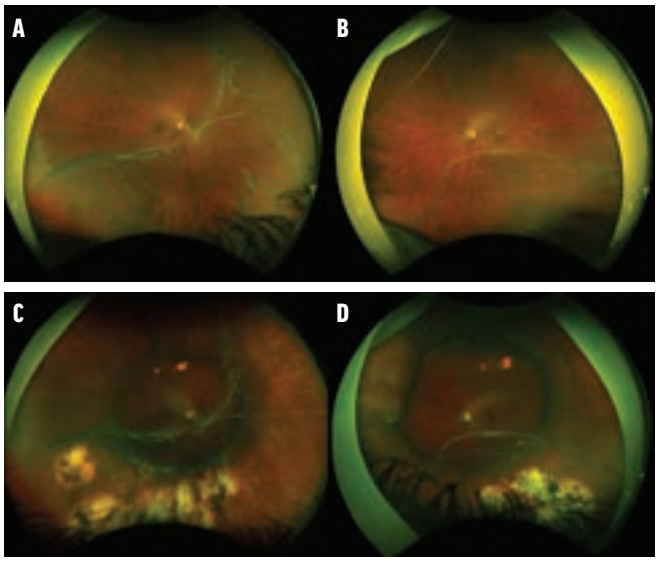


Figure. Preoperative widefield fundus photographs of the eyes of a 31-year-old woman with high myopia document RDs in the right (A) and left (B) eye with associated lattice degeneration and demarcation lines. One year after after primary SB surgery, the retina is attached in the right (C) and left (D) eye.

The remarkable degree to which SB relieves vitreoretinal traction is demonstrated in investigations showing that the addition of retinopexy does not result in better rates of reattachment compared with SB alone.[2,3]

The induced indentation beneath the break displaces the existing subretinal fluid, allowing reapposition of the retina to the underlying retinal pigment epithelium. Often, this leads to displacement of the liquified vitreous with more solidified gel that closes the break. In eyes with a detached retina and fibrocellular membrane formation, contraction of this tissue generates posteriorly directed radial forces that can create new retinal breaks and contribute to the expansion of existing breaks. SB changes the eyewall's contour from naturally concave to iatrogenically convex, redirecting these radial forces outward along the buckle. This enables relaxation and flattening of a foreshortened retina without the need for membrane peeling and retinectomy, often obviating the need for PPV entirely with proper case selection.

SUPPORTING DATA

The clinical efficacy of SB is substantiated by both landmark studies and more recent investigations. The Scleral Buckling Versus Primary Vitrectomy in Rhegmatogenous Retinal Detachment Study (SPR) was the first large prospective randomized clinical trial comparing the outcomes of SB and PPV in the management of noncomplex RD.[4] Analysis showed comparable BCVA with SB in eyes that were phakic but a higher primary anatomic success rate with PPV in pseudophakic eyes. However, the study protocol permitted supplemental SB at the time of PPV based on surgeon discretion; ancillary analysis of the data showed that primary anatomic success was improved with PPV/SB compared with PPV alone in these pseudophakic eyes.[4]

Thus, the declining popularity of SB since the SPR study is not based on outcomes data. Instead, it is largely attributed to surgeons becoming increasingly acclimated to advanced retinal imaging and evolving vitrectomy technologies, while growing less familiar with careful ophthalmoscopy, detailed retinal drawings, and the nuances of SB.

This notion is bolstered by current research that substantiates the excellent visual and anatomic outcomes achieved by surgeons who continue to prefer and remain experienced in the art of SB. In a meta-analysis of 41 studies, Dhoot et al reported comparable rates of primary surgical success (> 85%) and final surgical success (> 95%) for both SB and PPV but significantly improved postoperative visual acuity with SB.[5] Znaor et al conducted a Cochrane analysis of PPV and SB performed in clinical trials across North America, Asia, and Europe and similarly reported no significant differences in primary or final surgical success between the operations.[6] Most recently, Kowano et al performed a propensity score-matched analysis of 882 phakic eyes with noncomplex macula-on RRD, and advanced analytics demonstrated that the proportion of surgical failure is significantly higher with PPV versus SB (risk difference 0.10, $P = .01$).[7]

The Primary Retinal Detachment Outcomes Study (PROS) included approximately 3,000 patients with noncomplex RD managed across six institutions with academic surgeons experienced in performing and teaching both SB and PPV.[8] The first PROS report noted that single-surgery success was greatest for the SB group, and eyes treated with SB (91.2%) and PPV/SB (90.2%) had higher rates of primary success compared with PPV alone (84.2%).[9]

Akin to the SPR study, subsequent PROS reports stratified eyes by lens status and reported similar outcomes with SB, PPV, and PPV/SB. In phakic eyes, primary surgical success was significantly higher with SB (91.7%) and PPV/SB (91.2%) compared with PPV alone (83.1%).[10] Furthermore, postoperative vision in eyes with macula-splitting RD was significantly better in the SB group even when controlling for cataract progression ($P < .001$). All pseudophakic eyes in PROS underwent PPV, and eyes managed using supplemental SB demonstrated significantly better single-surgery success for both macula-on RD (PPV/SB, 100%; PPV, 88%) and macula-off RD (PPV/SB, 89%; PPV, 81%). Notably, single-surgery success for PPV/SB was also significantly higher compared with PPV (96% vs 82%) in eyes with inferior RD.[11]

MAKE IT YOUR OWN

SB is an intricate and dynamic operation that empowers each surgeon to develop a unique approach in the OR.

ALTHOUGH PPV HAS BECOME THE DOMINANT FOCUS OF MODERN VITREORETINAL SURGERY, SB IS NOT AN OBSOLETE SURGICAL OPTION. RATHER, SURGEONS SHOULD RECOGNIZE SB AS A CORNERSTONE IN THE FRAMEWORK OF RD REPAIR.

Nearly every surgical step is customizable. Common variants of SB include the creation of lamellar scleral flaps or scleral sutures; choice of radial element, segmental exoplant, or encircling band; consideration for draining subretinal fluid; and the use of intraocular tamponade. More recently, the use of noncontact viewing systems with chandelier endoillumination has gained increasing popularity. Many surgeons advocate that this setup provides enhanced magnification and localization of peripheral pathology, enables safer completion of retinopexy and drainage, and allows for improved instruction of trainees. Recent comparative investigations have shown that anatomic success and postoperative outcomes are comparable among these different surgical techniques.[12-14]

OUR APPROACH

Our personal approach is to perform primary SB in phakic eyes (particularly in younger patients with an attached hyaloid), when pathology is in multiple quadrants, and when there is likely to be densely adherent vitreous (eg, high myopes with lattice degeneration [Figure]). We also use SB in eyes with a known history of trauma, retinal dialysis, or retinoschisis, in patients who are monocular, and in those with significant asymptomatic RD.

We further advocate supplementing PPV with SB in eyes that are at high risk for recurrent detachment (ie, eyes that have failed previous RD repair, have inferior pathology or existing proliferative vitreoretinopathy, and eyes with a history of inherited vitreoretinopathy, giant retinal tear, or RD in the fellow eye). We prefer to use an encircling band for its multifaceted advantages of diffusely reducing transvitreal traction, addressing pathology in multiple quadrants, and maintaining adequate buckle height throughout prolonged follow-up.

The use of sutures minimizes trauma to the sclera, especially in cases with existing ectasia, staphylomatous change, or large myopic eyes with thin tissue. Drainage is considered on a case-by-case basis and is generally reserved for eyes with large RDs that will remain reasonably bullous after finalizing the buckle position, extensive inferior subretinal fluid, and chronic fluid that presumably requires prolonged time to resolve spontaneously.

DON'T FORGET THE BUCKLE

In the current era of vitreoretinal surgery, maintaining familiarity with the practice of SB is essential to tailoring RD repair surgery and maximizing success for each patient. Among the myriad ways to perform SB, surgeons should employ the techniques they are most experienced with to consistently yield optimal outcomes. ■

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RISING STARS IN RETINA

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

Lauren Kiryakoza, MD

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

My exposure to retina was serendipitous. I applied for an endocrinology research position through the National Institutes of Health as a medical student and was assigned to a diabetic retinopathy research lab. This introduced me to the field and to people who were very excited about their work and study. As a resident at Bascom Palmer Eye Institute, I saw how diverse vitreoretinal diseases were, especially in our eye emergency department. I had a wonderful experience with the retina faculty and decided it was for me!

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

I am lucky to have mentors who have dedicated their time and energy to help me grow in my career. Steven J. Gedde, MD; Chris R. Alabiad, MD; and Jayanth Sridhar, MD, guided me through ophthalmology residency. My chief residents, Jesse D. Sengillo, MD, and Julia L. Hudson, MD, taught me vitreoretinal surgery fundamentals and how to approach ocular trauma. In fellowship, Audina M. Berrocal, MD; Harry W. Flynn Jr, MD; and Thomas A. Albini, MD, have guided me through research and challenging cases. William E. Smiddy, MD; Justin H. Townsend, MD; Basil K. Williams Jr, MD; Nicolas A. Yannuzzi, MD; and Hong-Hyuen Hua, MD, have taught me incredible surgical management skills. Jorge Fortun, MD, and Luis J. Haddock, MD, are my dedicated surgical mentors up north who taught me about 3D heads-up surgery. I am forever grateful for all my mentors and their selfless devotion to education and patient care.

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

I will never forget being in Dr. Berrocal's pediatric retina clinic and meeting a family with more than six children affected by Stickler syndrome. These visits showed me that some cases require unique doctor-patient relationships and that clinical decisions can deeply affect the patient's daily life. Clinically, it was my first in-depth exposure to the complicated counseling involved in retinal detachment prophylaxis. One of these siblings, now a teen, had a prophylactic procedure at 2 years of age and is still seeing well.

FIRST CAREER MILESTONE

In the fall of 2025, Dr. Kiryakoza will begin her position as Chief Resident and Co-Director of Ocular Trauma at Bascom Palmer Eye Institute.

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

I would like to practice in Southeast Michigan (where I grew up) and develop long-term patient relationships. I loved being an English-as-a-second-language tutor in my hometown, and I would like to mesh that work with my interest in community health by participating in eye care screenings in vulnerable communities. Another important goal is to work directly with trainees. I think these two interests can complement each other.

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

Retina specialists are uniquely positioned to care for diverse patients with diverse pathologies. It is a specialty that delivers good and bad news daily, and that has enriched my experience as a physician. It is an exciting field with very interesting surgical options. ■

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AN UNUSUAL CASE OF PEDIATRIC IRD


This patient developed an associated macular hole and retinal detachment, prompting further investigation.

BY NATASHA FERREIRA SANTOS DA CRUZ, MD, PHD, AND AUDINA M. BERROCAL, MD

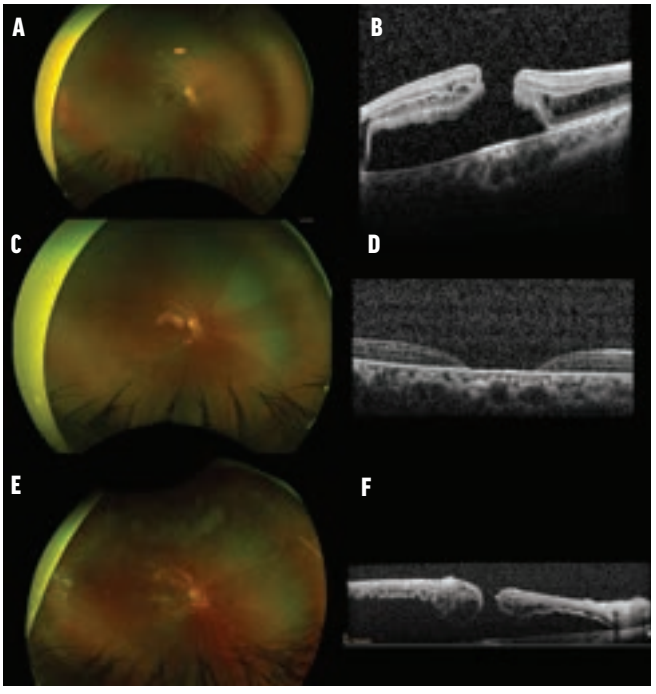
Over the past few years, our understanding of inherited vitreoretinopathies and vitreoretinal degenerations has significantly advanced, particularly when it comes to the identification of causative genes.[1] Vitreoretinal degenerations are a group of retinal disorders marked by early-onset cataracts, liquefaction of the vitreous humor, variable retinal degeneration, and abnormalities at the interface between the vitreous and the retina. These abnormalities increase traction on the retina, leading to retinal detachment (RD). Most of these conditions, including snowflake vitreoretinal degeneration (SVD), are autosomal dominant diseases with variable expressivity and nearly complete penetrance of vitreoretinal degeneration.[2,3] It is important to consider SVD in the differential diagnosis of patients with fibrillar vitreous anomalies.[4,5]

Here, we discuss a patient diagnosed with SVD with a macular hole, RD, and complications in the left eye who followed up with complications in the right eye.[6]

THE CASE

A healthy 18-year-old female patient presented with a history of amblyopia, high myopia, and increased blurry vision in the right eye for the past 2 years. Her BCVA was 20/200 OD and 20/25 OS. Anterior segment examination was unremarkable. Indirect fundoscopy revealed flattened, small optic nerves, cystic changes in the macula and retinal periphery of each eye, and a full-thickness macular hole (FTMH) in the right eye. Fluorescein angiography demonstrated peripheral straightening of vessels and no retinal vascular leakage. OCT confirmed the flat macular schisis and FTMH in the right eye. OCT also showed macular schisis and vitreomacular traction in the left eye. As FTMHs are rare in the pediatric population, further investigation was necessary. Genetic studies disclosed a heterozygous pathogenic variant in the *KCNJ13* gene, consistent with SVD. The patient elected for observation of the FTMH.

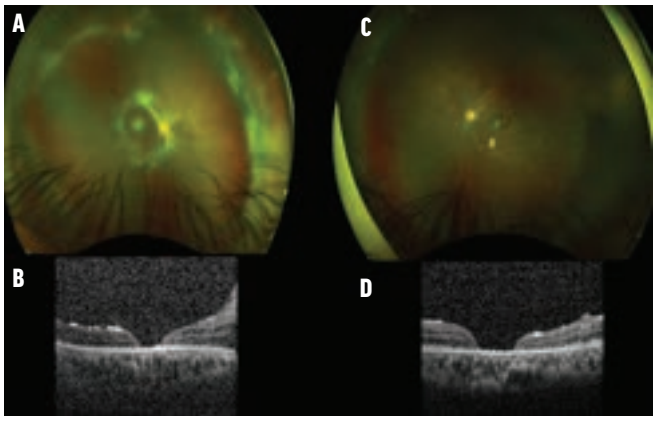
The patient developed a FTMH in the left eye 17 months later, followed by a rhegmatogenous RD (RRD) with a VA of light perception requiring two surgical repairs, including a scleral buckle, external drainage, cryopexy, and 100% C_3F_8 gas for the first attempt and an RRD/FTMH repair with pars plana vitrectomy (PPV), membrane and internal limiting membrane peeling, PFO, endolaser, and silicone oil injection (1,000 centistokes) for the second. One month later, there was an RD from the FTMH in the right eye with a VA of counting fingers (Figure 1A and B).



Courtesy of Giselle de Oliveira

Figure 1. Eighteen months after surgical intervention for the left eye, fundus (A) and OCT (B) imaging of the right eye reveal an RD through the macular hole. At postoperative day 30 after PPV in the right eye (C and D), the retina is attached. At postoperative month 3 (E and F), the retina is redetached with accompanying proliferative vitreoretinopathy.

PPV was pursued in the right eye to repair the RRD with membrane peeling, PFO, endolaser, and silicone oil injection (1,000 centistokes). Intraoperatively, the vitreous was noted to be adherent and fibrillar. The retina was attached on postoperative day 30 (Figure 1C and D), but by postoperative month 3 (Figure 1E and F), the patient developed a redetachment with proliferative vitreoretinopathy. She underwent another RRD repair with PPV, membrane peeling, PFO, endolaser, and silicone oil injection (5,000 centistokes). The retina remained attached in each eye, but the FTMHs



Courtesy of Giselle de Oliveira

Figure 2. Fundus and OCT imaging of the right (A and B) and left (C and D) eyes at postoperative month 6 after the final intervention in the right eye.

persisted in each eye with a VA of 20/200 OD and 20/250 OS at postoperative month 6 (Figure 2).

DISCUSSION

SVD is a rare genetic condition that significantly affects the retina. This disorder is characterized by distinctive crystalline deposits in the vitreous and retina, resembling snowflakes that give the condition its name.[7] These deposits are indicative of the underlying degenerative processes that affect retinal structure and function. While there were no corneal guttata, cataracts, or perivascular sheathing in this case, salient features of SVD included a fibrillar vitreous structure, crystalline retinopathy, and flattened optic nerves.

The primary challenges in managing SVD are its genetic basis and rarity. As an inherited condition, it often requires genetic counseling and family screening to understand the inheritance patterns and identify at-risk individuals. The rarity means there is limited data available, making diagnosis and treatment particularly challenging, especially with the oftentimes subtle and variable initial presentation.

Although pathological myopia and RRD have been described in SVD,[2,5,8] retinoschisis and FTMHs have not been previously associated with this syndrome. No participants in the Hirose et al study were reported to have a macular hole, a finding that is often related to blunt trauma in pediatric patients.[2,5,9] While abnormal vitreous traction has been described in myopic degeneration, it may also be associated with SVD.[10,11] We speculate that the fibrillar vitreous structure is anchored abnormally to the retina in SVD, contributing to vitreomacular traction, FTMHs, and RRD.

RD has been reported in up to 21% of SVD patients.[5] Compared with other retinal degenerations, such as Stickler syndrome, SVD patients have a much higher rate of RD (65%).[12] Pediatric RDs are often more complex than those in adults due to late presentation, associated ocular anomalies, pathology in the fellow eye, and a tendency for bilateral occurrence.[13] These detachments frequently require multiple surgeries to achieve anatomical success, with each procedure carrying risks such as infection, cataract formation, inflammation, and additional retinal damage.[14]

Pediatric patients with SVD require lifelong monitoring to manage the recurrent and progressive nature of the disease. Decision making in pediatric vitrectomies must be individualized and consider the patient's overall development, progression of the disease, and psychosocial effect on the patient and their family. Multidisciplinary care teams, including retina specialists, pediatric ophthalmologists, and geneticists, play a vital role in managing these young patients and providing comprehensive care.

PROCEED WITH CAUTION

SVD presents significant challenges due to its rarity and genetic basis. The retinal complications of macular holes and RD necessitate timely and often repeated surgical intervention, which can be particularly challenging in young patients. Pediatric vitrectomies require long-term follow-up and careful, individualized decision making to preserve vision and quality of life for these patients. ■

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Empowering the Next Generation: Mentorship and Networking at the 2024 AAO Annual Meeting

YoungMD Connect (YMDC) hosted its capstone mentorship and networking event at the 2024 AAO Annual Meeting in Chicago, offering a unique opportunity for early-career ophthalmologists to connect with leaders in the field and representatives from top industry organizations. Specifically designed for medical students, residents, and fellows, the event showcased the power of building connections, collaborating across the profession, and preparing for a thriving future in ophthalmology.

A COMMUNITY FOR ASPIRING OPHTHALMOLOGISTS

The evening drew 285 attendees, 72% of whom were residents, fellows, and early-career ophthalmologists. They participated in a dynamic program featuring a panel discussion, interactive mentorship rotations, and a vibrant networking reception (Figure 1).

Insights on Industry Collaboration

The evening began with an engaging panel discussion led by Paul C. Kang, MD; Tara Capalbo (AbbVie); and Lori Tierney (Johnson & Johnson Vision; Figure 2). The panel explored how partnerships between ophthalmologists and industry stakeholders propel innovation and bolster clinical growth.

Dr. Kang underscored the impact of such collaborations, urging attendees to take the initiative: "Partnering with industry has been pivotal in moving our practices and the field of ophthalmology forward. I urge attendees to seize opportunities to engage with industry leaders."

Capalbo and Tierney complemented his perspective by offering actionable advice. Capalbo discussed strategies for effective cocreation, while Tierney highlighted practical steps for building professional networks and advocating for career advancement. Their insights set the tone for an evening aimed at empowering attendees with tools for success.

Personalized Guidance Through Mentorship Rotations

A hallmark of the event, the mentorship rotations featured 24 faculty mentors representing diverse subspecialties, including retina, cornea, glaucoma, global health, pediatric ophthalmology, oculoplastics, and cataract/refractive (Figure 3). Using an ask-me-anything format, these sessions encouraged candid discussions on critical career topics, including:

- Choosing between private practice and academia;
- Selecting a subspecialty;
- Balancing work and life;
- Engaging with industry; and
- Pursuing research opportunities.

Figure 1. Attendees gather during the YMDC Capstone event.

Figure 2. Panelists Tara Capalbo, Lori Tierney, and Paul C. Kang, MD, in discussion.

Figure 3. William B. Trattler, MD, with attendees during the mentorship rotations.

Robert F. Melendez, MD, MBA (Figure 4), reflected on the significance of these face-to-face interactions: "Meeting in person creates a relaxed environment to connect and explore ideas. YMDC makes it easy for mentees to approach mentors and ask questions directly."

Figure 4. Dr. Melendez poses with (from left to right) Dagny Zhu, MD; Heather Broyles, DO; and Sayena Jabbehdari, MD, MPH, at the networking reception.

Photo courtesy of Judy Kim, MD.

Figure 5. Dr. Kim connects with attendees during the networking reception.

Figure 6. Mentors and mentees connect at the networking reception.

Key Takeaways for Early-Career Ophthalmologists

- No. 1: Build your network. Seek mentors, connect with industry, and collaborate with peers.
- No. 2: Stay curious and proactive. Take charge of your career by asking questions and embracing opportunities.
- No. 3: Trust the process. Focus on growth and relationships during training.
- No. 4: Define your niche. Develop expertise in areas you are passionate about.
- No. 5: Lead with integrity. Treat mentors and colleagues with respect to shape long-term success.

Mentors also shared personal reflections. Emily Schehlein, MD, encouraged attendees to savor their training years: "Residency and fellowship were my favorite stages of my career. The connections I made then have shaped my life and career. I always tell mentees to trust the process and enjoy the journey."

Gary Wörtz, MD, urged participants to define their passions and build their professional brand: "Focus on what excites you most and build expertise around it. Events like YMDC help refine your goals and connect you with mentors who can guide you."

Judy E. Kim, MD, emphasized the importance of integrity and collaboration: "Raise your hand, speak up, and deliver results. Respect and compassion go a long way in building a successful career and leadership pathway" (Figure 5).

BUILDING LASTING CONNECTIONS

The networking reception that followed the mentorship rotations allowed attendees to solidify relationships and exchange ideas in an informal setting (Figure 6).

Eric Rosenberg, DO, highlighted the value of mentorship in shaping the field: "These events provide young ophthalmologists with platforms to connect, learn, and advance. They are essential for fostering the next generation of leaders."

Dr. Wörtz recounted a moment of connection: "I introduced a young ophthalmologist to her hero in the field. Witnessing such eagerness to learn and grow is incredibly rewarding."

Dr. Schehlein summed up the evening's ethos: "Ophthalmology is a small field, making connections easier but also long-lasting. Be mindful, kind, and respectful; you'll be working with these mentors and colleagues for decades."

LOOKING AHEAD TO 2025

The success of the 2024 Capstone event reaffirms YMDC's commitment to fostering mentorship and collaboration. The next YMDC Capstone event will take place at the 2025 AAO Annual Meeting in Orlando, Florida.

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

MEMBRANE PEELING: TIPS AND TRICKS

Surgical videos illustrate several intricate surgical techniques.

BY HUDSON DE CARVALHO NAKAMURA, MD

Recent advances in surgical techniques, particularly the continuous refinement of small-gauge, sutureless vitrectomy approaches, have significantly increased the safety and efficacy of internal limiting membrane (ILM) peeling. Wide-angle viewing systems provide enhanced visibility during the procedure, while macular lenses enable detailed visualization when managing epiretinal membranes (ERMs) and ILMs.

The intricate nature of retinal surgery has always posed significant challenges to retina surgeons. ILM peeling stands out as a critical intervention for conditions such as idiopathic macular holes, vitreomacular traction, and ERM, among others. Certain indications remain controversial, such as diabetic macular edema and primary retinal detachments. Recent advances in surgical techniques and technologies have ushered in a new era of retina peeling, promising better outcomes and fewer complications.

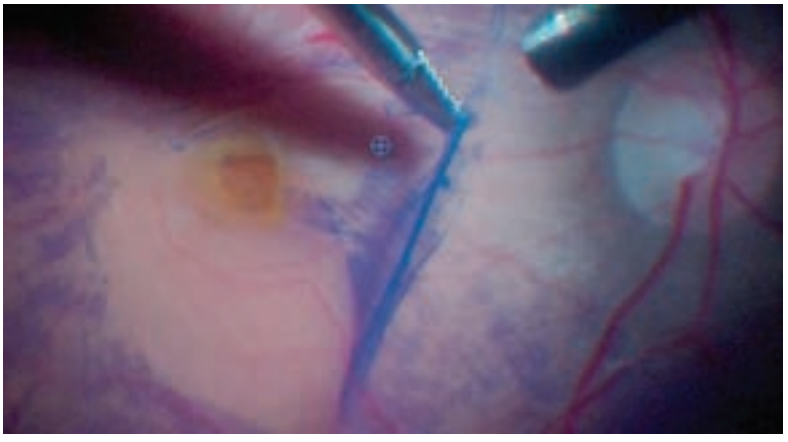


Figure. A 25-gauge serrated forceps was used to peel the ILM. The membrane was removed carefully in a counterclockwise direction with a horizontal pull to minimize complications.

The following three complex surgical cases illustrate useful tips and techniques for ERM and ILM peeling.

CASE NO. 1: PSEUDOMACULAR HOLES

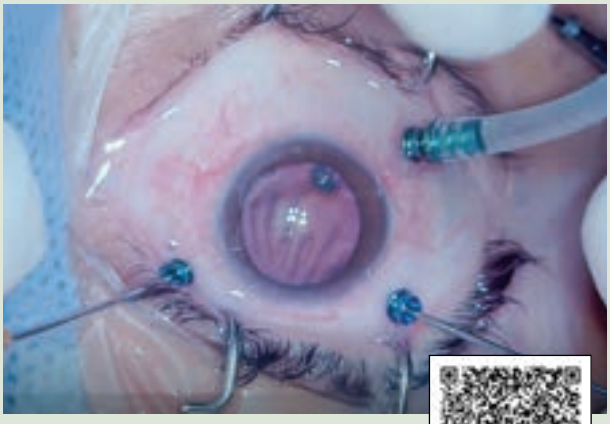
The surgical maneuvers for managing pseudomacular holes can vary based on the specific case, diagnosis, consistency, and tissues involved. When using forceps during retinal surgery (Video 1), it is crucial to hold them halfway open initially to avoid asymmetrical contact with the retina and unintended damage. When peeling the ILM, surgeons should use slow horizontal movements in a clockwise or counterclockwise direction to minimize complications that can arise from vertical traction (Figure). In some cases, loosening the ILM tissue may be challenging because it may be adherent and tense. Closing the forceps' blades symmetrically, ensuring they remain equidistant to secure a proper grip, potentially offers the retina further protection from trauma. After membrane peeling, surgeons may consider employing a gentle, rhythmic motion with a 25-gauge backflush cannula to clear small hemorrhages from the macular region, particularly in cases with resistant ILM.

CASE NO. 2: RETINITIS PIGMENTOSA

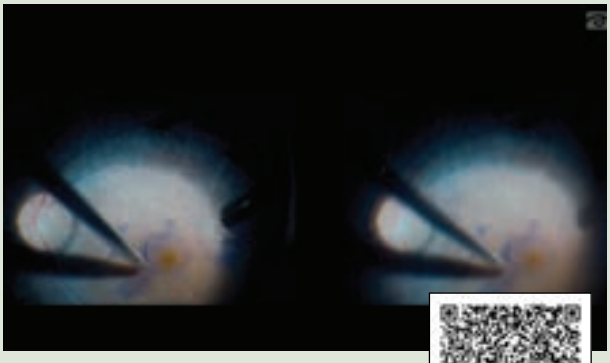
When managing a case of retinitis pigmentosa (RP), I used two different forceps to manipulate the epiretinal tissues and the ILM (Video 2): a 23-gauge endgrip ILM forceps and a serrated 25-gauge forceps. I began the approach with the 23-gauge forceps, which was tilted almost parallel to the retina. To further avoid touching the retina, an edge was created by lifting the ILM, potentially causing less harm than reaching the retina vertically. As the ILM was so adherent that only parts of it could be grabbed, I used the 25-gauge forceps to grab the ILM in a pinch maneuver (opened only halfway).

Of note, the ILM measurement itself does not typically differ between patients with RP and those without the condition; however, the retinal thickness and structural integrity can be different in patients with RP due to the

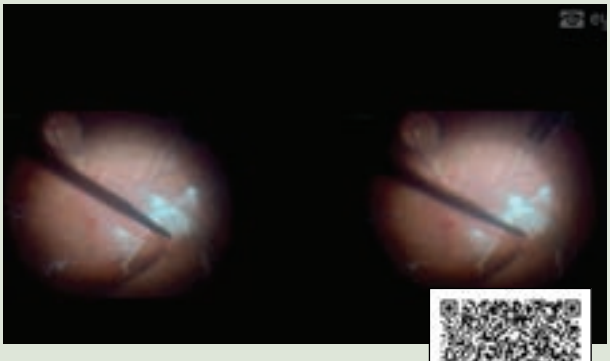
WATCH IT NOW



Video 1. Optimal Timing for ERM Surgery in Patients With Pseudomacular Holes.



Video 2. Complex Membrane Peeling for Vitreomacular Traction in Retinitis Pigmentosa.



Video 3. Fibrovascular Tissue and ILM Peel for Severe Diabetic Retinopathy With Retinal Detachments.

degenerative nature of the disease. Thus, in patients with RP, the outer retinal layers are often thinner, and there can be more pronounced thinning of the photoreceptor outer segments and the retinal pigment epithelium. These changes can be observed using imaging techniques, such as OCT.

CASE NO. 3: SEVERE DIABETIC RETINOPATHY WITH RETINAL DETACHMENTS

Tissue characteristics, such as resistance and thickness, make management of diabetic retinopathy cases increasingly reliant on the surgeon's skill. Proper force application and consideration of vectors and directions are essential to accurately target specific tissues. In the context of diabetic retinopathy, fibrovascular tissue peeling must be conducted with utmost care and delicacy.

When managing a patient with severe diabetic retinopathy and retinal detachments (Video 3), I used 25-gauge serrated forceps, which provides excellent grip on both the ILM and some ERM, allowing the use of gentle and controlled movements. Rushing the procedure or applying excessive force can lead to tearing of the membrane, potentially causing hemorrhage and other complications.

This technique involves securing the fibrovascular tissue and employing horizontal movements, which allows the forceps to engage the membrane with minimal traction. Some ERMs may not be stained with brilliant blue G (the dye that was used in this procedure). As a result, when the ILM is peeled horizontally, it also removes the unstained ERM, achieving a double peel. By removing both membranes from the macular area, this technique effectively relieves traction.

PEELING STRATEGIES AND FUTURE OUTCOMES

The field of retinal surgery is constantly advancing, thanks to ongoing research into bioengineered materials and robotic-assisted procedures. These innovations promise greater precision, reduced human error, and an expanded range of treatable conditions. However, ensuring safety during vitreoretinal surgery requires more than just advanced visualization systems and lenses. It demands the surgeon's tactile sensitivity to feel the membrane through the forceps. The skills, tips, and tricks discussed here can help surgeons make precise movements and determine the direction and force needed without damaging the delicate tissues involved. Ultimately, this blend of technology and human expertise allows for the most successful surgical outcomes. ■

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EVOLVING THE TREATMENT PARADIGM IN GEOGRAPHIC ATROPHY: CONSIDERATIONS FOR EARLY INITIATION OF THERAPY

Complement inhibitors have transformed the landscape, changing how patients with intermediate AMD are followed in the clinic.

Scan this QR code to read the extended article.

Chirag D. Jhaveri, MD

Although geographic atrophy (GA) is irreversible, the recent availability of treatment, in the form of complement inhibitors, is changing the long-term prognosis for patients affected by this eye disease. Because the goal of therapy is to slow down disease progression, early treatment may improve the prospect of preserving viable retina, and with it, functional vision. **Success will depend on understanding what to look for** in the clinic and on imaging, **how to discuss treatment** with patients, and, ultimately, **whether community eye care practitioners are diligent** in recognizing early warning signs and referring promptly.

What to Look For

Treatment option availability for GA has altered how patients with intermediate age-related macular degeneration (AMD) are followed over time. Prior to the advent of complement inhibitors, most patients with intermediate AMD were seen on an annual schedule for an examination and OCT imaging. Now, for patients with findings on OCT that are indicative of progression to GA, we prefer to see them back in the clinic every 6 months at a minimum, and even sooner if the eye is showing nascent GA on imaging. Furthermore, we are incorporating fundus autofluorescence (FAF) imaging more often and earlier in the patient's journey to look for the hallmark hypofluorescence associated with GA and for signs of hyperfluorescence (bright areas at the lesion margin), which show areas of potential GA expansion.[1]

Although FAF is a crucial modality for recognizing GA—it was used during the pivotal trials of each on-market complement inhibitor to track, measure, and follow lesion growth over time—OCT still has a critical role in following patients over time, and even before GA becomes apparent. For example, **certain imaging biomarkers that can be identified on OCT are associated with a higher risk of GA development,** including:

- subretinal drusenoid deposits (also known as reticular pseudodrusen),
- large soft drusen collapse,
- loss of the ellipsoid zone,
- sinking of the inner nuclear layer (INL) and outer plexiform layer (OPL),
- hyporeflective wedges,
- and hyperreflective foci.[2]

As well, OCT is useful for detecting both incomplete retinal pigment epithelium (RPE) and outer retinal atrophy (iRORA) and complete RPE and outer retinal atrophy (cRORA); each of these are considered nascent forms of GA, and their detection may identify patients who would benefit from therapy.[3] Finally, OCT is used to monitor for development of neovascularization, which may be especially important for those on complement inhibitors, as there was an increased risk of choroidal neovascularization in treated patients compared to sham in each of the pivotal studies for avacincaptad pegol (Izervay, Astellas)[4] and pegcetacoplan (Syfovre, Apellis).[5]

Patient Conversations

With complement inhibitors, the objective is to slow down the disease state, and, importantly, not to reverse or stop GA lesion growth. Because patients will not experience improved vision, and because at the current time there are not objective parameters for gauging treatment success, getting patients to commit to long-term treatment can be challenging, especially if they are asymptomatic. Nevertheless, a commitment to educating patients about what is going on in their eye, their options for treatment, and their potential for future loss of functional vision is fundamental to gaining their buy-in to long-term treatment.

Showing patients their own imaging gives them a visual perspective on the changes taking place at the back of the eye. FAF clearly shows GA lesions, and even near-infrared reflectance imaging, which shows GA as areas of hyperreflectivity,[6] can be helpful for education purposes.

Working With Community Partners

In a paradigm in which we want to encourage patients to think about treatment options early in their disease continuum, perhaps even before they are symptomatic, **success will hinge on whether community eye care practitioners recognize the earliest warning signs and refer promptly.** For this reason, it is important to **educate referral sources about the availability of treatment options, and particularly about the early imaging findings associated with progression to GA.** Community eye care practitioners already play an important role in educating patients about the health of their eyes; advancing their knowledge about GA empowers them to have meaningful conversations with prospective patients about their options so they are more informed when they arrive in our clinics. ■

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DOES IRIS COLOR MATTER IN UVEAL MELANOMA?

Research confirms that light eyes are a risk factor.

BY CHARLES DEYOUNG, BA; ALEXANDRA R. ZALOGA, BA; ROLIKA BANSAL, MD; AND CAROL L. SHIELDS, MD

Uveal melanoma (UM) is an ocular malignancy that most often affects individuals of European descent.[1] This tumor can arise de novo or via transformation of a benign nevus,[2,3] and epidemiological risk factors include older age, male gender, White race, fair skin color, blond hair, light iris color, sunlight exposure, and history of cutaneous melanoma.[4-6] Thus, the incidence of UM varies substantially worldwide, with individuals of lighter skin tone and with lighter irises being more at risk.[7] In addition to higher UM rates in White individuals, there is a notable increase in the incidence of UM from southern to northern Europe.[1,7]

The most common iris color globally is brown, accounting for approximately 70% to 80% of the world population,[8] but many northern European countries demonstrate a majority of individuals with blue eyes (Figure).[8] Moreover, populations with lighter irises, such as those in Northern Europe, exhibit higher rates of UM compared with populations with darker irises, such as those in Africa and Asia.[6] Incidence rates of UM are greater than or equal to eight cases per one million in northern Europe, western Europe, and Oceania; two to eight cases per one million in North America, eastern Europe, and southern Europe; and more than two cases per one million in South America, Asia, and Africa.[7]

IRIS COLOR AND RISK OF UVEAL MELANOMA

Iris pigmentation is determined by the ratio of pheomelanin to eumelanin in the iris, with a higher pheomelanin to eumelanin ratio found in individuals with lighter irises.[9] In contrast, eumelanin, which is photoprotective, is found to be elevated in darker irises. Pheomelanin is phototoxic, which can induce DNA damage in pigmented tissues via prooxidant activity. This damage can also be exacerbated by UV radiation exposure,[9] a phenomenon that may be a potential factor in the pathogenesis of UM.[10]

A meta-analysis by Weis et al that included 10 case-controlled studies assessed UM risk and reported that individuals with lighter irises are at a 1.75-times greater risk of developing UM compared with those with darker irises.[11] Other studies have shown an odds ratio (OR) ranging from 1.3 to 3.1 for green irises and 1.1 to 3.4 for blue irises when compared with brown irises.[1,12-19] While the increased likelihood of developing UM in individuals with lighter irises is well-documented, there are little data available about outcomes in darker irises.[12,13]

In 2020, Houtzagers et al analyzed UM rates based on iris color in a Dutch population.[1] This study included 412 patients who were matched with controls based on eye color. Unsurprisingly, the results indicated that individuals of White/European ancestry with green/hazel iris color (OR = 3.64) and those with blue/gray iris color (OR = 1.38) had a significantly higher risk of developing UM compared with those with brown irises, which supports prior reports.[11] While this study demonstrated a strong correlation between iris color and UM risk, the differences in clinical features or outcomes based on eye color were not explored.

IRIS COLOR AND CLINICAL OUTCOMES OF UVEAL MELANOMA

Zaloga et al sought to further explore the clinical characteristics and outcomes of UM based on iris color.[19] They analyzed 7,245 patients with UM who were treated at a single ocular oncology center and observed that most patients were White (n = 7,075; 98%) and had blue

Figure. This world map shows the most common iris color by country.

Adapted with permission from: Eye color by country. World Population Review. Accessed June 14, 2024. worldpopulationreview.com/country-rankings/eye-color-by-country

irises (51%), followed by brown (29%) and green irises (20%).[19] Initial treatment approaches included plaque radiotherapy (63%), enucleation (27%), partial lamellar sclerouvectomy (5.3%), and transpupillary thermotherapy (4.4%). The only difference in the initial treatment distribution based on iris color was a higher rate of primary enucleation in those with brown irises. No difference was noted in the presence of subretinal fluid or extraocular extension among the groups; however, patients with brown irises (brown irises vs blue irises vs green irises) were more likely to demonstrate Bruch membrane rupture (24% vs 19% vs 21%, $P < .01$) and subretinal and/or vitreous hemorrhage (12% vs 9% vs 9%, $P = .02$).

The researchers also found no difference in overall survival, globe salvage, or vision outcomes based on iris color.[19] Although iris color did not consistently lead to differences in tumor features, outcomes, or death, independent risk factors for UM-related metastasis were tumor thickness (OR = 1.16) and subretinal and/or vitreous hemorrhage (OR = 1.52). The independent risk factors for UM-related death included patient age (OR = 1.01), tumor thickness (OR = 1.15), and subretinal and/or vitreous hemorrhage (OR = 1.59).[19]

A comparison of iris color revealed that green irises showed significantly greater risk of UM-related death than blue irises ($P = .02$), which was a bit surprising and unexplained. However, when comparing blue irises with brown irises, there was no significant difference in UM-related death. Despite similar proven risk factors for metastasis and death (eg, tumor thickness, melanocytosis, heterochromia) between the blue and green iris groups, a difference in UM-related death persisted, suggesting eye color alone may play a role in UM-related outcomes. Therefore, iris color may be included as a risk factor for death, especially given that Sen et al found that individuals with lighter skin tones demonstrated greater UM tumor cytogenetic mutations that are known to be related to increased metastasis and death.[20]

FUTURE DIRECTIONS

Iris color does appear to matter in UM. Individuals with lighter irises have higher rates of UM compared with those who have darker irises, which could influence screening, treatment, and overall outcomes of UM. Although Zaloga et al identified variations in tumor characteristics and mortality rates in UM patients based on iris color, further research is needed to better understand precisely how eye color affects the pathogenesis and disease course of UM. ■

Carol L. Shields, MD, has had full access to all the information in the study and takes responsibility for the integrity of the information provided. Support was provided in part by the Jerry A. Shields, MD, Eye Cancer Fund, Philadelphia (CLS) and the Eye Tumor Research Foundation, Philadelphia (CLS). The funders had no role in the design and conduct of the study, in the collection, analysis and interpretation of the data, or in the preparation, review, and approval of the manuscript.

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SURGICAL TECHNIQUES AND TECHNOLOGIES

(Continued from page 39)

all patients.[11] However, none of these cases specified the amount of time that the PFO was left in the eye. There are fewer reported cases of hAM positioned under PFO to treat refractory MHs without RD.[12] Our case supports the idea that allowing hAM to remain under PFO for several minutes may improve graft adhesion and help prevent graft dislocation in the case of a refractory MH.

A NOVEL APPROACH TO TRY

We postulate that using a larger graft and waiting for at least 2 minutes with the graft under PFO allows for displacement of fluid from underneath the graft and promotes adhesion to the macular surface, thereby decreasing postoperative graft dislocation. ■

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CODING ADVISOR
A Collaboration Between *Retina Today* and AMERICAN ACADEMY OF OPHTHALMOLOGY

DECODING THE NUANCES OF INJECTABLE ANTIBIOTICS IN RETINA

Here is a brief overview of the claim process for injectables.

BY JOY WOODKE, COE, OCS, OCSR

Treating patients with endophthalmitis is common in retina practices. When injecting antibiotics, most likely vancomycin and ceftazidime, the coding can be daunting, and ensuring proper reimbursement is often a challenge. Let's review various clinical scenarios, the correct coding for each, and any additional claim requirements.

MEDICATION PACKAGING

The form of the medication—whether it is compounded, a liquid vial, or a powdered vial requiring reconstitution—will guide the coding and claim submission process (Table).

Compounded

Compounded antibiotics are often preferred and should be reported using HCPCS code J7999, compounded drug, not otherwise classified. Modifier -JZ should be appended to J7999, as there is no waste. Additionally, report the name of the drug(s), dosage(s) in milligrams per milliliters, and the invoice amount(s) in item 19 of the CMS-1500.[1]

Report the NDC in item 24a of the CMS-1500 per the payer policy. Some payers require the NDC of the original ingredient(s) and all drug NDCs if the compounded medication consists of more than one drug.[2] Medicare, however, does not associate compounded medications with an NDC.[1]

The unit of measure (UOM) should be reported following the NDC in item 24a of the CMS-1500. Report the volume injected in milliliters; for example, a volume of 0.1 ml (liquid form) would be reported as ML0.1.

Liquid Vial

When the medication is packaged as a liquid vial, report the HCPCS code for the medication injected. For example:

- J0713 injection, ceftazidime, per 500 mg
- J3370 injection, vancomycin, per 500 mg

Based on the HCPCS descriptor, one unit should be

TABLE. ANTIBIOTIC CODING IN RETINA

	HCPCS Code	Unit	Modifier	NDC	UOM
Compounded	J7999*	1	-JZ	Per payer policy	Volume, ML (eg, ML0.1)
Vial, liquid form	J0713, ceftazidime J3370, vancomycin	1	-JZ for single-dose vials	Unique per vial	Volume, ML (eg, ML0.1)
Vial, powder form	J0713, ceftazidime J3370, vancomycin	1	-JZ for single-dose vials	Unique per vial	Units, UN (eg, UN1)

*Report medication name, dosage in milligrams per milliliters, and invoice amount in item 19 of the CMS-1500.

For an overview of antibiotic coding, visit the following AAO sites:

Practice Management for Retina

Coding for Injectable Drugs

reported when 500 mg or less is injected. Modifier -JZ should be appended to the appropriate HCPCS code, as there is no waste, 1 unit or greater. Make sure to document the amount of medication in milligrams per milliliters injected.

Report the NDC as indicated on the vial in item 24a of the CMS-1500, followed by the UOM in ML.

Powdered Vial

If the medication used was reconstituted from a powder form, report the appropriate HCPCS code and unit, along with modifier -JZ. Document the dosage in milligrams per milliliters. Note that the NDC will vary by medication, as will the UOM. Vial quantity should be reported in units; when one powdered vial is used, report the UOM as UN1.[3]

COVER YOUR BASES

Confirm that your chart documentation and inventory system are tracking each patient's medication and its packaging so that both match your claim submission. In the event of an audit, the reviewer may also request your documentation and inventory to confirm the appropriate HCPCS code/modifier, unit, NDC, and UOM were reported. ■

1. Billing and coding: approved drugs and biologicals; includes cancer chemotherapeutic agents. Centers for Medicare & Medicaid Services. Revised November 2, 2023. Accessed December 5, 2024. www.cms.gov/medicare-coverage-database/view/article.aspx?articleId=53049
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Want to learn more about the -JZ modifier?

Check out *How to Implement the -JZ Modifier* From the October 2023 issue of *Retina Today*

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THROUGH THE EYES OF THE RESEARCH FELLOW

Here's how these former and current fellows got their start—and what it took to get to where they are now.

BY ROSELIND NI, BS; TURNER D. WIBBELSMAN, MD; BITA MOMENAEI, MD; RAZIYEH MAHMOUDZADEH, MD; AND JASON HSU, MD

Dedicating time to research opens doors for fostering connections, growing careers, and gaining new skills and knowledge, but it also presents new challenges. Research has become an increasingly important factor in residency applications and can help fellows determine whether they want to pursue an academic career. There are many considerations to keep in mind when deciding to participate in research. Here, three current or former Wills Eye research fellows—Turner D. Wibbelsman, MD; Raziyeh Mahmoudzadeh, MD; and Bita Momenaei, MD—share their journeys to success and offer advice for those considering the research fellowship path.

ROSELIND NI, BS: WHY DID YOU CHOOSE TO PURSUE A RESEARCH FELLOWSHIP, AND HOW HAS IT AFFECTED YOUR CAREER TRAJECTORY?

Dr. Mahmoudzadeh: I discovered my passion for research early in medical school, starting with bench research, then transitioning to clinical research. I realized that research made my day-to-day work more meaningful, pushed me to stay up to date on the rapidly expanding knowledge in ophthalmology, and helped me explore the unknowns within the field of medicine. My passion for clinical research grew during residency in Iran (my home country), and I recognized the need to broaden my experiences to design and conduct higher-quality research. I saw the retina research fellowship as an opportunity to deepen my skills and further explore how to address important clinical questions. After meeting with US mentors at international conferences, I decided to further my expertise in the United States.

Dr. Wibbelsman's Advice: "It is well-understood that dedicated time for research prolongs the completion of training. Regardless, view the opportunity as time on, rather than time off. Research allows you to connect with mentors, learn about the field, and hone technical research skills; most importantly, the product of the work is a contribution to advancing the field and improving the lives of our patients."

Dr. Momenaei: I became interested in research during my residency in Iran and found it incredibly rewarding. However, in Iran, we did not have access to electronic health records or the ability to conduct large-scale data research. This motivated me to pursue a research fellowship in the United States. At Wills Eye Hospital, I now have the privilege of collaborating with leading experts who serve as valuable resources and mentors. Having access to large-scale data allows me to engage in comprehensive data analysis and contribute to impactful research projects. I have deepened my understanding of how to refine research questions, found novel ways to approach complex problems analytically, and improved my teamwork and multitasking skills. Additionally, attending and presenting at meetings offers excellent opportunities to network and stay informed about advancements at other research centers.

Dr. Wibbelsman: As an undergraduate student pursuing medical school, I saw clinical research as an avenue to learn

INTERNATIONAL RESEARCH FELLOW PERSPECTIVES

"I arrived in Philadelphia for my research fellowship on the first day of the COVID-19 lockdown in 2020. On top of the pandemic restrictions, I had to learn to navigate life in a different country and adapt to a new research setting. One of the biggest challenges I faced was working through the Visa process. I wanted to get my green card before applying to residency—I knew how difficult it would be to match without one. My advice is to be persistent and adaptable. The process made me more resilient and resourceful."

— Raziyeh Mahmoudzadeh, MD

"Securing a Visa required traveling to neighboring countries for US embassy appointments. Leaving behind my family and an established career to start anew in the United States was a significant challenge. Overcoming these obstacles reaffirmed that sacrifices are often necessary to achieve ambitious goals. My advice is to find your passion, stay focused, and give your absolute best effort. Believe in yourself and your ability to navigate the journey—each step will bring you closer to where you want to be."

— Bita Momenaei, MD

about and contribute to the health care field. I was curious about the technical and logistical aspects of conducting high-quality research and worked as a research assistant in college. When I became interested in ophthalmology as a career, I decided to pursue a research position in the field between undergraduate and medical school. During my research year, I worked with forward-thinking senior trainees and attending mentors. Having this experience early in my medical career provided me with a focused and intentional approach to the rest of my training.

MS. NI: WHAT WERE YOUR GOALS GOING INTO THE RESEARCH FELLOWSHIP, AND WHAT ARE THEY NOW?

Dr. Mahmoudzadeh: During my research fellowship, one of my goals was to refine my ability to design and conduct meaningful clinical studies. I wanted to address practical questions that could improve patient outcomes, particularly in retinal surgery. Another goal was to expand my skills in data analysis and manuscript writing to ensure that my research would have a lasting effect. Research has inspired me to pursue academic ophthalmology. Now, my primary goal is to combine patient care with research to continue answering clinical questions and developing innovative solutions. I also hope to mentor future ophthalmologists.

Dr. Momenaei: I have focused on learning how to develop a new study idea and see it to completion, work with large-scale data, and refine my analytical and problem-solving skills. Another goal was to better understand evidence-based ophthalmology. Additionally, I have prioritized mentoring medical students interested in ophthalmology, guiding them in research, and helping them engage with the field. I am applying to ophthalmology residency with plans to pursue a retina fellowship after. My long-term goal is to integrate clinical practice with research in academic medicine and combine patient care with innovation and education. I am passionate about mentoring and advancing the field through collaboration and participation in clinical trials.

Dr. Wibbelsman: When I began my research fellowship, I had relatively little knowledge of clinical ophthalmology. After absorbing as much information as possible in the first few months, I set a goal of leading my own projects from start to finish. Under the guidance of my mentors, I was able to devise my own study concepts and execute these projects. This invaluable process provided me with much-needed experience with every step of the research process. As an ophthalmology resident, I now lead medical students on several of my projects, teaching them about ophthalmology and clinical research. My long-term goal is to have an academic career dedicated to patient care and advancement through clinical research. ■

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VABYSMO™
faricimab-svoa injection 6 mg

VABYSMO® (faricimab-svoa) injection, for intravitreal use

This is a brief summary. Before prescribing, please refer to the full Prescribing Information

1 INDICATIONS AND USAGE

VABYSMO is a vascular endothelial growth factor (VEGF) and angiopoietin 2 (Ang-2) inhibitor indicated for the treatment of patients with:

1.1 Neovascular (wet) Age-Related Macular Degeneration (nAMD)

1.2 Diabetic Macular Edema (DME)

1.3 Macular Edema Following Retinal Vein Occlusion (RVO)

4 CONTRAINDICATIONS

4.1 Ocular or Periocular Infections

VABYSMO is contraindicated in patients with ocular or periocular infections.

4.2 Active Intraocular Inflammation

VABYSMO is contraindicated in patients with active intraocular inflammation.

4.3 Hypersensitivity

VABYSMO is contraindicated in patients with known hypersensitivity to faricimab or any of the excipients in VABYSMO. Hypersensitivity reactions may manifest as rash, pruritus, urticaria, erythema, or severe intraocular inflammation.

5 WARNINGS AND PRECAUTIONS

5.1 Endophthalmitis and Retinal Detachments

Intravitreal injections have been associated with endophthalmitis and retinal detachments *[see Adverse Reactions (6.1)]*. Proper aseptic injection techniques must always be used when administering VABYSMO. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay, to permit prompt and appropriate management *[see Dosage and Administration (2.6) and Patient Counseling Information (17)]*.

5.2 Increase in Intraocular Pressure

Transient increases in intraocular pressure (IOP) have been seen within 60 minutes of intravitreal injection, including with VABYSMO *[see Adverse Reactions (6.1)]*. IOP and the perfusion of the optic nerve head should be monitored and managed appropriately *[see Dosage and Administration (2.6)]*.

5.3 Thromboembolic Events

Although there was a low rate of arterial thromboembolic events (ATEs) observed in the VABYSMO clinical trials, there is a potential risk of ATEs following intravitreal use of VEGF inhibitors. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause).

The incidence of reported ATEs in the nAMD studies during the first year was 1% (7 out of 664) in patients treated with VABYSMO compared with 1% (6 out of 662) in patients treated with aflibercept *[see Clinical Studies (14.1)]*.

The incidence of reported ATEs in the DME studies from baseline to week 100 was 5% (64 out of 1,262) in patients treated with VABYSMO compared with 5% (32 out of 625) in patients treated with aflibercept *[see Clinical Studies (14.2)]*.

The incidence of reported ATEs in the RVO studies during the first 6 months was 1.1% (7 out of 641) in patients treated with VABYSMO compared with 1.4% (9 out of 635) in patients treated with aflibercept *[see Clinical Studies (14.3)]*.

5.4 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 VABYSMO *[see Adverse Reactions (6.2)]*. Discontinue treatment with VABYSMO in patients who develop these events. Patients should be instructed to report any change in vision without delay.

6 ADVERSE REACTIONS

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

- Hypersensitivity *[see Contraindications (4)]*
- Endophthalmitis and retinal detachments *[see Warnings and Precautions (5.1)]*
- Increase in intraocular pressure *[see Warnings and Precautions (5.2)]*
- Thromboembolic events *[see Warnings and Precautions (5.3)]*
- Retinal Vasculitis and/or Retinal Vascular Occlusion *[see Warnings and Precautions (5.4)]*

6.1 Clinical Trial 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 other clinical trials of the same or another drug and may not reflect the rates observed in practice.

The data described below reflect exposure to VABYSMO in 2,567 patients, which constituted the safety population in six Phase 3 studies *[see Clinical Studies (14.1, 14.2, 14.3)]*.

Table 1: Common Adverse Reactions (≥ 1%)

Adverse Reactions	VABYSMO			Active Control (aflibercept)		
	AMD N=664	DME N=1,262	RVO N=641	AMD N=662	DME N=625	RVO N=635
Cataract	3%	15%	< 1%	2%	12%	1%
Conjunctival hemorrhage	7%	8%	3%	8%	7%	4%
Vitreous detachment	3%	5%	2%	3%	4%	2%
Vitreous floaters	3%	4%	2%	2%	3%	2%
Retinal pigment epithelial tear[a]	3%			1%		
Intraocular pressure increased	3%	4%	1%	2%	3%	3%
Eye pain	3%	3%	< 1%	3%	3%	< 1%
Intraocular inflammation[b]	2%	1%	1%	1%	1%	< 1%
Eye irritation	1%	< 1%	< 1%	< 1%	1%	< 1%
Lacrimation increased	1%	1%	0%	1%	< 1%	< 1%
Ocular discomfort	1%	1%	< 1%	< 1%	< 1%	< 1%

[a]AMD only
[b]Including iridocyclitis, iritis, uveitis, vitritis

Less common adverse reactions reported in < 1% of the patients treated with VABYSMO were corneal abrasion, eye pruritus, ocular hyperemia, blurred vision, sensation of foreign body, endophthalmitis, conjunctival hyperaemia, visual acuity reduced, visual acuity reduced transiently, vitreous hemorrhage, retinal tear and rhegmatogenous retinal detachment.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of VABYSMO. 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.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies of VABYSMO administration in pregnant women.

Administration of VABYSMO to pregnant monkeys throughout the period of organogenesis resulted in an increased incidence of abortions at intravenous (IV) doses 158 times the human exposure (based on C_{max}) of the maximum recommended human dose *[see Animal Data]*. Based on the mechanism of action of VEGF and Ang-2 inhibitors, there is a potential risk to female reproductive capacity, and to embryo-fetal development. VABYSMO should not be used during pregnancy unless the potential benefit to the patient outweighs the potential risk to the fetus.

All pregnancies have a background risk of birth defect, loss, and other adverse outcomes. The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects is 2%-4% and of miscarriage is 15%-20% of clinically recognized pregnancies.

Data

Animal Data

An embryo fetal developmental toxicity study was performed on pregnant cynomolgus monkeys. Pregnant animals received 5 weekly IV injections of VABYSMO starting on day 20 of gestation at 1 or 3 mg/kg. A non-dose dependent increase in pregnancy loss (abortions) was observed at both doses evaluated. Serum exposure (C_{max}) in pregnant monkeys at the low dose of 1 mg/kg was 158 times the human exposure at the maximum recommended intravitreal dose of 6 mg once every 4 weeks. A no observed adverse effect level (NOAEL) was not identified in this study.

8.2 Lactation

Risk Summary

There is no information regarding the presence of faricimab in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production. Many drugs are transferred in human milk with the potential for absorption and adverse reactions in the breastfed child.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for VABYSMO and any potential adverse effects on the breastfed child from VABYSMO.

8.3 Females and Males of Reproductive Potential

Contraception

Females of reproductive potential are advised to use effective contraception prior to the initial dose, during treatment and for at least 3 months following the last dose of VABYSMO.

Infertility

No studies on the effects of faricimab on human fertility have been conducted and it is not known whether faricimab can affect reproduction capacity. Based on the mechanism of action, treatment with VABYSMO may pose a risk to reproductive capacity.

8.4 Pediatric Use

The safety and efficacy of VABYSMO in pediatric patients have not been established.

8.5 Geriatric Use

In the six clinical studies, approximately 58% (1,496/2,571) of patients randomized to treatment with VABYSMO were ≥ 65 years of age. No significant differences in efficacy or safety of faricimab were seen with increasing age in these studies. No dose adjustment is required in patients 65 years and above.

17 PATIENT COUNSELING INFORMATION

Advise patients that in the days following VABYSMO administration, patients are at risk of developing endophthalmitis. If the eye becomes red, sensitive to light, painful, or develops a change in vision, advise the patient to seek immediate care from an ophthalmologist *[see Warnings and Precautions (5)]*.

Patients may experience temporary visual disturbances after an intravitreal injection with VABYSMO and the associated eye examinations *[see Adverse Reactions (6)]*. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

VABYSMO® [faricimab-svoa]
Manufactured by:
Genentech, Inc.
A Member of the Roche Group
1 DNA Way
South San Francisco, CA 94080-4990
U.S. License No.: 1048

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INDICATIONS

VABYSMO (faricimab-svoa) is a vascular endothelial growth factor (VEGF) inhibitor and angiopoietin-2 (Ang-2) inhibitor indicated for the treatment of patients with Neovascular (Wet) Age-Related Macular Degeneration (nAMD), Diabetic Macular Edema (DME), and Macular Edema following Retinal Vein Occlusion (RVO).

IMPORTANT SAFETY INFORMATION

Contraindications

VABYSMO is contraindicated in patients with ocular or periocular infection, in patients with active intraocular inflammation, and in patients with known hypersensitivity to faricimab or any of the excipients in VABYSMO.

Warnings and Precautions

- Endophthalmitis and retinal detachments may occur following intravitreal injections. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay, to permit prompt and appropriate management.
- Increases in intraocular pressure have been seen within 60 minutes of an intravitreal injection.
- There is a potential risk of arterial thromboembolic events (ATEs) associated with VEGF inhibition.
- Retinal vasculitis and/or retinal vascular occlusion have been reported. Patients should be instructed to report any change in vision without delay.

Adverse Reactions

The most common adverse reactions (≥5%) reported in patients receiving VABYSMO were cataract (15%) and conjunctival hemorrhage (8%).

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at (888) 835-2555.

Please see additional Important Safety Information throughout and in the VABYSMO Brief Summary of full Prescribing Information on the following page.

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Scan the QR code to discover more or visit www.vabysmo-hcp.com/namd

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