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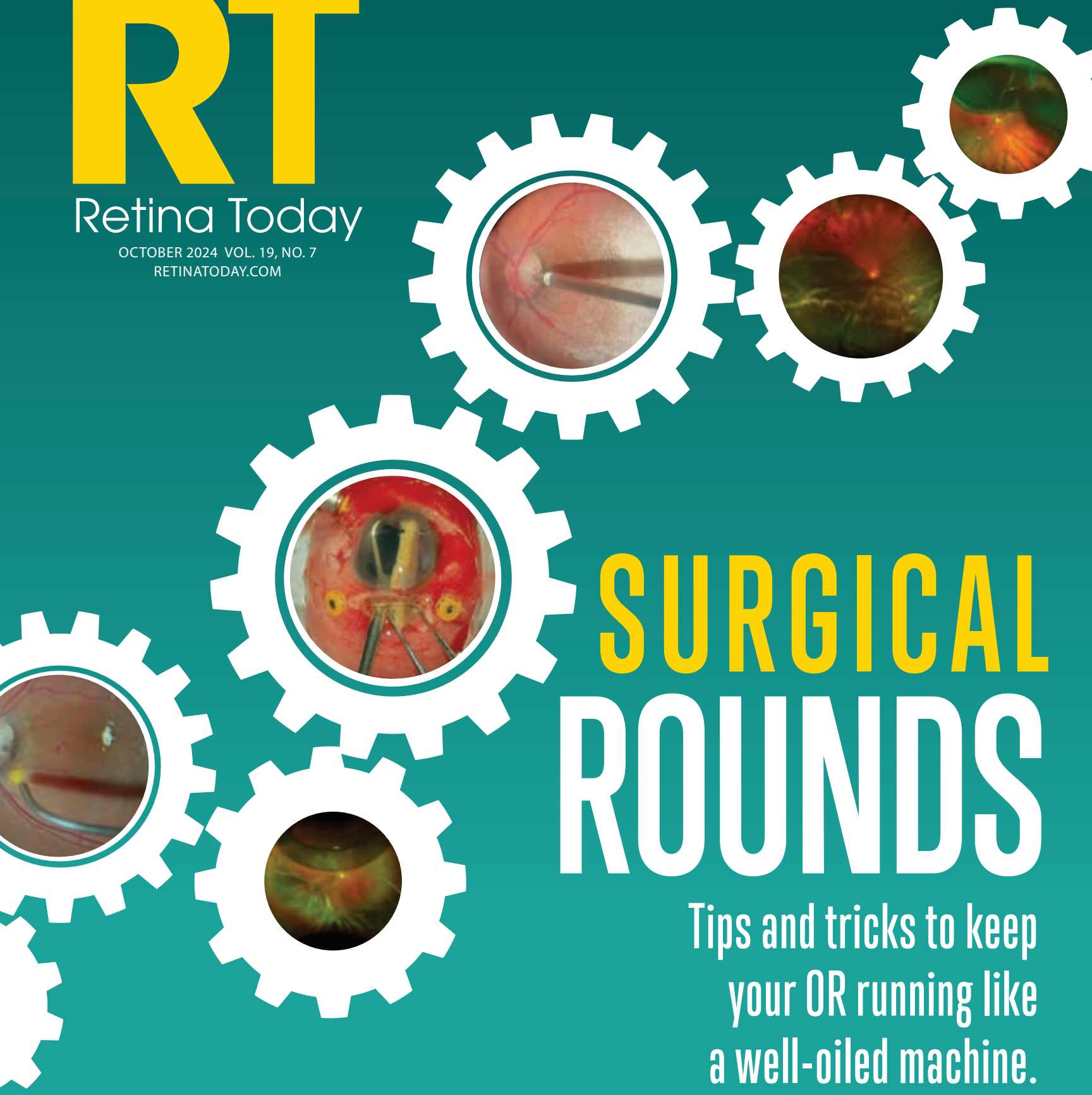
eyetube



SURGICAL ROUNDS

Tips and tricks to keep your OR running like a well-oiled machine.

CONSIDERATIONS FOR OPTIC PIT MACULOPATHY

MANAGING CHALLENGING MACULAR HOLES

ADVICE FROM THE OR: RD AND PVR

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:
IVERIC bio, Inc., An Astellas Company. Parsippany, NJ 07054

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FEATURED ARTICLES

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ONLINE EXCLUSIVE:

Understanding the ROP Epidemic in Africa
By Catherine Manthorp, BA, Senior Editor

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A new dawn is on the horizon

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PROBLEM SOLVERS UNITE

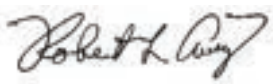

The annual surgical rounds issue is a favorite for many of us. It captures one of the most fun aspects of being a retina specialist: collaborating with each other to solve clinical problems. This one just happens to focus on the surgical side of things. When you read through these pages, we hope it transports you to the break room where some fellows tracked you down to discuss a tough macular hole case on the schedule. Or to a call made to a colleague to pick their brain about adding a scleral buckle to the surgical plan for a patient with proliferative vitreoretinopathy (PVR) who's heading back to the OR. Better yet, to a conference hall jotting down surgical pearls from lectures on optic pit maculopathy, visually significant vitreous opacities, and intraocular foreign bodies. The goal here is to bring these shared experiences to life for everyone to learn from.

We love the teamwork that is inherent in our field. We look forward to learning from each other and are always eager to try out a new surgical technique or tool. None of our cases are "routine," and every surgical encounter is unique. That means we need to be flexible in the OR, ready to change surgical plans and call a friend when we need advice. (Of course, the longer you are in the OR, the fewer calls you make and the more you take.) There is always a challenging case that has us sifting through the literature to see how others have handled it. If it's particularly interesting, we might find ourselves adding to that body of literature.

Every featured article in this issue addresses a scenario that's anything but routine—they are controversial, up for debate, challenging, or have no set management guidelines. See the theme? We are continually refining our surgical approaches, and these types of conversations are crucial to help us find better ways to preserve our patients' vision.

In this issue, Luke Mavrofrides and Matthew A. Cunningham, MD, FASRS, provide their guidance on managing optic pit maculopathy in the OR, and Tamer H. Mahmoud, MD, PhD, and Omar M. Moinuddin, MD, discuss our ever-expanding armamentarium for challenging macular holes. (Have you tried the retracting door inverted internal limiting membrane flap technique? That's a mouthful.) Haemoglobin Parida, MBBS, MS, and Juan Carlos Gutierrez Hernandez, MD, share their approaches to organic and glass intraocular foreign bodies (with videos!), and Linnet Rodriguez, MD, teases out expert advice on retinal detachment repair in the setting of PVR from her colleagues at Wills Eye Hospital. Nita Valikodath, MD, MS, and her team review postoperative face-down positioning after retinal detachment repair, and Peter Karth, MD, MBA, FASRS, FACS, tackles one of the latest controversies in retina: vitrectomy for visually significant vitreous opacities. If medical retina is your jam, we have an interesting article on detecting infective endocarditis during a routine retinal examination by Mathew W. MacCumber, MD, PhD, and colleagues.

Whether you read cover-to-cover or pick through your favorite topics within, we hope you find this issue as fun as we do, learn something new, and are reminded that we are all united in our efforts to preserve our patients' vision, especially when a condition, complication, or trauma sends them to the OR. Stay tuned for our last issue of the year, which focuses on the therapeutic pipeline. ■

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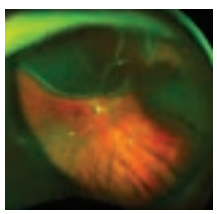
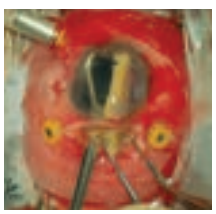
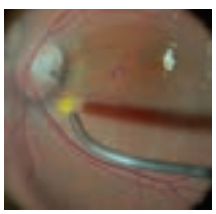


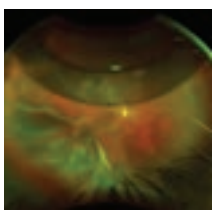
A 69-year-old man presented with a macula-splitting retinal detachment in the right eye with retinal breaks superiorly, temporally, and nasally. In: *Head Positioning After RD Surgery: A Review.*



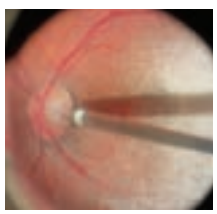
A wooden splinter, measuring 15 mm x 5 mm, was removed with the help of McPherson forceps and an irrigating vectus. In: *Material Matters: Managing IOFBs.*



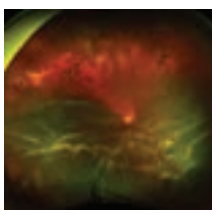
During vitrectomy for optic pit maculopathy, performing endolaser may help to lower the risk of blind-spot enlargement. In: *Surgical Considerations for Optic Pit Maculopathy.*



Fundus imaging revealed a retinal detachment with retinal folds, a detached macula, and proliferative vitreoretinopathy (PVR). In: *Advice From the OR: RD and PVR.*



To address vitreous traction on the optic pit, stain the hyaloid with triamcinolone to ensure complete hyaloid elevation during vitrectomy. In: *Surgical Considerations for Optic Pit Maculopathy.*



Fundus photography revealed a retinal detachment with PVR and macular involvement, which prompted a trip to the OR. In: *Advice From the OR: RD and PVR.*

DIAGNOSTICS · LASERS

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THE CLINICAL EFFECTS OF BEVACIZUMAB RECALLS

Recalls of large quantities of off-label intravitreal bevacizumab (Avastin, Genentech/Roche) have caused clinical disruptions and delays in patient care, according to a new study published in *Ophthalmology Retina*. Researchers, led by Hasenin Al-khersan, MD, recently studied the Pine Pharmaceuticals intravitreal bevacizumab recall in October 2023 and its effect on patients and retina practices.[1,2] They found that, compared with the year prior, eyes were more than five-times more likely to switch from bevacizumab to another anti-VEGF agent after the recall. The effects of this recall may have disproportionately affected uninsured patients, who were less likely to switch, and patients treated with bevacizumab were also more likely to experience delays in treatment.

"Our data demonstrate that large recalls cause disruption in patient care," says Dr. Al-khersan. "More than 10% of our cohort showed an increase in their injection interval of 28 days or more after the recall compared with the interval beforehand—this jump in the interval likely reflects treatment delays."

The retrospective review included 19 retina practices in 16 states and was conducted using the Health Analytics in Ophthalmology (HALO) registry of the Retina Consultants of America. "The HALO registry houses clinical data from more than 29 practices in 24 states and more than 300 retina physicians," says Dr. Al-khersan. "More than 1.7 million visits are available, with capabilities to review imaging data on the way."

Patients receiving at least two intravitreal bevacizumab injections within 6 months prior to the recall were included (25,689 eyes, the recall cohort). A comparative analysis for the same interval 1 year prior was also performed to determine comparative usage rates of bevacizumab within the same practices (29,366 eyes, comparator cohort).

Of the eyes in the recall cohort, 39.4% switched to an anti-VEGF agent other than bevacizumab after the recall. Eyes of uninsured patients were less likely to switch post-recall (20.5%) compared with those of insured patients (39.5%). The switch rate was significantly lower in the comparator cohort (7.6%).[1]

Many insurance plans require step therapy with bevacizumab as the first agent, and they require unique authorizations to bypass step therapy. During the Pine Pharmaceuticals recall, the American Society of Retina Specialists met with the Centers for Medicare and Medicaid Services to discuss the effects of the recall on patients required to follow step therapy and advocated for a contingency plan to bypass step therapy in cases of recalls.[3]

"Many retina practices across the country receive their bevacizumab from a handful of compounding pharmacies," says Dr. Al-khersan. "Therefore, large recalls have the capacity to be very disruptive to clinic workflows, particularly in the era of step therapy when many patients are required to receive bevacizumab for their initial treatments. Given the prevalence of bevacizumab-first step therapies, we believe that insurance carriers should have contingency plans in place to bypass step therapies when recalls occur so as to ensure patient treatments are not delayed."

Dr. Al-khersan and his team also found that eyes switching to agents other than bevacizumab after the recall had better visual acuity gains than those remaining on bevacizumab. "Though early studies reported noninferiority of bevacizumab to ranibizumab, newer anti-VEGF agents may demonstrate improved outcomes in certain patient populations, which would be important to understand," he explains. "Our current work lacked anatomical data, so further research is warranted to investigate the visual acuity findings observed."

1. Al-khersan H, Garcia E, Fan KC, et al. Impact of a recall of intravitreal bevacizumab: a HALO registry review [published online ahead of print September 2, 2024]. *Ophthalmol Retina*.
2. Pine Pharmaceuticals announces voluntary recalls, including Avastin. American Society of Retina Specialists. October 2, 2023. Accessed September 9, 2024. bit.ly/3XCXYKb
3. ASRS to meet with CMS on Avastin shortage; will urge an end to step therapy. American Society of Retina Specialists. October 18, 2023. Accessed September 9, 2024. bit.ly/3zgBuFv

ANTI-VEGF INJECTION PRIOR TO PRP YIELDS MORE SUCCESSFUL OUTCOMES IN PDR

A recent study published in *JAMA Ophthalmology* reported that patients with proliferative diabetic retinopathy (PDR) treated with panretinal photocoagulation (PRP) first and subsequent anti-VEGF injection are more likely to undergo vitrectomy for vitreous hemorrhage (VH) and tractional retinal detachment (TRD) compared with eyes treated with anti-VEGF injection before PRP.[1]

This retrospective cohort study analyzed data from January 2003 to January 2024. A total of 1,377 patients with PDR treated with PRP first and subsequent anti-VEGF injection

and 1,377 patients with PDR treated with anti-VEGF injection first and subsequent PRP were included.[1]

The researchers found that treatment with PRP and subsequent anti-VEGF injection was associated with higher rates of vitrectomy at 5 years (relative risk [RR]: 1.88), with similar associations at 6 months, 1 year, and 3 years. Treatment with PRP first and subsequent anti-VEGF injection was also associated with higher rates of VH (RR: 1.40) and TRD (RR: 1.85) at 5 years, with similar findings at 6 months, 1 year, and 3 years.[1]

"These findings support the need for further investigations to determine if the order of PRP and anti-VEGF injections should be considered when treating patients with PDR," the investigators concluded in their paper.[1]

1. Alsoudi AF, Wai KM, Koo E, Parrikh R, Mruthyunjaya P, Rahimy E. Initial therapy of panretinal photocoagulation vs anti-VEGF injection for proliferative diabetic retinopathy [published online ahead of print August 29, 2024]. *JAMA Ophthalmol.*

FDA RECEIVES FTC SUPPORT TO STREAMLINE THE BIOSIMILAR APPROVAL PROCESS

The Federal Trade Commission (FTC) has expressed support for the FDA's recent draft guidance on interchangeable biosimilar drugs to enhance patient access to affordable prescription medications. The FDA's draft guidance proposes changes that aim to streamline the approval process for biosimilars and make it easier for these drugs to be used in place of more expensive brand-name biologics.[1]

Biologic drugs are among the most expensive on the market, placing a significant financial burden on patients, the FDA stated in a press release. Biosimilar drugs offer a cost-effective alternative to treat the same conditions as their brand-name counterparts with no clinically meaningful differences in safety or effectiveness.[1]

A key aspect of the FDA's draft guidance is the removal of the previous requirement for biosimilar drug applicants to submit clinical switching studies to prove that their product is interchangeable with the reference biologic drug. The new guidance would allow biosimilar applicants to provide a rationale, supported by existing data from their biologic license application, to demonstrate interchangeability. This change would allow pharmacists to substitute a biologic with a biosimilar without needing prescriber approval.[1]

1. FTC backs FDA draft guidance on interchangeable biosimilar drugs [press release]. Eyewire+. August 21, 2024. Accessed September 9, 2024. bit.ly/3MLEi0G

INTERIM RESULTS REPORT 4-YEAR VISUAL MAINTENANCE WITH PDS

Interim results from the Portal extension trial evaluating the port delivery system (PDS) with ranibizumab (Susvimo, Genentech/Roche) for the treatment of wet AMD demonstrate the maintenance of visual and anatomical outcomes through 4 years with PDS 100 mg/ml. The results also show that the PDS was preferred to monthly injections and the implant has a well-characterized long-term safety profile.[1]

This multicenter, nonrandomized, open-label extension clinical trial included 555 patients who completed the phase 2 Ladder or phase 3 Archway trials.[1]

A total of 137 (24.7%) patients had at least one ocular adverse event of special interest; the most common were cataract (11.4%), conjunctival thickening (bleb)/filtering bleb leak (6.3%), and vitreous hemorrhage (6.1%). Endophthalmitis occurred in 11 (2.0%) patients. Approximately 95% of patients did not need supplemental treatment before each refill-exchange for > 2 years since Portal enrollment.[1]

For Ladder-to-Portal patients previously treated with PDS 100 mg/ml or monthly ranibizumab (Lucentis, Genentech/Roche), BCVA remained stable from baseline to month 48; the mean change from baseline was 0.1 and 2.3 letters, respectively. Center point thickness remained stable through month 48 in these patients. Of the Ladder-to-Portal monthly ranibizumab patients, 92% preferred the PDS over injections.[1] ■

1. Campochiaro PA, Eichenbaum D, Chang MA, et al. Interim results of the phase III Portal extension trial of the Port Delivery System with ranibizumab in neovascular age-related macular degeneration [published online ahead of print August 27, 2024]. *Ophthalmol Retina.*

Eyewire+ Pharma Update

- **Atsena Therapeutics** received rare pediatric disease designation from the FDA for **ATSN-201**, its gene therapy candidate for the treatment of X-linked retinoschisis. The phase 1/2 LIGHTHOUSE trial is underway to evaluate the therapy's safety and tolerability.
- The FDA granted investigational new drug clearance for **OpCT-001 (BlueRock Therapeutics)**, an induced pluripotent stem cell-derived therapy for the treatment of primary photoreceptor conditions, such as retinitis pigmentosa (RP) and rod-cone dystrophy.
- **Ocugen** received approval from Health Canada to initiate its phase 3 Limelight trial of **OCU400**, a modifier gene therapy candidate for the treatment of RP. The trial will enroll up to 50 participants across five sites. The drug candidate targets more than 200 different genetic mutations associated with RP.
- **OPGx-LCA5 (Opus Genetics)**, a gene therapy in development for the treatment of Leber congenital amaurosis type 5, received rare pediatric disease designation by the FDA. This severe early-onset inherited retinal degeneration affects approximately 1.7 million individuals in the United States.
- **Tern Therapeutics**, a gene therapy company, officially launched following the closing of a $15 million financing round. At the same time, the company announced an agreement with Regenxbio to acquire two gene therapy programs: RGX-381 and RGX-181, now known as TTX-381 and TTX-181, respectively.

Want more retina news from *Eyewire+*?

HIGHLIGHTS FROM ARDS 2024

This year's event included lectures on geographic atrophy, ocular oncology, and myopic traction maculopathy.

BY JASON C. FAN, MD, PHD

The 52nd Annual Aspen Retinal Detachment Society Meeting, held March 2-6, 2024, in Snowmass Village, Colorado, boasted many excellent lectures from world-renowned experts in retina. Here, I highlight the hot topics that kept the attendees engaged (Figure).

TREATING GEOGRAPHIC ATROPHY

Daniel F. Martin, MD, provided his perspective on pegcetacoplan (Syfovre, Apellis) and avacincaptad pegol (Izervay, Iveric Bio/Astellas), beginning with a review of the history of complement pathway research in AMD. Although variants in complement factor H (CFH) have been linked to the onset of advanced AMD, CFH has not been significantly correlated with the growth of geographic atrophy (GA), he said. Many clinical trials targeting complement for the treatment of GA have failed, including the SPECTRI and CHROMA trials for lampalizumab. The AREDS2 cohort paradoxically showed an inverse relationship between complement C3 AMD risk alleles and GA expansion.[1] A more recent AREDS study showed that ARMS2/HTRA1 is highly predictive of the growth rate of small GA lesions, suggesting that there are other pathogenic pathways in the progression of GA.[2]

Dr. Martin then summarized the OAKS/DERBY trials, reminding the audience that OAKS met its primary endpoint but not DERBY, and that both trials showed significant reduction in GA lesion growth at 2 years. However, there were no significant differences in functional endpoints. A subgroup analysis showed that patients with extrafoveal GA did have slower vision loss, but this cohort included only 22% of all trial participants. Most patients (78%) with GA lesions closer to the fovea did not show this benefit.

Similarly, the GATHER trials for avacincaptad pegol showed a significant reduction in GA lesion growth. A post-hoc analysis looking at trial patients who lost 15 letters or more at two consecutive visits showed significantly less loss in the avacincaptad pegol-treated cohort.

Dr. Martin reminded the audience that although the approximate 20% reduction in GA growth rate seen for both pegcetacoplan and avacincaptad pegol might seem impressive, this difference corresponded to an absolute area of approximately 1 mm^2 at 24 months—not a significant clinical change for 2 years of therapy. In fact, he stated that AREDS2 supplementation had the same clinical efficacy. He calculated that, when aggregating the mean baseline characteristics from all trials for these two agents, treatment changes the average time from diagnosis to foveal involvement from 4 years to 5 years if it was extrafoveal at baseline.

Dr. Martin then discussed safety profiles. Pegcetacoplan had a four-fold increased risk for conversion to wet AMD, a 4% rate of intraocular inflammation, and a 2% rate of ischemic optic neuropathy for monthly dosing. Avacincaptad pegol had a 1.7-fold increased risk for conversion to wet AMD and no episodes of intraocular inflammation or ischemic optic neuropathy. Dr. Martin briefly discussed the retinal vasculitis reported by the ASRS

ABOUT THE SPEAKERS

Daniel F. Martin, MD
- Chair, Cleveland Clinic Cole Eye Institute; Barbara and A. Malachi Mixon III Institute Chair in Ophthalmology; Professor of Ophthalmology, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland

Barbara Parolini, MD
- Head of Vitreoretinal Unit, Eyecare Clinic, Brescia, Italia

Basil K. William Jr, MD
- Associate Professor of Clinical Ophthalmology, Bascom Palmer Eye Institute, Miami

Check out our video coverage of the 52nd ARDS Meeting at eyetube.net/meeting-coverage/ards:

Images courtesy of Kevin Caldwell Photography

Figure. Drs. Martin (left), Williams (middle), and Parolini (right) engaged the ARDS 2024 attendees with top-notch education and clinical insights.

Research and Safety in Therapeutics committee and noted that it remains to be seen whether avacincaptad pegol will cause similar inflammatory reactions.

SURGERY AND COMPLICATIONS IN OCULAR ONCOLOGY

Basil K. Williams Jr, MD, discussed the unique risks, surgical precautions, and potential complications of intraocular surgery for patients with malignant intraocular tumors. Surgeons must be cautious of tumor seeding, he said, which is more likely when the tumor has broken through Bruch membrane or when there is a release of subretinal fluid. Dr. Williams shared several precautions to mitigate tumor seeding, including precise identification of the tumor location, localized peritomy in the area surrounding each trocar, cryotherapy at the time of trocar removal, and sclerotomy closure with sutures. During fine needle aspiration biopsy, tumor seeding may occur if the biopsy needle penetrates too deeply into or through the sclera. Vitrectomy-assisted biopsy with subretinal cannulas, on the other hand, may allow more control and prevent this complication.

The greatest challenges usually occur when surgeons are not aware of an intraocular tumor. Dr. Williams shared the case of a 69-year-old woman who underwent vitrectomy with silicone oil for a rhegmatogenous retinal detachment (RD). The surgeon identified a mound of subretinal hemorrhage intraoperatively, which continued to grow over 6 months of observation. Upon presentation to Dr. Williams, the patient had already developed neovascular glaucoma and required enucleation after a large hypoechoic mass was discovered. Pathology revealed spindle B melanoma. He further described a case series by Shields et al, in which vitrectomy was performed in eyes with unsuspected retinoblastoma.[3] With a median time to referral after vitrectomy of 4 days, one of 11 patients died due to pre-existing metastatic disease. In another series in India with a median time to referral of 7 months, eight of 14 patients died due to progressive disease.[4]

Rhegmatogenous RD is rare in patients with uveal melanoma, and repair is complex, with single-surgery success rates ranging from 40% to 60%.[5,6] Exudative RD is very common with intraocular tumors (up to 75% of cases) and can cause photoreceptor damage over time. Dr. Williams prefers to perform internal drainage but acknowledges the disadvantages, which include introducing a break, the potential for tumor seeding, and the creation of a nidus for proliferative vitreoretinopathy. Dr. Williams considers RD repair only in monocular patients or in those with bilateral disease and prefers a primary scleral buckle, if possible.

Lastly, Dr. Williams discussed the controversial topic of tumor endoresection. In the United States, endoresection is not the primary mode of treatment for choroidal melanomas due to the risk of local recurrence and tumor dissemination. However, recent studies with smaller-gauge vitrectomy and valved trocars have not shown increased rates of metastasis and mortality compared with enucleation or radiation. Dr. Williams reserves endoresection for specific situations (ie, monocular patients with toxic tumor syndrome where the tumor has already been treated with radiation).

MYOPIC TRACTION MACULOPATHY

Barbara Parolini, MD, gave an excellent talk on myopic traction maculopathy (MTM), covering pathogenesis, clinical staging, and surgical treatment. She began by describing the forces at play in the pathogenesis of MTM. A centripetal force mediated by the Müller cells, external limiting membrane, and internal limiting membrane holds the retina together. These are opposed by forces acting perpendicular to the fovea, which cause schisis and detachment, as well as forces tangential to the fovea, which induce foveal splitting. The perpendicular forces are caused by scleral ectasia, in which the sclera is stretched posteriorly away from the retina while the vitreous pulls the retina anteriorly. Ectasia of the sclera also causes tangential forces that pull away from the fovea, leading to macular holes. The combination of these

(Continued on page 20)

SAVE THE DATE

53rd Annual Aspen Retinal Detachment Society Meeting
March 1-5, 2025
The Viceroy, Snowmass, Colorado

COMBINING THE PRC AND INTRIS: A POWERHOUSE OF EDUCATION


The 10th Annual Pacific Retina Club and International Retinal Imaging Society Symposium had something for everyone.

BY ALESSANDRO FEO, MD, AND AHMAD SANTINA, MD

The 10th Annual Pacific Retina Club (PRC) and International Retinal Imaging Society (IntRIS) Symposium was held May 30 – June 1, 2024, at the University of California Los Angles Meyer & Renee Luskin Conference Center in Los Angeles. The meeting was expertly organized by David Sarraf, MD; Amani A. Fawzi, MD; K. Bailey Freund, MD; H. Richard McDonald, MD; and SriniVas Sadda, MD. Mark W. Johnson, MD, and James G. Fujimoto, PhD, were the award lecturers (Figures 1 and 2).

CASE PRESENTATIONS

The first day of PRC kicked off with 30 mystery cases presented by trainees as part of a lively session moderated by Dr. Sarraf. With only 5 minutes for each case, it was challenging to determine the correct diagnosis, which included atypical presentations of angioid streaks, ocular sarcoidosis, primary vitreoretinal lymphoma, Loeys-Dietz syndrome associated with familial exudative vitreoretinopathy, and acute idiopathic maculopathy due to Coxsackie virus. Genetic disorders, such as *A3243G* mitochondrial retinopathy, *PROM1* retinal dystrophy, and ocular albinism, were also discussed. Additional sessions were chaired by Anita Agarwal, MD, and Dr. McDonald, who moderated a second set of 30 compelling cases that included ophthalmomyasis, leiomyoma, and multifocal vitelliform maculopathy.

ALEXANDER R. IRVINE LECTURE

Dr. Johnson delivered the named lecture in honor of University of California San Francisco Professor Alexander R. Irvine, MD. The first part of his presentation focused on the clinical and surgical significance of internal limiting membrane tears associated with epiretinal membrane.

In the second part, Dr. Johnson discussed a new classification of maculopathies whose pathoanatomy and pathophysiology depend on Müller cells; he proposed the term *Müller cell gliopathies*. According to Dr. Johnson, the spectrum of these gliopathies may include traumatic, inflammatory, metabolic, and toxic diseases, such as lamellar macular holes, inner retinal dimples, macular teleangiectasia, and tamoxifen toxicity.

PRC 2024 RETINA UPDATE

The second day kicked off with sessions focusing on AI, inherited retinal diseases, pediatric surgery, and uveitis. During the imaging session, Dr. Fawzi discussed the thin double layer sign as a biomarker for geographic atrophy, while Dr. Freund introduced the concept of sealed versus unsealed retinal pigment epithelium (RPE) defects in different macular diseases, including AMD and pachychoroid disorder. Finally, Alain Gaudric, MD, explained the various types of acute choroidal ischemia and triangular syndrome.

Dr. Johnson presented a whirlwind of cases of macular disease to an expert panel of retinal imaging gurus and reviewed various novel disorders and new OCT findings, such as "snowflake-like" paracentral acute middle maculopathy.

After two panels on cutting-edge surgical and oncology cases led by David R. Chow, MD, and William F. Mieler, MD, respectively, the focus shifted to medical retina disorders, including sessions dedicated to AMD, retinal vascular disease, and diabetic retinopathy. During the AMD session, Dr. Sarraf discussed the clinical utility of OCT angiography (OCTA) in the diagnosis of type 1, 2, and 3 macular neovascularization and in the assessment of macular neovascularization growth and treatment response. Special attention in these sessions was also given to the latest clinical trial results.

INTRIS 2024 SYMPOSIUM

The first half of this year's IntRIS Symposium was dedicated to technology innovations and advances in OCT and OCTA imaging. This was followed by a session on inherited retinal disease, during which Claudio Iovino, MD, gave a wonderful talk on the development of chorioretinal atrophy as a complication of voretigene neparvovec-ryzl (Luxturna, Spark Therapeutics) subretinal gene therapy. The data were

Figure 1. Dr. McDonald (left) and Dr. Sarraf (right) present Dr. Johnson (middle) with the 2024 Alexander R. Irvine Award.

Figure 2. Dr. Fujimoto was the 5th Annual Lawrence A. Yannuzzi lecturer.

based on one of the largest cohorts of patients in the world treated with this groundbreaking therapy for *RPE65*-related inherited retinal dystrophy.

The next session on dry AMD included presentations on the outcomes of various dry AMD lesions, including subretinal drusenoid deposits, acquired vitelliform lesions, and the progression of large drusen to a state of collapse.

The vitreoretinal disease section included talks about the findings of ultra-widefield OCT and fluorescein angiography in peripheral retinal disease and after epiretinal membrane surgery (by Anibal A. Francone, MD; Iksoo Byon, MD, PhD; and Dr. Gaudric). Another lecture by Fiammetta Catania, MD, FEBO, touched on the natural course of lamellar macular holes in pathologic myopia and pachychoroid disease, as studied by en face OCT and OCTA.

Important updates on the advanced multimodal imaging of diabetic retinopathy and geographic atrophy were provided during two sessions focusing on retinal vascular disease and dry AMD. The newly recognized entity of multizonal outer retinopathy and retinal pigment epitheliopathy was presented by Prithvi Ramtohul, MD, during the inflammatory and infectious disease session. Central serous chorioretinopathy was the focus of the next session, and Dr. Sarraf presented a novel theory regarding the potential link between the reversal of the RPE pump function and the pathogenesis of acute central serous chorioretinopathy.

LAWRENCE A. YANNUZZI AWARD LECTURE

Dr. Fujimoto presented the 5th Annual Lawrence A. Yannuzzi lecture focused on OCT. After explaining the evolution of this revolutionary imaging tool, Dr. Fujimoto provided a lesson in perseverance. He explained that after the first demonstration of in vitro OCT in 1991 and the first commercial introduction of the ophthalmic OCT device in 1996, only approximately 400 units were sold worldwide by 2001. Today, an OCT device is ubiquitous in retina practices worldwide and is an indispensable tool for retinal evaluation.

MEMBERS-IN-TRAINING

Eleven presentations by young IntRIS members-in-training concluded this year's meeting. Key topics on advanced retinal imaging included en face OCT and OCTA of diabetic retinopathy, tamoxifen retinopathy, retinal ischemic perivascular lesions, pentosan polysulfate sodium maculopathy, and hyperreflective foci as a predictor of geographic atrophy.

SEE YOU NEXT YEAR!

The 2024 combined PRC-IntRIS meeting was a major success and exceeded expectations; it highlighted current updates on the evaluation and management of a broad spectrum of retinal disorders and offered exciting presentations of novel imaging systems. The discussions were dynamic and insightful, and the overall exchange among the participants was energetic and rewarding. The organizers, presenters, and participants are already looking forward to next year's meeting, which will take place June 5 – 7, 2025, at the the University of California Los Angles Meyer & Renee Luskin Conference Center in Los Angeles. ■

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KAPIL MISHRA, MD

WHERE IT ALL BEGAN

I grew up in Riverside, California, and went to Brown University, double-majoring in neuroscience and film studies before attending medical school at Icahn School of Medicine at Mount Sinai. I was interested in medicine at an early age because my father, whom I deeply admire, is an astute clinician; to this day, I have never heard him complain about anything, ever.

MY PATH TO RETINA

I entered residency at the Wilmer Eye Institute interested in oculoplastics but quickly gravitated toward the retina consults. My first-year assistant chief of service, Roomasa Channa, MD, taught me the fundamentals of retina, and I am grateful to all the Wilmer retina faculty for solidifying my choice to pursue retina.

SUPPORT ALONG THE WAY

Two of my biggest mentors are Prithvi Mruthyunjaya, MD, and Jim Handa, MD. They are both brilliant clinicians, and I can only hope to one day influence a mentee as much as they have me. I also frequently seek advice from Fasika A. Woreta, MD, an academic machine and a wonderful human being. I was fortunate to learn from fantastic clinician scientists during my fellowship at Stanford under the strong leadership of Darius Moshfeghi, MD (and all the Stanford faculty). I am also grateful to learn from the impressively productive Ehsan Rahimy, MD, and Arshad M. Khanani, MD.

Finally, the best part of my current position at the University of California Irvine is learning from my colleagues who have quickly become close mentors. Our chairperson Baruch D. Kuppermann, MD, PhD, is a true polymath who has been immensely supportive, and Stephanie Lu, MD, our retina division chief, is a natural leader who has guided me in countless ways.

AN EXPERIENCE TO REMEMBER

During my year as co-assistant chief of service with my close friend Narine Viruni, MD, we had the opportunity to engage with some of the best minds in our field. I will always remember when Albert M. Maguire, MD, during a conference presented a talk on the journey of voretigene neparvovec-ryzl (Luxturna, Spark Therapeutics). At the end of the talk, a tearful Morton F. Goldberg, MD, stood up and congratulated Dr. Maguire on finally bringing a treatment to those seemingly destined for blindness.

Another memorable experience was visiting the Aravind Eye Institute in Pondicherry, India, run by Rengaraj Venkatesh, MD. Every member of the eye hospital embodied the founder's mission to eliminate preventable blindness. I watched clinicians work full-time Monday through Saturday, then travel for hours on Sunday to a remote village to screen patients for ocular disease. They subscribed to their mission and worked tirelessly to achieve it. ■

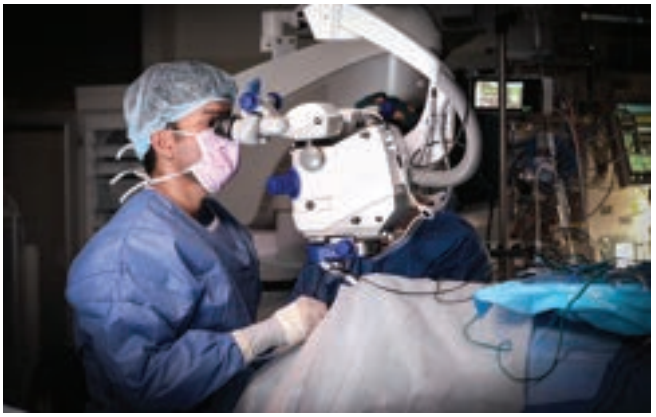

Image courtesy of John Barret

Dr. Mishra's advice: Always be available, affable, and able. Stay humble and respect every procedure—from a simple injection to an end-stage tractional retinal detachment. Finally, never forget that even on your worst clinic day, you still go home at the end of the day.

Kapil Mishra, MD, is a clinical assistant professor of ophthalmology at the Gavin Herbert Eye Institute, University of California, Irvine. He practices adult surgical retina and ocular oncology and is initiating the plaque brachytherapy program at the University of California, Irvine. Dr. Mishra is a consultant for Bausch + Lomb, Carl Zeiss Meditec, and Regenxbio. He can be reached at **mishra.kap@gmail.com.**

USING A MOBILE FUNDUS CAMERA TO EVALUATE SCHEMATIC EYES

Our study suggests this method of imaging the retina is safe and effective.

BY SUPAPORN TENGTRISORN, MD; SOMYOT CHIRASATITSIN, PHD; PRAWIT KAEONARONG, BENG; DUANGRAT GANSAWAT, PHD; SITTHICHOK CHAICHULEE, DPHIL; AND VIRASAKDI CHONGSUVIVATWONG, MD, PHD

While screening for retinal conditions with a commercial fundus camera is beneficial, the currently available portable handheld fundus cameras (HFCs) are expensive. A mobile fundus camera (MFC) may be useful for mass screening to detect early lesions, especially in remote areas. We conducted a study to assess the quality of retinal images captured with various MFC systems. The secondary objectives were to assess the usability of the images and evaluate any potential safety issues associated with the light emission. Here's what we found.

THE STUDY: LIGHTS, CAMERA, ACTION

In this cross-sectional study, 10 ophthalmologists were trained to use a commercial HFC and eight different MFC systems to capture fundus photographs of schematic eyes,

TABLE. COMPARISON OF IMAGE QUALITY CAPTURED WITH A HANDHELD FUNDUS CAMERA VERSUS MOBILE FUNDUS CAMERAS

System No. and Device Combination	Sharpness Index Mean (SD)	Relative Redness Mean (SD)	Red-Green Difference Mean (SD)	Red-Blue Difference Mean (SD)	Disc-to-Image Ratio Mean (SD)
1. Handheld Fundus Camera	6.97 (1.94)	0.57 (0.04)	149.52 (19.01)	6.09 (3.31)	0.3081 (0.0736)
2. iPhone 12 + Volk 20D	2.86 (0.90)	0.49 (0.06)	125.02 (39.80)	3.42 (2.11)	0.2301 (0.0597)
3. iPhone 12 + oDocs 20D	2.54 (0.77)	0.51 (0.06)	136.69 (36.03)	4.33 (3.26)	0.2601 (0.0773)
4. iPhone 12 + Volk 28D	2.93 (1.02)	0.49 (0.05)	116.88 (32.30)	2.52 (1.79)	0.2949 (0.0871)
5. iPhone 12 + oDocs 30D	3.02 (1.22)	0.46 (0.04)	102.57 (31.68)	2.10 (2.12)	0.3218 (0.1146)
6. Samsung S21 + Volk 20D	4.82 (1.78)	0.44 (0.04)	101.27 (42.31)	2.65 (1.62)	0.2380 (0.0580)
7. Samsung S21 + oDocs 20D	4.72 (1.64)	0.45 (0.08)	113.37 (42.34)	3.18 (2.43)	0.2570 (0.0676)
8. Samsung S21 + Volk 28D	6.36 (1.95)	0.44 (0.09)	98.52 (42.97)	2.02 (1.33)	0.3054 (0.0889)
9. Samsung S21 + oDocs 30D	5.50 (3.18)	0.35 (0.18)	70.53 (47.35)	1.23 (1.01)	0.3267 (0.1109)

after which the systems were compared. The MFC systems tested were comprised of a lens connected to a smartphone using a specially designed adjustable holding tube and a commercial locking interface. To standardize the lighting, the camera was operated in video mode using the flashlight. The study included different combinations of smartphone (Apple iPhone 12 and Samsung S21) and connecting lens (oDocs 20D, oDocs 30D, Volk 20D, and Volk 28D).

Each ophthalmologist evaluated the MFC using the Usability Experience Questionnaire (UEQ),[1] which measures attractiveness, perspicuity, efficiency, dependability, stimulation, and novelty using 26 questions. Image quality was evaluated without processing based on five quality metrics: relative redness, red-green difference, red-blue difference, sharpness index (SI), and disc-to-image ratio (Table). These metrics were calculated from the retinal areas in the photographs.[2-4] We used SI to measure the sharpness of an image by calculating the differences between adjacent pixels, with higher values indicating greater contrast.

THE FINDINGS

For each device, we summarized the five quality parameters with the overall mean and standard deviation. The independent effects of the operating system (iOS vs Android) and connecting lens were evaluated using a multiple regression model. The key quality value was sharpness, which was plotted against the relative value of each prime color. The metric of the best device for each parameter was compared with that of the HFC. Inter-participant differences were analyzed using the Conover post-hoc test.

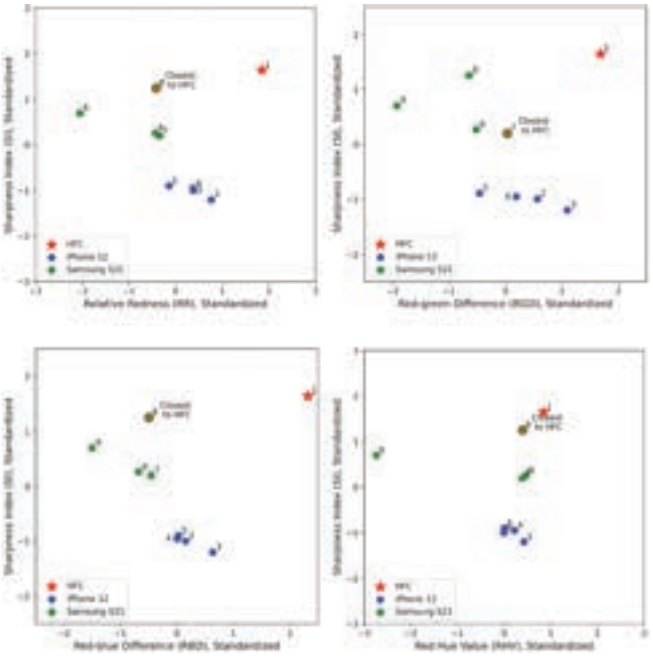

Figure 1. Interaction plots of the SI, relative redness, and disc-to-image ratio, which represent clarity, color, and scale, respectively. The Samsung S21 + Volk 20D MFC system was closest to the HFC in the SI versus relative redness versus disc-to-image ratio, SI versus relative redness, and SI versus disc-to-image ratio plots.

DIFFERENCES BETWEEN DEVICES

We excluded 12 images due to poor quality of the flashlight reflex; the remaining 348 images were evaluated using the five quality metrics mentioned earlier.

Each MFC system had a lower SI value than the HFC; however, the SI values for four MFC systems were closer to those of the HFC than all other devices, indicating better sharpness with the Samsung S21, although they had poorer color discrimination than the iPhone 12 ($P < .05$). The effect of the connecting lens (ie, oDocs vs Volk) was not significant. The SI of device 8 (Samsung S21 + Volk 28D) and all color indices of device 3 (iPhone 12 + oDocs 20D) were close to that of the HFC (Figure 1). Consequently, the combination of the Samsung S21 with the Volk 28D provided the best SI (91.2% of HFC), and the iPhone 12 with the oDocs 20D provided the best color discrimination (71.1% to 91.6% of HFC). The quality parameters were found to be consistent among the devices tested (Figure 2), indicating good reliability.

Safety

For both the iPhone 12 and Samsung S21, the light safety parameters for photochemical and thermal hazards were below the limits defined in the ISO 15004-2 Ophthalmic Instruments Fundamental Requirements and Test Methods Part 2: Light Hazard Protection.[5] In addition, our results were in line with those of a previous study that used a smartphone for fundoscopy.[6]

UEQ Assessment

The UEQ scores in this study showed mixed results. The ophthalmologists were satisfied with attractiveness, dependability, stimulation, and novelty but were unsatisfied with efficiency and perspicuity. The system was perceived as inefficient because the users had to connect and disconnect the smartphones using different connecting lenses throughout the assessment period; this issue was resolved when only the optimal combination was used. Regarding perspicuity, the reviewers rarely operated HFCs before this study, and the

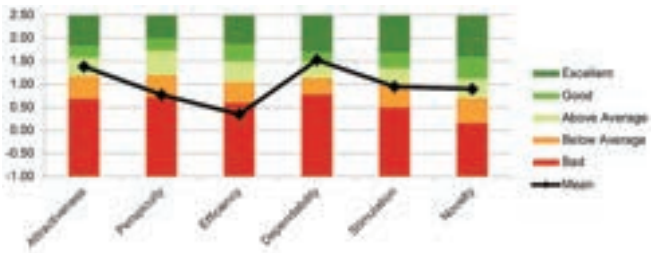

Figure 2. The overall UEQ for the MFCs showed unsatisfactory scores for perceived efficiency and perspicuity.

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MFC was new to all participants, who required an extensive explanation before use. Jansen et al reported that image quality was not affected by shorter time spent in training[6]; Gosheva et al reported no significant effects on users' learning with the use of a mobile device.[7]

RESULTS POINT TO GOOD CLINICAL UTILITY

Our results suggest use of an MFC system is safe and effective for retinal screening. Based on the SI criteria, the Samsung S21 with the Volk 28D lens was closest to the HFC and should therefore be considered for further development, especially for primary care providers. ■

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ARDS

(Continued from page 13)

forces causes a macular hole with macular detachment.

Dr. Parolini then described her staging system for MTM, which was validated internationally with high interobserver agreement.[7] Stage 1 consists of inner-outer macular schisis, and stage 2 involves predominantly outer macular schisis. In stage 3, there is macular schisis with RD. Stage 4 is an RD. Each stage is further subclassified into A, B, or C based on the foveal morphology. Grade A indicates a normal foveal morphology, grade B indicates a lamellar macular hole, and grade C refers to a full-thickness macular hole.

Dr. Parolini then transitioned the discussion to treatment, emphasizing the importance of understanding the pathogenesis of MTM to inform treatment decisions. She asserted the necessity of treating MTM, presenting evidence that observation alone yields poorer outcomes compared with treatment. Dr. Parolini then questioned the efficacy of vitrectomy, citing literature reporting 60% functional and 80% anatomical success, noting the higher failure rates in advanced stages. In her opinion, the surgical approach should counteract the tractional forces. Forces perpendicular to the fovea need to be counteracted by macular buckling, whereas forces tangential to the fovea may require vitrectomy with internal limiting membrane peeling.

Finally, Dr. Parolini discussed the development of macular buckles and shared her own New Parolini Buckle, which has four eyelets for anterior scleral fixation, a curved arm to extend posteriorly, and a terminal ovoid bump for macular buckling effect. Furthermore, a canal within the curved arm allows insertion of a transilluminator to confirm positioning. Dr. Parolini has also created a preliminary nomogram for optimal suture placement positioning based on axial length. In total, she has performed more than 400 macular buckles and collected the outcomes of 236 cases with 1 to 15 years of follow-up. She reports an anatomical and functional success rate of nearly 100%. ■

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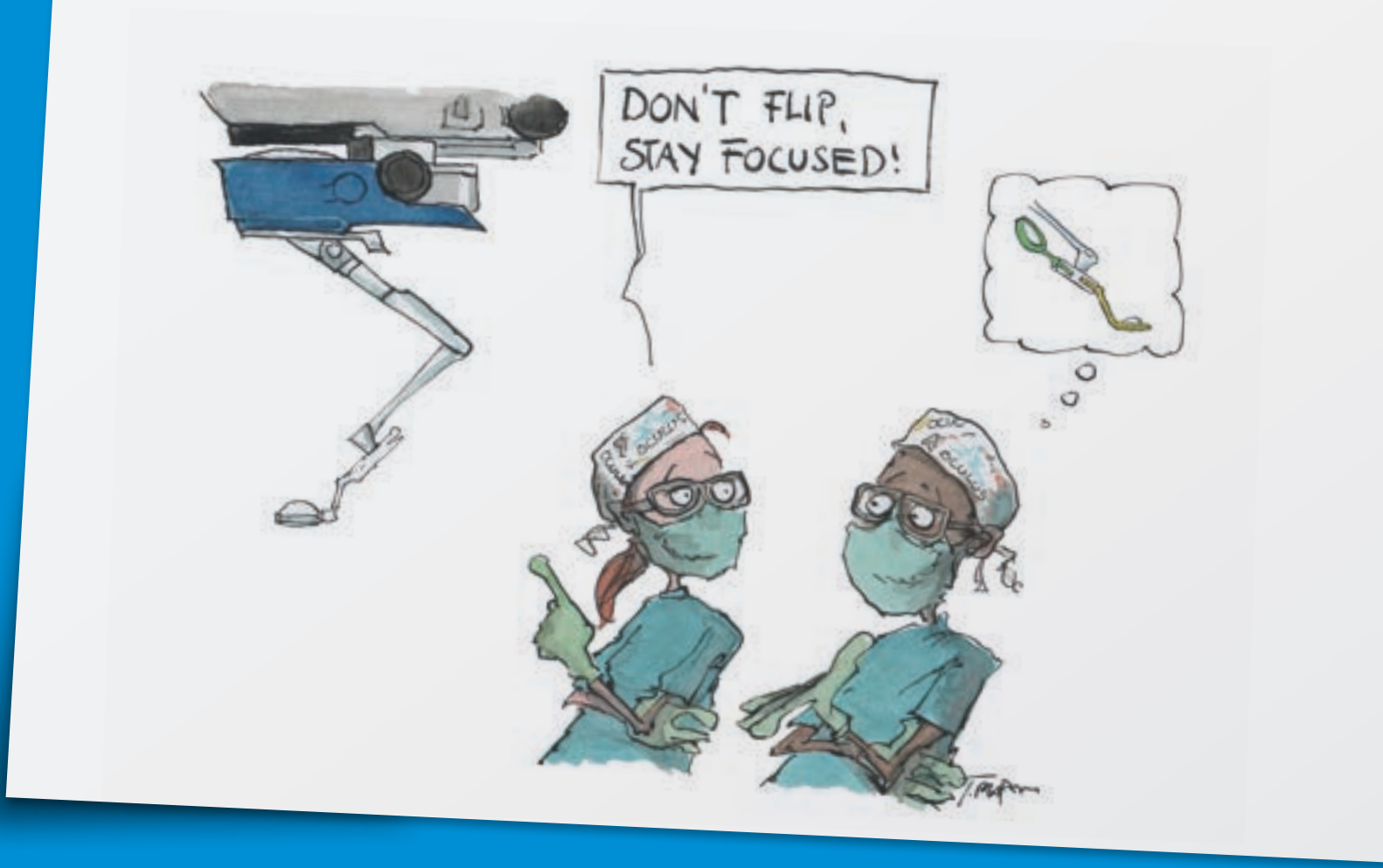

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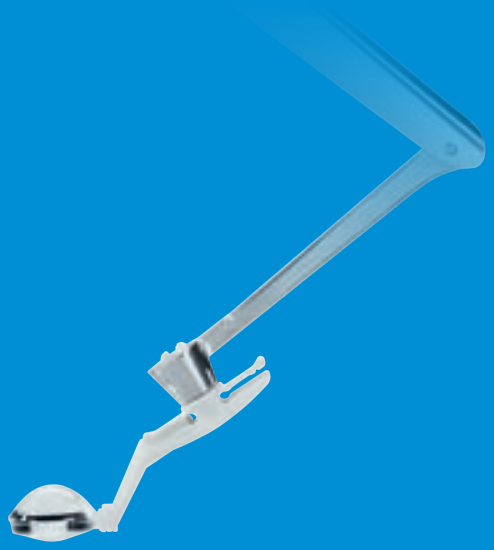

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SURGICAL CONSIDERATIONS FOR OPTIC PIT MACULOPATHY

A review of the various surgical techniques to address this rare disorder.

BY LUKE MAVROFRIDES AND MATTHEW A. CUNNINGHAM, MD, FASRS


Optic disc pit (ODP) is a rare congenital disorder characterized by an excavation of the optic nerve head. These excavations typically appear at the temporal or inferotemporal segment of the optic disc, although central and nasal excavations have also been reported.[1] ODP occurs in approximately one in 10,000 individuals with no racial or sex predilection. While most patients with ODP are asymptomatic, some can develop optic pit maculopathy (OPM), which is characterized by the presence of subretinal and intraretinal fluid extending from the pit into the macula. This can lead to progressive visual deterioration and usually presents in patients in their 30s and 40s.[2,3]

The exact pathogenesis of OPM remains unclear with significant debate on the origin of the subretinal and intraretinal fluid.[4,5] Most believe that the source of the fluid is related to either the vitreous or the cerebrospinal fluid (CSF). For those who believe the fluid originates from the vitreous, it is postulated that vitreous traction on the macula allows fluid to enter the subretinal space through the optic pit more readily.[6] Others argue that the fluid originates from the CSF through the subarachnoid space. Modern OCT imaging may suggest a connection between the subarachnoid space and ODP.[7] This theory is further supported by a case report of silicone oil migration from the vitreous cavity into the intracranial space.[8]

MANAGEMENT OPTIONS

There is no universally accepted approach to managing patients with OPM. Early literature recommended conservative management, as spontaneous resolution of the fluid has been reported after a posterior vitreous detachment (PVD) develops.[5,9] However, most patients will have chronic

AT A GLANCE

- There is no universally accepted approach to managing patients with optic pit maculopathy (OPM).
- The most common approach to OPM is vitrectomy, and advances in surgical techniques have made this approach safer and more effective.
- Regardless of technique, complete fluid resolution often takes more than a year, and patients must be educated on the expected postoperative course.

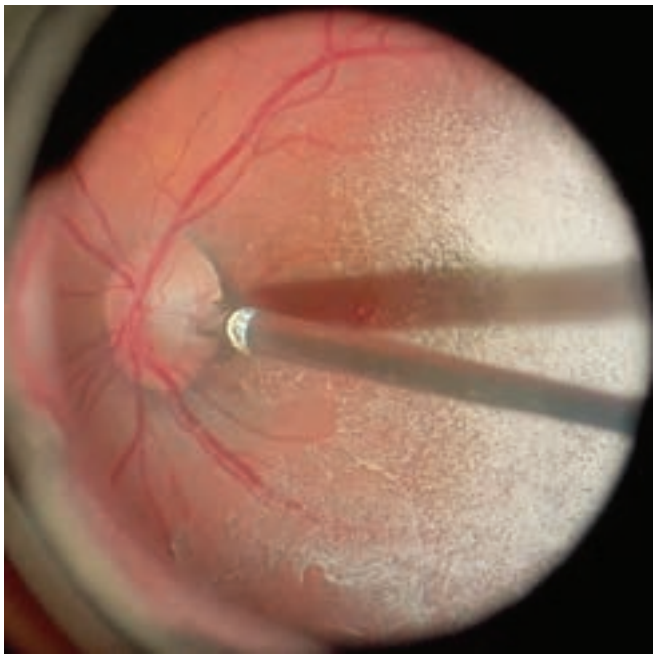

Figure 1. To address vitreous traction on the optic pit, stain the hyaloid with triamcinolone to ensure complete hyaloid elevation during vitrectomy.

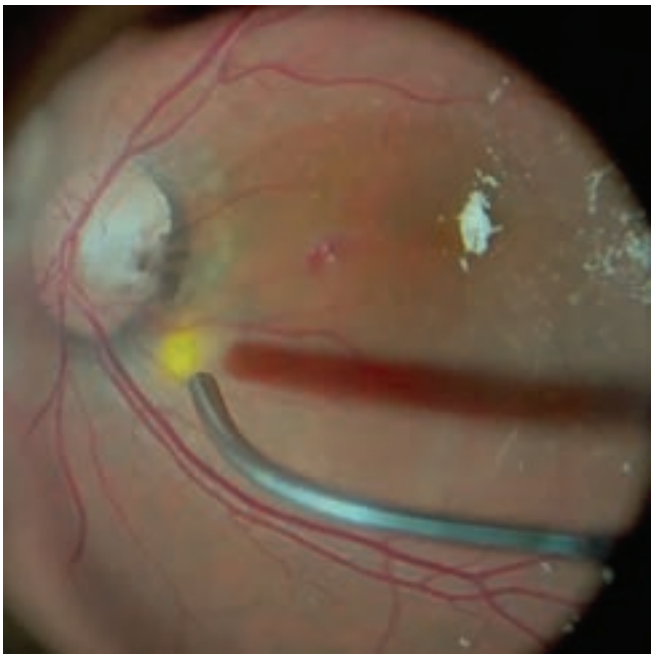

Figure 2. Surgeons can apply a single light-intensity row of laser at the temporal edge of the optic nerve to prevent fluid from entering the subretinal space.

persistence of fluid with a risk for progressive central vision loss. Thus, retina specialists must be prepared to choose between several treatment approaches for OPM.

Laser photocoagulation to the temporal edge of the optic nerve is one of the earliest interventions reported—the theory being that a chorioretinal adhesion in the peripapillary region would prevent fluid from entering the subretinal space through the optic pit.[10,11] This approach was limited by inconsistent results with low rates of complete fluid resolution. In addition, there is a risk for enlarging the blind spot by damaging the papillomacular bundle.[10] The use of light laser burns can limit the damage to the nerve fiber layer.

Intravitreal gas injection is another minimally invasive approach that has been previously described. Injecting gas into the vitreous may be beneficial by inducing a PVD, alleviating vitreomacular traction, and even sealing the pit itself. Akiyama et al demonstrated a success rate of approximately 50%, but multiple injections were often necessary.[12] Intravitreal gas injection can be combined with laser photocoagulation to potentially improve fluid resolution; using this technique, Lei et al had a 75% complete resolution rate of subretinal and intraretinal fluid, although some patients required repeat treatments.[13]

Theodossiadis et al described a macular buckling technique in which a scleral sponge is fixed externally in the area of the macula to reduce the anterior-posterior tractional forces. This technique showed a high rate of anatomical and functional success on long-term follow-up.[14] However, the procedure is technically difficult with a steep learning curve and has not gained widespread use.

The most common approach to OPM is vitrectomy. Advances in surgical techniques—with the continued improvement of small-gauge, sutureless vitrectomy instrumentation—have made this approach safer and more effective. Because vitreous traction on the optic pit likely contributes to OPM, induction of a complete PVD during vitrectomy can be extremely beneficial.[1,3,4] Staining of the hyaloid with triamcinolone can help to ensure complete hyaloid elevation during surgery (Figure 1). Vitrectomy also provides the opportunity to include other treatment modalities, such as endolaser, internal limiting membrane (ILM) peeling, and gas tamponade, to name a few.[1,3,4] Some surgeons believe that laser photocoagulation to the edge of the temporal aspect of the optic pit can be more effective following vitrectomy.[15] Others feel the laser is not necessary and remain concerned about possible complications.[16] When performing endolaser at the time of the vitrectomy, surgeons can apply a lighter laser treatment in an attempt to reduce the risk of blind-spot enlargement (Figure 2).

Intraocular gas injection during vitrectomy may also enhance outcomes, as it can provide a longer-acting tamponade of the optic pit, facilitating resolution of the fluid. Adjuvant face-down positioning can further enhance the efficacy of the gas tamponade.

Some surgeons advocate for ILM peeling to further reduce tangential traction on the macula beyond hyaloid elevation alone.[17] However, there is always a risk of causing a full-thickness macular hole with ILM peeling due to the thinned nature of the inner retinal layers.[17,18] Several studies have shown successful management of OPM with

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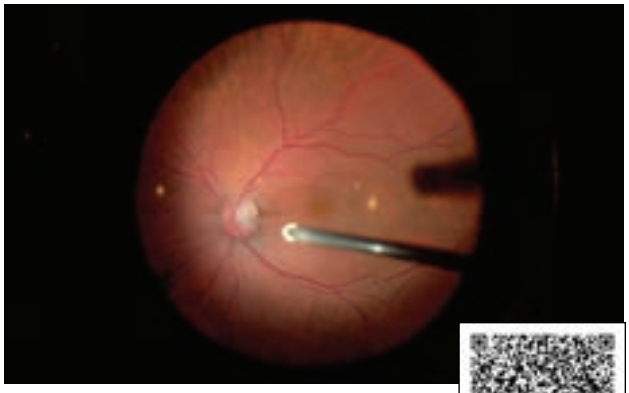

A Case of Optic Pit Maculopathy
By Matthew A. Cunningham, MD, FASRS

RETINA SPECIALISTS MUST BE PREPARED TO CHOOSE BETWEEN SEVERAL TREATMENT APPROACHES FOR OPM.

vitrectomy without ILM peeling, and many surgeons choose to forego ILM peeling in these cases.[15,19]

Recently, numerous techniques have been described to cover or plug the pit at the time of surgery. Rather than a complete idiopathic macular pucker peel, some authors have advocated for creating an ILM flap that can be placed over or into the pit.[20,21] Autologous scleral patch graft, amniotic membrane, autologous fibrin, and exogenous fibrin glue have all been described as ways to seal the optic pit.[22-25] Although these modalities may result in faster resolution of the fluid, they do not necessarily provide better anatomical or visual outcomes. Each approach creates an added level of complexity or expense that must be compared with more traditional approaches.

SET EXPECTATIONS

When managing patients with OPM, patient education to set appropriate expectations is paramount. Regardless of surgical technique, we have found that complete fluid resolution often takes more than 12 months. The rate of visual improvement and the final visual outcome are also highly variable. Patients should be informed that multiple procedures may be necessary to achieve the best anatomical outcome.

Although ODP and OPM are rare conditions, retina specialists must be aware of the evolving management options. Many treatment approaches exist without any universally accepted standard. Understanding the potential benefits and limitations of each approach is necessary when deciding the optimal treatment for each patient. ■

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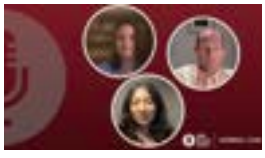

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THE MODERN MANAGEMENT OF CHALLENGING MACULAR HOLES

New surgical tools and techniques are changing how we approach large and myopic macular holes.

BY OMAR M. MOINUDDIN, MD, AND TAMER H. MAHMOUD, MD, PHD


Fueled by continued advances in retinal imaging, operative technologies, and surgical techniques, the treatment of full-thickness macular holes (FTMHs) has improved dramatically. Pars plana vitrectomy, elevation of the posterior hyaloid, peeling of the internal limiting membrane (ILM), and fluid-air exchange followed by gas tamponade remains a standardized and highly successful approach,[1] with rates of anatomic hole closure approaching ≥ 90% and improved BCVA of at least two lines seen in ≥ 70% of eyes.[2,3] Still, up to 10% of FTMHs fail to close, despite seamless execution of this classic technique.[4] These poorer outcomes most commonly occur in eyes that are myopic and MHs with a minimum linear diameter (MLD) ≥ 500 µm.[5,6] The comparatively lower rates of anatomic hole closure in such eyes requires refined surgical techniques to provide an enhanced treatment benefit.

AT A GLANCE

- Several variants of the internal limiting membrane flap technique have emerged showing increased success in treating challenging macular holes.
- Each technique poses its own set of advantages and challenges that must be considered based on the configuration of the macular hole, the eye's anatomy, and the surgeon's preference and experience.
- Very large macular holes that fail to close with conventional surgical interventions may benefit from human amniotic membrane graft, macular hydrodissection, and autologous retinal transplantation techniques.

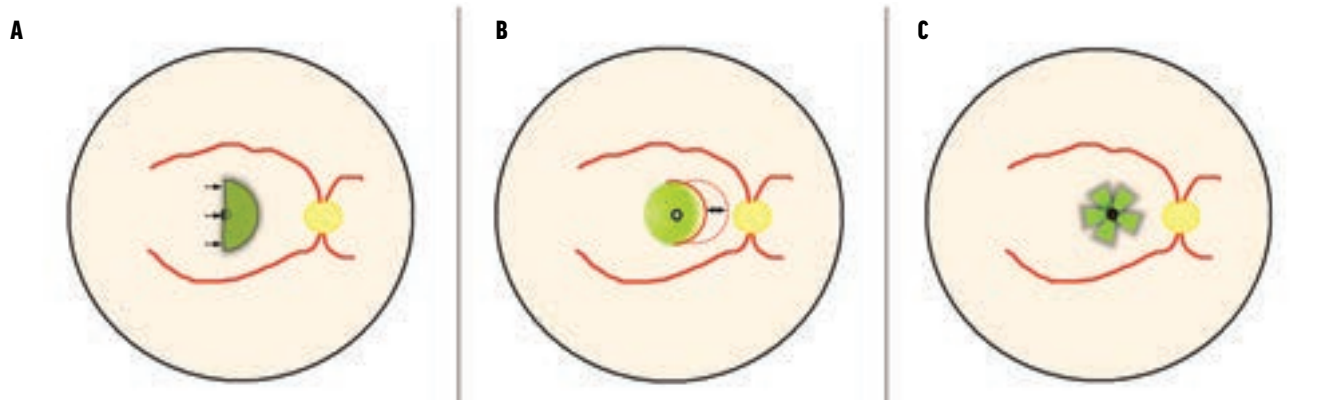

Figure 1. These images depict various ILM flap techniques, including the inverted ILM flap (A), with a semicircular flap that remains attached and inverted (arrows) along the temporal edge of the hole; the retracting door ILM flap (B), with the ILM now assuming a retracted position (solid red line) compared with its original position (dotted red line) still along its same natural orientation; and the flower-petal inverted ILM flap (C), with multiple ILM leaflets hinged circumferentially around the hole edge and subsequently inverted to cover the hole.

UPDATED APPROACHES

In 2010, Michalewska et al devised the inverted ILM flap.[7] In their series, anatomic closure was achieved in 98% of eyes with FTMHs with an MLD ≥ 400 µm treated with the inverted ILM flap technique compared with 88% of eyes treated with conventional ILM peel alone.[7]

Subsequent reports confirmed the superior surgical outcomes achieved with the inverted ILM flap technique. In a large retrospective series of 620 eyes, Rizzo et al reported significantly greater anatomic success in MHs with an MLD ≥ 400 µm treated using an inverted ILM flap (95.6%) versus ILM peeling (78.6%).[4] Moreover, the rate of anatomic hole closure in myopic eyes with an axial length (AL) ≥ 26 mm managed with an inverted ILM flap (88.4%) was also significantly greater than myopic eyes that underwent ILM peeling (38.9%).

Mete et al reported a superior rate of anatomic hole closure in a series of 68 eyes with large myopic FTMHs treated with an ILM flap (94%) compared with a complete ILM peel (61%) and, more importantly, showed that the inverted ILM flap technique is associated with a 22-times higher probability of anatomic success for all sizes of FTMH (P = .001).[8]

Furthermore, a meta-analysis of more than 1,400 eyes demonstrated that the inverted ILM flap technique achieves significantly greater rates of closure compared with ILM peeling alone for varying sizes of FTMH, eyes that are myopic, and in patients with retinal detachment.[9]

UNMET NEEDS

Despite the success of the inverted ILM flap technique, the management of large and atypical FTMHs remains challenging, particularly in patients with high myopia and holes with a MLD ≥ 500 µm (see *Measuring Macular Holes*). For example, the Manchester Large Macular Hole Study showed that MHs with a diameter ≥ 630 µm were significantly less likely to close.[6] The study concluded that this revised MLD threshold may more accurately classify a MH as *large* based on the probability of surgical closure with conventional ILM peeling, and the comparatively lower closure rates warrant adjuvant techniques such as ILM flaps.

Likewise, the BEAVRS Macular Hole Study Group demonstrated a stepwise decline in anatomic hole closure beyond a MLD ≥ 500 µm, further highlighting the unmet need for new macular hole surgery techniques.[5]

New Flap Techniques

Several variants of the ILM flap technique have emerged showing increased success in more challenging MH scenarios (Figure 1). Shin et al described the use of PFO to prevent movement of the flap during fluid-air exchange.[10] The investigators showed that a PFO-assisted inverted ILM flap achieved hole closure in 100% of patients with MHs with a mean MLD of 590.8 µm. They also reported a significantly higher rate of anatomic success compared with conventional ILM peeling at 6 months.

Song et al described a technique in which viscoat is injected into and around the FTMH, ICG is injected, and the ILM is peeled to create a superior inverted ILM flap. Viscoat is then applied on top of the inverted ILM flap prior to performing fluid-air exchange.[11] In highly myopic eyes (mean AL of 29.83 mm) with MHs with a mean MLD of 597.6 µm, Song et al reported anatomic closure in 100% of eyes and improved BCVA in 66.7% of cases.

To address the anatomic and surgical intricacies of myopic MHs, Finn and Mahmoud described the retracting door ILM flap technique.[12] This technique involves creating a large ILM flap starting nasal to the hole, carrying the flap over the fovea such that it remains attached temporally, and then carefully draping the ILM back over the MH. This technique requires minimal manipulation beyond the flap creation, relieves tractional forces, and achieves relaxation of the taut ILM as the flap retracts to assume a natural

Figure 2. Our personal surgical algorithm for primary FTMHs.

position and orientation. Marlow et al demonstrated that the retracting door ILM flap technique can be modified to find success in eyes with FTMH and associated epiretinal membrane (ERM).[13] With this technique, ICG is applied to start the ILM peel nasally, the peel is propagated to engage the negatively staining ERM, and a temporal hinge is maintained to allow the combined ERM/ILM tissue to drape over the hole as a single flap. The authors reported anatomic hole closure in 83% of FTMHs with a mean MLD of 681 µm and concurrent ERM and showed that this technique minimized loss of ILM.[13]

Another ILM flap variant that has demonstrated success is the flower-petal inverted ILM flap, which involves multiple ILM leaflets that are inverted in sequence to form a multilayered ILM scaffold covering the hole.[14] In a series of 103 eyes with large FTMHs with a mean MLD of 712 µm, Joshi et al described this technique under PFO and

Figure 3. Our personal surgical algorithm for refractory FTMHs that have previously undergone surgery.

reported anatomic hole closure in 92.2% of cases.[15] This flower-petal technique may be particularly useful in highly myopic eyes with posterior staphyloma, in which there is often fragmentation and discontinuity of the ILM.

Several variants of the ILM flap technique have proven successful over the last decade, and each technique poses its own set of advantages and challenges that must be considered based on the configuration of the FTMH, the eye's anatomy, and the surgeon's preference and experience (Figure 2).

MEASURING MACULAR HOLES

Obtaining an accurate measurement of a macular hole (MH) is inherently challenging. Because OCT is conventionally based on a set axial length (AL) of 24 mm, measurements in longer eyes are prone to inaccuracy. To account for this discrepancy, the size of the measured hole must be adjusted as a ratio of the patient's actual AL to the machine's assumed AL (Table).[1] For example, a 500 µm MH as measured on OCT in an eye with an AL of 30 mm has a true minimum linear diameter (MLD) of 625 µm, which should be calculated by multiplying the measured MLD by the eye's correct AL and then dividing by 24.

This presumed underestimation in size may explain, in part, the historically limited anatomic success reported in myopic MHs managed with ILM peeling. Calculating the accurate size of myopic MHs can guide the type of surgical approach to successfully close those holes and achieve better visual acuity.

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TABLE. ADJUSTED MACULAR HOLE SIZE BASED ON AXIAL LENGTH

Axial Length	24 mm	27 mm	30 mm	33 mm	36 mm
Minimum Linear Diameter	400 µm	450 µm	500 µm	550 µm	600 µm
	500 µm	562 µm	625 µm	687 µm	750 µm
	600 µm	675 µm	750 µm	825 µm	900 µm
	700 µm	787 µm	875 µm	962 µm	1,050 µm
	800 µm	900 µm	1,000 µm	1,100 µm	1,200 µm

DESPITE THE SUCCESS OF THE INVERTED ILM FLAP TECHNIQUE, THE MANAGEMENT OF LARGE AND ATYPICAL FTMHS REMAINS CHALLENGING.

Managing Complex Cases

The use of more invasive techniques is reserved for patients with very large MHs, in which success using ILM flaps has been shown to decline significantly and proportional to MLD exceeding 750 µm. Such eyes may benefit from the use of human amniotic membrane graft (hAM), macular hydrodissection, and autologous retinal transplantation (ART) techniques that have had comparatively greater success in recent investigations.[2,16] The CLOSE Study Group analyzed outcomes using these adjuvant techniques in FTMHs ≥ 800 µm and reported anatomic success rates of 100% with hAM, 90.5% with ART, and 83.3% with macular hydrodissection. Notably, only eyes treated with ART demonstrated a significant improvement in vision with a mean BCVA improvement of approximately four lines in eyes with MHs ≥ 1,000 µm.[2] More recently, a combined hAM-ART technique in eyes with large myopic MHs and associated outer retinal atrophy has shown promise.[17]

The management of refractory FTMHs is equally complex. These types of MHs are frequently larger, commonly associated with higher orders of myopia or chronicity, and often have little remaining ILM. Our personal treatment algorithm for refractory MHs is initially guided by MLD (Figure 3). For holes ≤ 750 µm with insufficient residual ILM following previous repair surgery, surgical options include the use of an ILM free flap, ART, hAM, and macular hydrodissection.

Surgeons must consider that ILM free flaps are prone to displacement, involve "stuffing" ILM into the hole in an orientation that is not physiologic, and may be less effective in inducing subsequent glial cell proliferation; furthermore, the MH remains without neurosensory retina. Although the ART and hAM techniques provide a neurosensory tissue plug, they may be better suited for larger holes. In eyes with sufficient residual ILM following previous peel, the superior wide-base ILM flap transposition technique has shown anatomic success and improved vision.[18] This technique involves a wide-based ILM flap harvested distal to the area of previous peeling that is then manipulated to assume an inverted position draping the area of the MH. In cases previously treated using an ILM flap technique, the flap may be repositioned under PFO to cover the hole, followed by a careful and slow fluid-air exchange and long-acting gas tamponade to prevent displacement. For refractory MHs ≥ 750 µm, our preferred surgical treatment choice is ART or combined hAM-ART, similar to very large primary FTMHs. ■

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ADVICE FROM THE OR: RD AND PVR

These tips and tricks can help you better manage patients who return with postoperative proliferative vitreoretinopathy.

BY LINNET RODRIGUEZ, MD; JORDAN D. DEANER, MD; SONIA MEHTA, MD; AND JASON HSU, MD

Proliferative vitreoretinopathy (PVR)—the proliferation of retinal pigment epithelium cells and the collateral inflammatory cells that are deposited on the retinal surface and vitreous—can cause contraction of and traction on the retina. This leads to retinal detachments (RDs) that can be tractional, rhegmatogenous, or a combination of both. PVR is the most common cause of failure for RD repair surgery; thus, surgeons must identify the risk factors and early signs of PVR and modify treatment plans to achieve better anatomical and functional outcomes.[1] Here, I share the surgical pearls gleaned from conversations with experts on RD repair in the setting of PVR.

– Linnet Rodriguez, MD

TACKLING MEMBRANES

By Jordan D. Deaner, MD

When peeling membranes, I recommend starting from the nerve and proceeding peripherally. The nerve is an anchor, and it is always easier to peel against countertraction. Consider using ICG or brilliant blue G to stain the internal limiting membrane (ILM) and reveal negative staining of posterior membranes. Preservative-free triamcinolone is also useful in highlighting and peeling both posterior and more peripheral membranes.

Look for valleys and star folds in the retina. These are

AT A GLANCE

- If the proliferative vitreoretinopathy (PVR) is mild and peripheral, consider adding a scleral buckle.
- Consider vitrectomy with PVR membrane peel in patients who are older, pseudophakic, and present with preretinal membranes.
- Because a shorter time to surgery after PVR redetachment is associated with better outcomes, get these eyes back to the OR quickly.

clues that PVR membranes are contracting and pulling the retina together. The grooves within the folded retina are your friend and can help you locate membranes that are easier to peel. If the PVR is mild and peripheral, don't underestimate the benefits of adding a scleral buckle to the surgery. This may save the patient a retinectomy. All membranes should be peeled, if possible, prior to considering a retinectomy. If membranes are left on the residual retina, there will likely be further proliferation, contraction, and surgical failure.

In severe cases of PVR, especially those that are circumferential at the vitreous base or anterior loop, a chandelier and bimanual dissection may be necessary. I prefer bimanual dissection with either two Maxgrip forceps (Alcon) to sheer or pull apart the circumferential PVR or a Maxgrip forceps and vitreous cutter to pick up and cut the circumferential traction.

Finally, if a retinectomy is necessary, plan carefully. When the traction is minimal, I place PFO prior to cutting the retina to stabilize the macula and prevent progression of the RD due to changes in fluidics post-retinectomy.

Mark and cut the retina as peripherally as possible, saving as much retina as you can while still removing all the PVR membranes that are preventing successful retinal attachment. In general, localized retinectomies carry a high risk for redetachment. I recommend doing at least a 180° inferior retinectomy. The milieu of PVR tends to deposit gravitationally at the inferior aspect of the eye; leaving a retinectomy horn inferiorly is just asking for a PVR redetachment.

FOCUS ON PATIENT SELECTION

By Sonia Mehta, MD

For patients presenting with RDs with grade C or worse PVR, multiple factors affect my surgical approach. If the patient is young and phakic with subretinal bands or mild preretinal membranes limited to one quadrant, I may consider a straight scleral buckle with external drainage.

If the patient is older, pseudophakic, and presents with multiple preretinal membranes, my typical approach is vitrectomy with PVR membrane peel. If I am not planning for a retinectomy, I may also add a scleral buckle. I also typically inject ICG and peel the ILM. After the membrane peel, if the retina appears stiff and will not reattach, I proceed with an inferior 180° retinectomy. For advanced pathology, a 360° retinectomy may be necessary. I reattach the retina with PFO, laser, fluid-air exchange, and conclude with 1,000 cSt silicone oil (see *Case No. 1*). For patients with advanced PVR whom I am planning to leave the silicone oil in long term, I typically use 5,000 cSt silicone oil (see *Case No. 2*). If a retinectomy was not required, I may use a gas tamponade.

Postoperatively, I monitor for cystoid macular edema, epiretinal membrane, recurrent PVR formation, and silicone oil emulsification.

CASE NO. 1

A 59-year-old woman was referred for retinal detachment (RD) with proliferative vitreoretinopathy (PVR) in the right eye 7 weeks after vitrectomy for RD repair. Her VA was counting fingers at 5 ft OD and 20/30 OS. IOP was 4 mm Hg OD and 18 mm Hg OS. Fundus examination of the right eye showed a post-vitrectomized eye with a C_3F_8 bubble (Figure 1). There was an RD from the 1 to 10 clock positions with fixed retinal folds from the 6 to 10 clock positions. The macula was detached. OCT showed an RD involving the macula with intraretinal fluid and PVR temporally. The left eye was unremarkable.

The patient underwent vitrectomy, brilliant blue G-assisted membrane peel, an inferior 180° retinectomy, PFO, endolaser, and 1,000 cSt silicone oil tamponade. Four months later, the patient returned for silicone oil removal, at which time the macula was attached, and her VA was 20/60 OD (Figure 2).

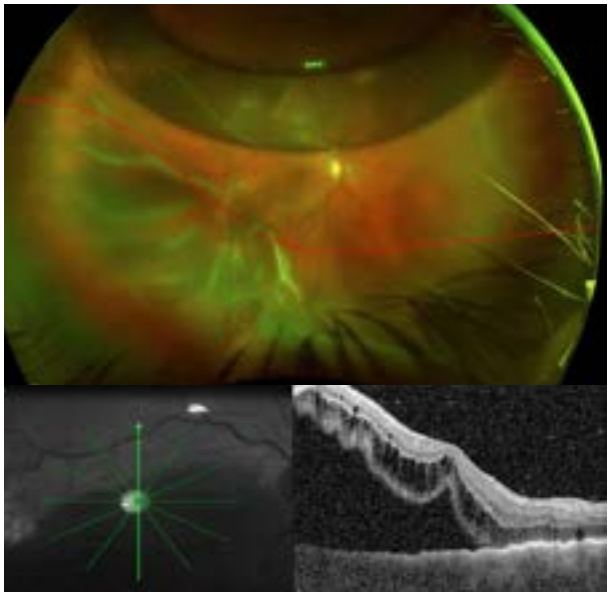

Figure 1. Imaging of the right eye revealed an RD with fixed retinal folds, a detached macula, and PVR. The patient underwent vitrectomy, membrane peel, inferior 180° retinectomy (red line), PFO, endolaser, and silicone oil tamponade.

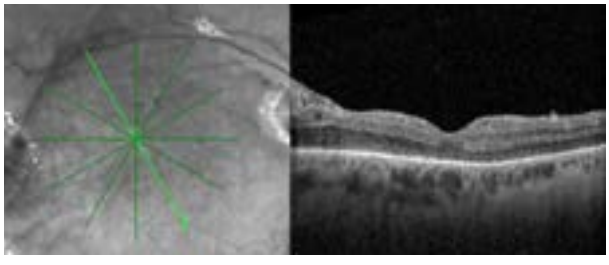

Figure 2. After silicone oil removal 4 months later, OCT imaging showed an attached macula with laser marks in the temporal macula from the previous retinectomy.

For eyes that present with recurrent PVR and a history of multiple surgeries, I may consider using intravitreal methotrexate injections as per the GUARD clinical trial protocol (NCT04136366).

ONE STEP AT A TIME

By Jason Hsu, MD

I first consider how I am going to approach the case—with vitrectomy or a combined scleral buckle-vitrectomy procedure. In most cases, I place a scleral buckle, unless there is a funnel RD with a severe anterior loop and I plan to perform a 360° retinectomy.

Lens status also influences my surgical approach. I often place a buckle in phakic eyes with PVR because I don't typically perform lensectomies (or concomitant cataract surgery) unless there is a significant cataract. Our group looked at the outcomes of vitrectomy with retinectomy without lensectomy for grade C PVR RDs in phakic eyes and found that the outcomes were similar to what has been reported in eyes that have undergone lensectomies.[2]

If a lensectomy is necessary, it's important to take the whole capsule; leaving the anterior capsule intact may act as a scaffold for PVR proliferation over the ciliary body, leading to hypotony and poorer outcomes.

During the vitrectomy, I use triamcinolone to ensure the posterior hyaloid is up, and I peel any membranes that are posterior to the equator. Identifying star folds and pinching with forceps in the center of the fold can often help initiate the peel. Alternatively, using a Finesse Flex Loop (Alcon) to massage the surface of the retina may help to identify additional membranes or edges from which to initiate a peel. Preretinal pigmentation, often presenting in clumps, typically signifies an associated membrane.

I rarely use ICG or brilliant blue G to peel the ILM but have done so in cases where the retina keeps redetaching from PVR recurrences. In these situations, I peel the ILM as extensively as possible, focusing on the macula and the area of the PVR, which is typically the inferior periphery. Using a lighted pick can help to dissect tenacious membranes that are adherent to the retina, but it's important not to be overly aggressive to avoid creating iatrogenic breaks.

In grade C PVR, I am more liberal about using retinectomy unless I'm confident I peeled all the membranes. I use diathermy to mark the edges and make sure to remove any retina that contains membranes that could not be peeled or areas of intrinsic PVR with thickening and folding. While I like to stay as anterior as possible, I also remove the vitreous base in the quadrants of the retinectomy. I place PFO over the macula, typically to the edges of the arcades, before initiating the retinectomy to help protect the macula and stabilize the retina.

When performing the retinectomy, I always watch the tip of my cutter to avoid hitting the choroid and causing a hemorrhage. I limit the amount of vacuum to avoid inadvertently eating more retina than is necessary. In addition, excessive hemorrhage may be a risk factor for recurrent PVR, and subretinal or preretinal hemorrhage at the retinectomy edge will block the laser uptake.

After completing the circumferential extent of the retinectomy, I remove the retina anteriorly. Although I

(Continued on page 45)

CASE NO. 2

A 61-year-old man presented with decreased vision in the right eye with an ocular history of vitrectomy for retinal detachment (RD) repair 2 years prior. His VA was counting fingers at 2 ft with an IOP of 14 mm Hg OD. The fundus examination showed a post-vitrectomized eye with an RD from the 1 to 10 clock positions with proliferative vitreoretinopathy and macular involvement (Figure 1).

The patient underwent vitrectomy, ICG-assisted membrane peel, 180° inferior relaxing retinectomy, PFO, endolaser, and 5,000 cSt silicone oil tamponade.

Four months postoperatively, the right eye had an attached macula under silicone oil with increased retinal thickness (Figure 2). The patient's final VA was 20/400 OD.

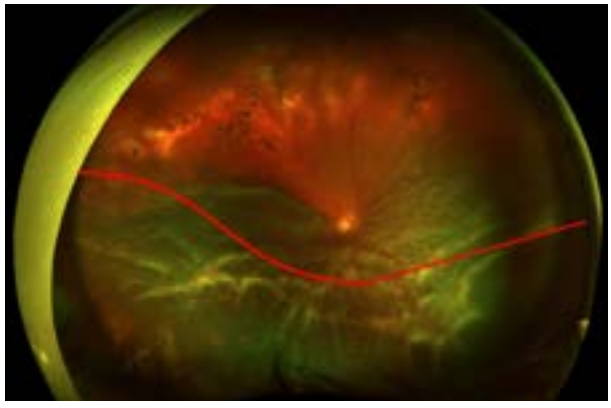

Figure 1. Fundus photography revealed an RD with proliferative vitreoretinopathy and macular involvement. The patient underwent vitrectomy, membrane peel, 180° inferior relaxing retinectomy (red line), PFO, endolaser, and silicone oil tamponade.

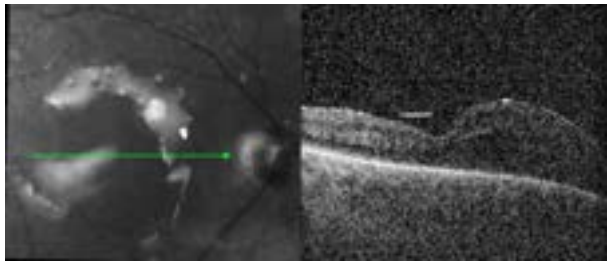

Figure 2. OCT imaging 4 months postoperatively showed an attached macula under silicone oil with increased retinal thickness.

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- *Use in pregnancy: Fetal harm can occur with first trimester use.*
- *Weight gain: May cause increased appetite.*

Adverse Reactions

- Based on a review of the available literature, the most commonly reported adverse events following ocular administration of triamcinolone acetonide were elevated intraocular pressure and cataract progression. These events have been reported to occur in 20-60% of patients.
- Less common reactions occurring in up to 2% of patients include: endophthalmitis (infectious and non-infectious), hypopyon, injection site reactions (described as blurring and transient discomfort), glaucoma, vitreous floaters, detachment of retinal pigment epithelium, optic disc vascular disorder, eye inflammation, conjunctival hemorrhage and visual acuity reduced. Cases of exophthalmos have also been reported.

Drug Interactions

- *Anticoagulant Agents* – Corticosteroids may enhance or diminish the anticoagulant effect of anticoagulant agents. Coagulation indices should be monitored.
- *Antidiabetic Agents* – Corticosteroids may increase blood glucose concentrations. Dose adjustments of antidiabetic agents may be required.
- *CYP 3A4 Inducers and Inhibitors* – CYP 3A4 inducers and inhibitors may respectively increase or decrease clearance of corticosteroids, necessitating dose adjustment.
- *NSAIDs* – Concomitant use of NSAIDS, including aspirin and salicylates, with a corticosteroid may increase the risk of GI side effects.

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CONTRAINDICATIONS

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- TRIESENCE® is a suspension; it should not be administered intravenously.
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- Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and hyperglycemia: Monitor patients for these conditions and taper doses gradually.
- Infections: Increased susceptibility to new infection and increased risk of exacerbation, dissemination, or reactivation of latent infection.
- Elevated blood pressure, salt and water retention, and hypokalemia: Monitor blood pressure and sodium, and potassium serum levels.
- GI perforation: Increased risk in patients with certain GI disorders.
- Behavioral and mood disturbances: May include euphoria, insomnia, mood swings, personality changes, severe depression, and psychosis.
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- Live or live attenuated vaccines: Do not administer to patients receiving immunosuppressive doses of corticosteroids.
- Negative effects on growth and development: Monitor pediatric patients on long-term corticosteroid therapy.
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- Weight gain: May cause increased appetite.

ADVERSE REACTIONS

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DRUG INTERACTIONS

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- *Antidiabetic Agents* – Corticosteroids may increase blood glucose concentrations. Dose adjustments of antidiabetic agents may be required.
- *CYP 3A4 Inducers and Inhibitors* – CYP 3A4 inducers and inhibitors may respectively increase or decrease clearance of corticosteroids, necessitating dose adjustment.
- *NSAIDs* – Concomitant use of NSAIDS, including aspirin and salicylates, with a corticosteroid may increase the risk of GI side effects.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

Two prospective case control studies showed decreased birth weight in infants exposed to maternal corticosteroids in utero. Triamcinolone acetonide was shown to be teratogenic in rats, rabbits, and monkeys at inhalation doses of 0.02 mg/kg and above and in monkeys, triamcinolone acetonide was teratogenic at an inhalation dose of 0.5 mg/kg (1/4 and 7 times the recommended human dose). Corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Infants born to mothers who received corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Nursing Mothers

Corticosteroids are secreted in human milk. The risk of infant exposure to steroids through breast milk should be weighed against the known benefits of breastfeeding for both the mother and baby.

Pediatric Use

The efficacy and safety of corticosteroids in the pediatric population are based on the well-established course of effect of corticosteroids which is similar in pediatric and adult populations. The adverse effects of corticosteroids in pediatric patients are similar to those in adults.

Geriatric Use

No overall differences in safety or effectiveness were observed between elderly subjects and younger subjects, and other reported clinical experience with triamcinolone has not identified differences in responses between the elderly and younger patients.

PATIENT COUNSELING INFORMATION

Patients should discuss with their physician if they have had recent or ongoing infections or if they have recently received a vaccine.

Patients should be advised of common adverse reactions that could occur with corticosteroid use such as elevated intraocular pressure, cataracts, fluid retention, alteration in glucose tolerance, elevation in blood pressure, behavioral and mood changes, increased appetite, and weight gain.

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MATERIAL MATTERS: MANAGING FOREIGN BODIES

Experts discuss the various surgical steps for removing wood and glass IOFBs.

BY HAEMOGLOBIN PARIDA, MBBS, MS, AND JUAN CARLOS GUTIERREZ HERNANDEZ, MD

Ocular trauma cases can be some of the most challenging experiences in the OR. Surgeons must review the patient's history carefully to fully understand the injury, the initial steps to repair it, and the possibility of an intraocular foreign body (IOFB). The type of object—organic, glass, or metal—and the size both play into the surgical plan. Here, two surgeons share their unique IOFB cases and how they handled them in the OR.

DEALING WITH ORGANIC MATERIAL

By Haemoglobin Parida, MBBS, MS

A 9-year-old boy presented the day after being hit in the eye by a stick. He had a scleral tear in the left eye at the 4 clock position, 2 mm from the limbus, and his VA was light perception OS. An outside provider had repaired the scleral wound the day of the injury. However, the postoperative B-scan showed an IOFB, vitreous hemorrhage, retinal detachment (RD), and thickened retinochoroidal complex of 2.19 mm. Due to severe chemosis and a concern for panophthalmitis, intravenous antibiotics were administered for 5 days, after which the chemosis subsided and the cornea was clearer.

During the 23-gauge vitrectomy after the 5-day course of antibiotics, the large wooden IOFB was released from the entangled vitreous (Video 1). Perfluorocarbon liquid (PFCL) was injected to stabilize the detached retina, and a scleral tunnel was made in the superior sclera. The IOFB, measuring 15 mm x 5 mm, was grasped with intravitreal forceps and removed through the scleral tunnel with McPherson forceps and the support of an irrigating vectus (Figure 1). The exudates over the inferior necrotic retina were trimmed,

AT A GLANCE

- Organic intraocular foreign bodies (IOFBs) have a high risk of endophthalmitis, and immediate removal is recommended at the time of primary repair.
- Removal of a tempered glass IOFB is especially challenging because of its non-magnetic nature, shape, smooth surfaces, and relatively large size.
- Although an uncommon tool in the ophthalmic OR, a nitinol stone basket has been used to extract intraocular square glass and pellets.

fluid-air exchange was performed, endolaser was applied to the inferior break, and silicone oil was added with intravitreal vancomycin, ceftazidime, and voriconazole.

Although the retina was attached postoperatively, the globe developed hypotony over the next 4 months, with a final VA of light perception.

DISCUSSION

Effort should be made to rule out an IOFB in every case of globe injury. B-scan ultrasonography with reduced gain should be performed gently to detect and localize any IOFBs and to assess the extent of intraocular damage. CT with thin cuts is the standard for detection and localization of all IOFBs.[1-3] MRI is preferred if a metallic IOFB is ruled out.

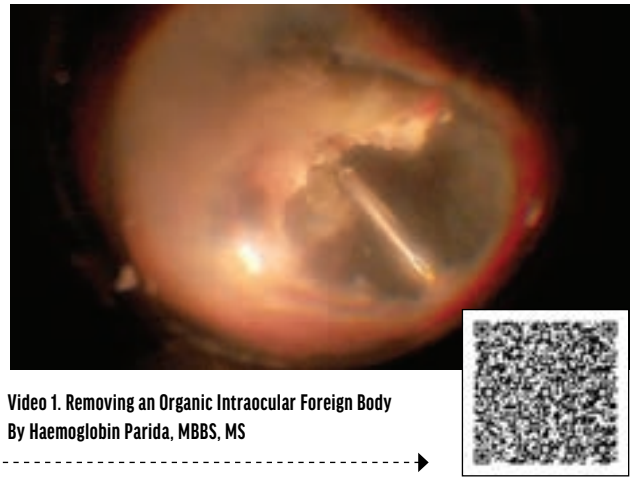
Organic IOFBs have a high risk of endophthalmitis, and immediate removal is recommended at the time of primary repair.[1,2,4,5] Associated vitreous hemorrhage and RD also prompt early intervention. Prophylactic intravenous antibiotics should be started as soon as possible.

Surgeons should consider repairing the entry wound first with a conjunctival peritomy and wound exploration in larger wounds. During standard 23- or 25-gauge vitrectomy, a 6 mm infusion cannula or anterior chamber maintainer should be placed if visibility is poor. Lensectomy may be done depending on lens damage or cataract presence or to facilitate large IOFB removal. Complete vitrectomy is preferred with induction of a posterior vitreous detachment.

The IOFB must be freed from vitreous adhesions with sharp dissection, if necessary. The sclerotomy size should be larger than the IOFB to prevent incarceration in the pars plana or fallback onto the retina. For larger sclerotomies, surgeons can use pre-placed sutures to prevent sudden hypotony after IOFB removal. When removing a large IOFB, scleral tunnels can be made superiorly. In some cases, PFCL may be used to float an organic IOFB and prevent retinal injury. Various forceps, snares, baskets, and loops can be used to grasp and remove the IOFB. To remove the IOFB, the object should be aligned perpendicular to the sclerotomy with the flatter end parallel to facilitate easy removal.

At the end of surgery, laser photocoagulation and intraocular tamponade can address associated retinal injuries. Intravitreal antimicrobials are recommended. Surgeons must monitor carefully for postoperative sequelae such as redetachment, proliferative vitreoretinopathy, and phthisis.

WATCH IT NOW



Video 1. Removing an Organic Intraocular Foreign Body
By Haemoglobin Parida, MBBS, MS

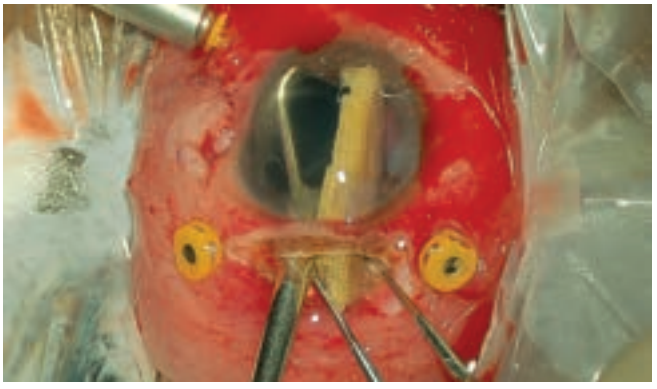


Figure 1. The wooden splinter was removed with the help of McPherson forceps and an irrigating vectus.

NOT-SO-SAFE SAFETY GLASS

By Juan Carlos Gutierrez Hernandez, MD

A 36-year-old patient who was involved in a motor vehicle accident presented with multiple glass fragment lacerations in the face and was taken to the OR for a primary scleral wound closure. Postoperatively, the patient was referred for a dilated fundus examination due to a non-clearing vitreous hemorrhage and a VA of counting fingers at 50 cm. No IOFB was identified on B-scan ultrasonography, and the anterior segment exploration was unremarkable; IOP was 16 mm Hg.

Despite the B-scan findings, the history of multiple glass fragment lacerations on the face and a scleral wound repair raised suspicions for an intraocular glass shard. Side vehicle windows are made of tempered glass, which shatters into small chunks rather than sharp fragments, the latter of which are more prone to producing significant damage.[6] However, if shattered tempered glass fragments achieve significant speed, they can penetrate the globe wall.

In this case, we took the patient to the OR for a complete vitrectomy, which revealed a 0.4 mm square-shaped tempered glass fragment lying over the posterior pole (Figure 2) and two retinal lesions in the periphery. Because the patient was young with a clear lens and preserved accommodation, we chose to extract the IOFB through the pars plana. Due to the size of the IOFB and the lack of special instrumentation at the time of surgery, we used 0.12 forceps to remove the glass shard; a wide non-valved incision and a firm and steady grasp were enough to extract the IOFB

without complications (Video 2). We repaired the scleral wound with interrupted 7-0 vicryl stiches. The retinal lesions were lasered, and a 12% C_3F_8 gas tamponade was added.

At the 9-week postoperative visit, the patient's VA was 20/40, the anterior chamber was unremarkable with a clear lens, IOP was 12 mm Hg, and the retina was attached with a normal macula.

DISCUSSION

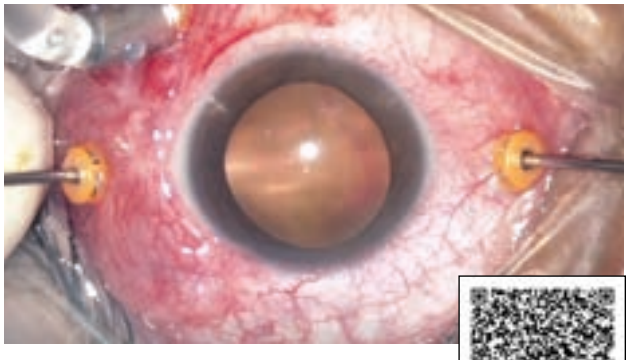
Removal of a tempered glass IOFB is especially challenging because of its non-magnetic nature, square or rectangular shape, smooth surfaces, and relatively large size. Thus, special considerations must be made prior to surgery, including extraction site, protection of the macula from dropout lesions, and instrumentation.

When planning the best extraction site, the lens status is a crucial consideration; if you are attempting to preserve a clear lens, a scleral incision is necessary. The incision must be long enough to allow you to pass a rectangular or square IOFB and the forceps holding it against the resistance of the sclera; generally, an incision 2 mm longer than the longitude of the fragment allows extraction without complications. Surgeons should avoid an incomplete incision in the uveal tissue, which could entangle the IOFB and lead to a drop.

The ideal incision should be tunneled to limit fluid loss and hypotony; nevertheless, when IOFBs are large or have a square or rectangular shape, the edges of the tunnel can be damaged by maneuvering the IOFB to get it angled with the tunnel and then removing it with its asymmetrical edges and large size. In these cases, consider using a linear incision, increasing the pressure of the balanced salt solution infusion, extracting the IOFB quickly, and closing the incision as fast as possible with interrupted stitches.

Protecting the macula from iatrogenic dropout lesions is fundamental. Some authors have used PFCL or viscoelastic to displace the IOFB and attempt to protect the macula from damage if the IOFB drops from the forceps, but no evidence suggests these approaches provide any protection.[7,8]

WATCH IT NOW



Video 2. Removing Tempered Glass From the Eye
By Juan Carlos Gutierrez Hernandez, MD

Figure 2. This patient presented with a non-clearing vitreous hemorrhage—and a 0.4 mm tempered glass IOFB—after a car accident and primary scleral wound repair.

The nitinol stone basket is an instrument created to extract kidney stones; since its first use described by McCarthy et al,[9] others have successfully used this tool to extract intraocular square glass and pellets.[7] However, it is an uncommon tool in an ophthalmic OR. Other potentially useful instruments for removing smooth-surface IOFBs include diamond-tipped forceps, lassos, snares, and aspiration cannulas.[10,11] ■

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HEAD POSITIONING AFTER RD SURGERY: A REVIEW

Optimal duration and type of head positioning are debated, despite ongoing research.

BY TIANYI WANG, BA; MOLLY BAUMHAUER, BS; SONIA PARVEEN; AND NITA VALIKODATH, MD, MS

Face-down positioning (FDP) is the most common post-surgical head positioning after retinal detachment (RD) repair via pars plana vitrectomy (PPV) with gas tamponade to minimize postoperative retinal translocation, retinal displacement, and metamorphopsia.[1-3] Since the introduction of FDP in the 1980s,[4] optimal type and duration have varied.[5]

VARIABILITY IN POSITIONING

There are no set guidelines for positioning after RD surgery, with some reports supporting FDP and others questioning the necessity of a specific position depending on the break location. Current literature supports initiation of FDP early in RD repair. Shiragami et al determined that immediately assuming FDP after surgery, compared with waiting 10 minutes, reduced retinal displacement at 6 months postoperatively.[2] Casswell et al found that FDP was beneficial compared with the support-the-break method for binocular diplopia and lowered retinal displacement rates at 8 weeks.[6] However, the redetachment and displacement rates at 6 months were the same in each group.

Nevertheless, the use of FDP as the standard is controversial. Abdelkader et al believed FDP to be of limited value when it pushed the retina back but did not tamponade breaks. In a prospective study of 32 patients excluding those with posterior breaks, the team found that face-up positioning for at least 10 days allowed 94% of patients

AT A GLANCE

- Duration and type of head positioning remain controversial with studies providing contradictory findings regarding its necessity.
- Face-down positioning (FDP) is the most common positioning recommendation after vitrectomy with gas tamponade for retinal detachment repair.
- A recent study found that FDP with side sleeping was the most recommended position at postoperative days 0 and 1. Upright positioning and FDP with side sleeping were recommended at similar frequencies at postoperative week 1.

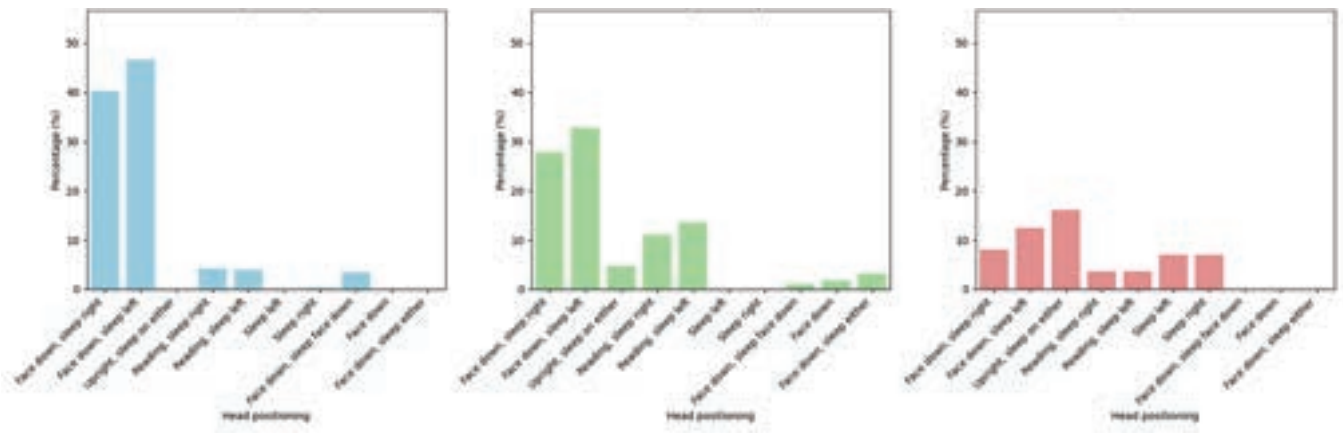

Figure 1. The recommended head positioning on postoperative days 0 (blue) and 1 (green) and postoperative week 1 (red) varied significantly.

to experience successful retinal attachment.[3] Otsuka et al found no differences in prone versus supine positioning for anatomical success rates, occurrence of macular pucker and retinal fold, or IOP after transconjunctival sutureless PPV for rhegmatogenous RD (RRD) that was not posterior. They also found no statistical differences in the location of retinal breaks between the groups. Of note, for both groups, Otsuka et al permitted patients with right temporal tears to lay in the left lateral recumbent position and those with inferior tears to lay in the lateral recumbent position on either side.[7]

Chen et al compared FDP with adjustable positioning and likewise found no difference in anatomical success rates, BCVA, or complication rates.[8]

Some literature even suggests that no recommended postoperative posture is viable. Martínez-Castillo et al found FDP was not necessary to achieve retinal reattachment in pseudophakic RDs with inferior breaks.[9] Similarly, Soliman et al found that PPV for primary RRD repair was associated with good anatomical outcomes without any restricted postoperative head positioning.[10]

VARIABILITY ON DURATION

Early literature suggested duration from 8 to 12 days.[11] A 2022 retrospective study found lower rates of redetachment in patients who were FDP ≥ 7 days compared with ≤ 6 days.[12] In contrast, a 2005 prospective interventional case series was the first to report that only 24 hours of postoperative prone positioning was effective in the management of pseudophakic RRD with breaks between the 4 and 8 clock hour positions.[11] In 2013, dell'Omo et al found that FDP 2 hours immediately post-PPV for RD in patients older than 60 years of age resulted in a lower rate of retinal displacement compared with 2010 reports of postoperative retinal displacement rates without any positioning.[1,13]

PATIENT FACTORS

Patients' quality of life (QoL) is often affected by FDP. Casswell et al found QoL scores to be 89.3 in the face-down group versus 89 in the support-the-break group, with sample size insufficiently powered to determine significance.[6] In addition, using the National Eye Institute Visual Function Questionnaire, Lina et al found that QoL after PPV correlated with metamorphopsia but not visual acuity or stereopsis.[14]

Patient adherence to FDP is a further challenge.[15,16] Li et al proposed several approaches to increase compliance, such as enhancing comfort, encouraging doctor-patient communication, providing comprehensive and community-based care, and strengthening family education.[17] Schaefer et al determined that compliance improved when patients were given inflatable prone position supports that were comfortable, inexpensive, and user-friendly.[16] In addition, Kim et al found reduced musculoskeletal pain after a 3-day structured exercise for patients required to maintain FDP post-PPV.[18]

MORE RESEARCH

While FDP is the most common post-surgical positioning after RD repair to reduce complications, optimal positioning type and duration remain a debate among retina surgeons. We conducted a retrospective study evaluating postoperative head positioning instructions following RD repair at a single tertiary academic institution from 2020 to 2021. We reviewed patient records for the duration and type of head positioning recommended by retina surgeons on postoperative day 0 (POD0), day 1 (POD1), and week 1 (POW1).

Among the 282 patients in the sample, the most common position at POD0 was FDP sleep left (46.5%) or right (40.1%). At POD1, the most common recommendations were FDP sleep left (32.6%) and FDP sleep right (27.7%), followed by reading position with sleeping on the left (13.5%) or right (11.0%). At POW1, the most common recommendations were upright with sleeping on either side (15.6%) and FDP sleep left (12.1%) or right (7.8%). Consistent with prior literature, FDP was the most recommended position at POD0 and POD1; however, at POW1, upright position and FDP sleeping either right or left were similar (Figure 1).

The duration of the recommended head positioning was

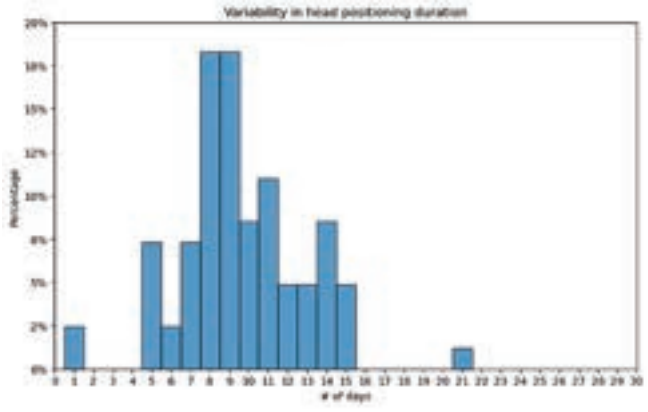

Figure 2. The recommended total duration of postoperative head positioning varied.

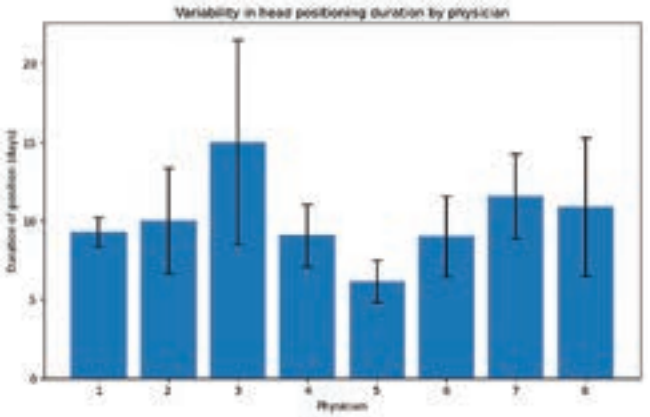

Figure 3. The recommended duration of postoperative head positioning varied by physician.

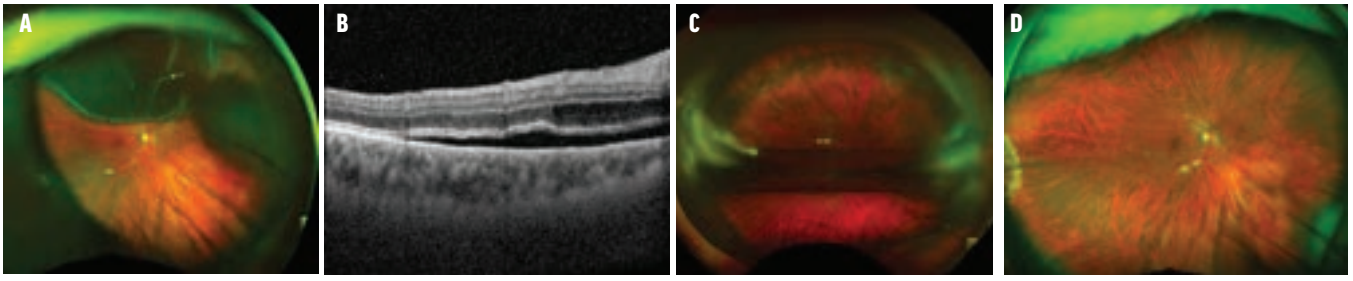

Figure 4. A 69-year-old man presented with a macula-splitting RD in the right eye (A, B) with retinal breaks superiorly, temporally, and nasally. The patient underwent 25-gauge vitrectomy with 14% C_3F_8. The patient was instructed to position face down and lie on his sides for 7 days. Follow-up at 1 (C) and 3 (D) months postoperatively showed that the retina was reattached.

an average of 9.6 days (Figure 2). Documented duration varied between physicians and within individual physicians based on the case (Figure 3). This could be related to patient factors, pathology, intraoperative factors, or postoperative findings (Figure 4).

Prior studies have tried to correlate positioning type and duration with surgical outcomes, but these studies are limited due to the difficulty of ensuring patient compliance and other confounding factors affecting surgical success rates. Randomized controlled trials evaluating positioning type, duration, patient QoL, and adherence can provide further guidance for retina surgeons on optimal recommendations for patients after RD surgery with PPV/gas. ■

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VITREOUS DYSFUNCTION: A FOCUS ON PATIENT SELECTION

These cases highlight the importance of active listening and proper classification and treatment when managing patients with visually significant vitreous opacities.

BY PETER KARTH, MD, MBA, FASRS, FACS

Research shows that the vitreous can have a significant negative effect on vision, often in aspects other than Snellen visual acuity.[1,2] Visual obscurations within the vitreous that become symptomatic, affecting a patient's activities of daily living and often prompting them to seek care, are labeled as *symptomatic vitreous opacities (SVOs)*.[3] Once thought to be incidental findings with no recommended treatment, SVO is now considered a treatable condition. Data show that 80% of retina specialists perform vitrectomy for SVOs, and more than 40,000 such surgeries are performed annually in the United States.[4] It is now standard of care to carefully evaluate SVOs and offer treatments to address the associated vision loss. Here, I describe ways in which patient selection and tailored treatment can help you succeed with the surgical treatment of SVOs.

AT A GLANCE

- Visual symptoms stemming from the vitreous itself (ie, degenerative vitreous syndrome) can be discrete myodysopsia or diffuse vitreous dysfunction.
- Discrete vitreous opacities may be best treated with low-risk laser vitreolysis, while diffuse vitreous dysfunction typically requires vitrectomy.
- Listen carefully to patients, as details of their complaints typically guide patient selection for maximum efficacy and minimal risk.

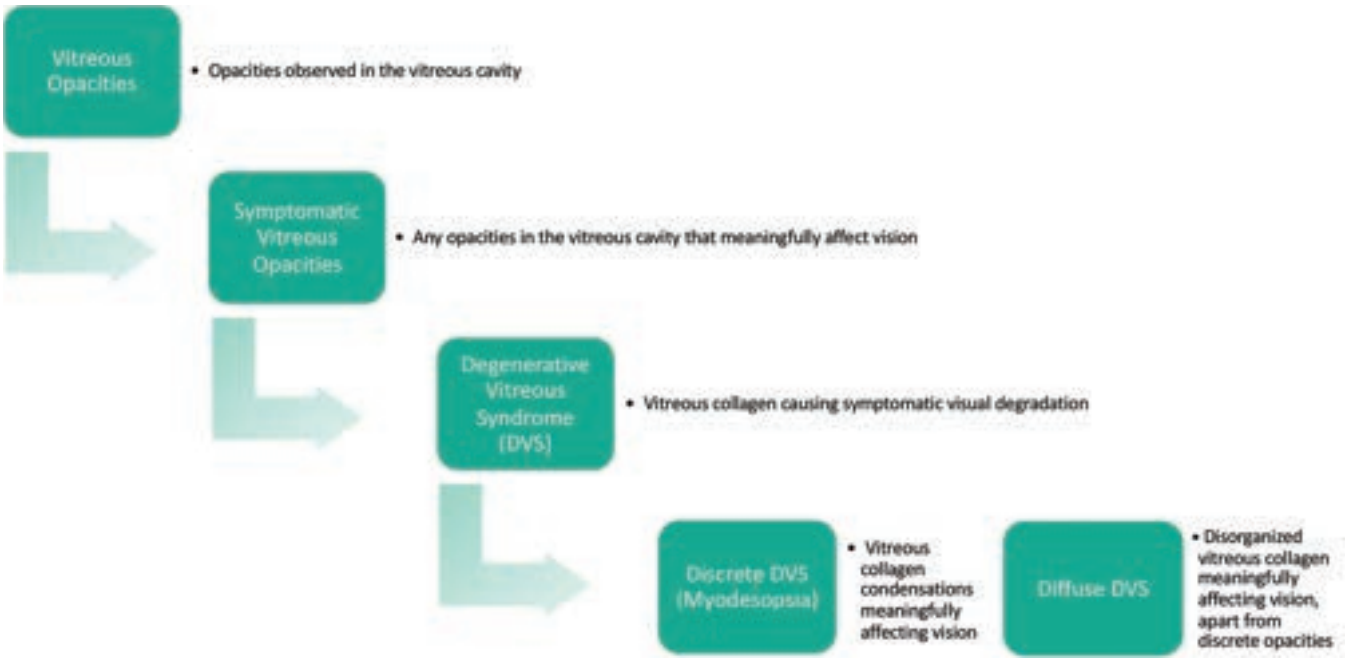

Figure. This flow chart shows the increasing specificity of terms to describe vitreous opacities.

UNDERSTANDING THE VITREOUS

The term *SVO* is nonspecific and does not guide treatment, as it can include conditions such as astroid hyalosis and inflammatory cell. Instead, Robert E. Morris, MD, uses the more specific term *degenerative vitreous syndrome (DVS)* to describe symptomatic visual dysfunction stemming from the vitreous body itself (Figure).[5,6] There are at least two different forms of DVS. Myodesopsia (often described by patients as dots, strands, or "flies" in their vision) are discrete opacities, often a Weiss ring, or other vitreous condensations. However, the vitreous body itself, apart from a Weiss ring, clumping, or stranding, can degrade vision in the full visual field and can have profound effects on visual function and especially contrast sensitivity.[7] In its detached state, the vitreous is both compressed and mobile, leading to persistent visual symptoms separate from myodesopsia. Patients often describe this as filmy, hazy vision, with reduced quality of vision. Recognition and diagnosis of these two types of DVS is critical.

As the vitreous deteriorates with age, it becomes more dysfunctional, with increased DVS. While patients may or may not adapt to discrete opacities, the increasingly dysfunctional vitreous remains in the eye with the potential to decrease visual acuity and reading speed,[8,9] reduce contrast sensitivity,[10] and even increase anxiety and depression.[11,12] Diffuse DVS is also a significant cause of dissatisfaction in the presence of multifocal IOLs.[13]

TREATING THE PROBLEM

Treatment selection and success depends on each patient's specific complaints and visual goals. Nd:YAG vitreolysis is proven to be excellent at removing specific discrete SVOs such as a Weiss ring.[14] Patients with diffuse DVS, however, may have better postoperative outcomes with vitrectomy to remove all the dysfunctional vitreous. In fact, research shows that treatment with vitrectomy resolves the symptoms listed above in nearly all cases.[15,16]

PATIENT SELECTION

Our understanding of what constitutes *visually significant* is still being refined. In fact, researchers in the Netherlands have studied the various VO-specific patient-reported outcome measurements (PROMS) in the literature, and they note that SVOs create unique quality-of-life (QoL) issues that are not properly addressed with our current PROMS.[17,18] Instead, clinicians must rely on careful clinical assessment of a patient's symptoms to determine the level of visual impairment beyond BCVA. I recommend documenting symptoms and their effect on activities of daily living through a patient survey and attestation.

Here, I share several cases that illustrate the critical role of active listening in the patient selection process for the treatment of DVS.

Case No. 1: Vision is More Than BCVA

A 76-year-old man presented with visual complaints in the right eye. His history included vitrectomy with membrane peel for an epiretinal membrane in the left eye a few years ago. He had a posterior vitreous detachment (PVD) in the right eye and was pseudophakic in each eye with standard monofocal IOLs. His BCVA was 20/20- OD and 20/40 OS.

OCT imaging was normal in the right eye and confirmed

BCVA DOES NOT REPRESENT VISUAL SATISFACTION, WHICH IS WHY WE HAVE PATIENTS WHO ARE *20/20 UNHAPPY*.

the PVD; in the left eye, the OCT revealed signs of a traumatic peel with significant nerve fiber layer defects. Stranding and other VOs were present in the right eye. An in-house vitreous-specific visual QoL questionnaire showed significantly reduced quality of vision in the right eye.

The patient confirmed that his right eye bothered him most because of the "hazy, filmy" visual effect. He felt it significantly detracted from his function, as was noted in his visual QoL. He had few discrete opacities in the right eye that did not bother him. I confirmed his visual acuity and asked why he felt his left eye was better even though his visual acuity was worse in that eye. He replied, "I can see letters better in the right eye, but everything is filmy, while my left eye can't see letters quite as well, but everything is clear!"—a surprising response, given his imaging and BCVA.

Based on his decreased visual QoL in the right eye and the presence of a PVD and vitreous syneresis, I recommended vitrectomy or observation. After a careful discussion of the risks, he chose vitrectomy in the right eye. A 27-gauge vitrectomy was performed with no complications. On his postoperative visits, his symptoms had resolved, and his vision was "the best it's ever been" in the right eye.

Discussion: This case illustrates that BCVA does not represent visual satisfaction, which is why we have patients who are *20/20 unhappy*. Clinicians must listen closely to each patient's complaints and realize that our methods of examination of the vitreous are currently lacking. Although we may not have imaging modalities or tools to quantify the dysfunction of the vitreous (yet), the issue still exists and is often something we can address.[19]

Case No. 2: Removing the Bug

A 67-year-old woman presented with complaints of symptomatic VOs in the left eye. She stated that a single large opacity appeared 6 months ago and has remained in her temporal visual field. She had a PVD in the left eye and mild cataracts in each eye. Her VA was 20/20- OD and 20/20 OS. OCT imaging showed normal retinas and confirmed the PVD in the left eye. The posterior examination revealed a Weiss ring in the left eye and no retinal tears or other issues. A visual QoL questionnaire showed a reduction in activities of daily living due to the opacity in the left eye, including difficulty reading, driving, and reduced enjoyment in visual tasks.

During our discussion, she explained that her only problem was the "big bug" in her left-eye vision, and if I could "get the bug out," she would be satisfied.

I suggested two possible treatment approaches: vitrectomy and Nd:YAG laser vitreolysis. After discussing each procedure, including the possibility of early cataract formation with vitrectomy, she chose laser vitreolysis. The laser procedure was performed with no complications. On her postoperative visit, she noted that the bothersome "bug" was gone and the residual floaters in her vision did not bother her. The posterior examination showed resolution of the Weiss ring and no retinal issues.

Discussion: Listening to the patient's specific complaints is critical to guide therapy. Not all opacities are the same or are treated in the same way. Laser vitreolysis was an excellent option, with a lower risk and side-effect profile than vitrectomy, in addition to lower cost, with the best outcomes in cases of discrete DVS/myodesopsia.

Case No. 3: Vitreous on the Move

A 64-year-old man presented with complaints of "terrible vision" after laser-assisted cataract surgery and premium multifocal IOL implantation in each eye. His UCVA was 20/20 OU, and he had 0.25 sphere of residual refractive error in the right eye with no astigmatism. He was J2 at near without correction. The posterior examination and imaging were unremarkable other than PVDs in each eye and typical vitreous stranding and opacities. The IOLs appeared well centered.

However, he scored poorly on the visual QoL questionnaire. I asked how he could consider his vision to be so poor with a VA of 20/20. He replied that "everything has a waxy film over it; nothing is clear." He said that his vision was better before cataract surgery (with a VA of 20/30 and 2+ nuclear sclerosis). He wanted his premium IOLs explanted and his out-of-pocket payments refunded.

I explained that vitreous, commonly in its detached state, can cause significant aberrations, especially in conjunction with multifocal IOLs. The patient admitted that his floaters didn't bother him but the "filmy vision" did. I explained that the vitreous can cause additional diffuse optical degradation without clumping, and removal of the vitreous body would remove this source of scatter. I explained that vitrectomy would yield the best results in this case.

After a careful discussion of the risks, he chose to undergo vitrectomy in the right eye. A 27-gauge vitrectomy was performed without complication. On his first postoperative visit, he was overjoyed, stating, "My vision is clearer than ever!" He opted for vitrectomy in the left eye, after which his UCVA was 20/20 OU.

Discussion: A key cause of vitreous dysfunction is the light scatter created by the disorganized vitreous body in the detached state,[20] and the defractive rings in a

multifocal IOL create additional opportunities for light scatter. A complete vitrectomy at the time of a multifocal IOL implantation has been shown to resolve light scatter issues.[13,21] In this patient's case, a second trip to the OR to remove the vitreous solved his visual complaints.

MANAGEMENT PEARLS

- Listen carefully to patients, as their specific complaints will guide patient selection for maximum efficacy and minimal risk.
- Current common imaging modalities are lacking in diagnosis and patient selection; instead, symptomology drives treatment selection.
- Visual QoL assessment is critical for patient selection to prevent unnecessary treatments.
- Discrete SVOs are often treated with low-risk vitreolysis, while diffuse DVS typically require vitrectomy.
- Diffuse DVS may cause significant reduction in QoL and is often more important to the patient's visual function than a discrete myodesopsia/Weiss ring.
- Treatment of DVS often leads to high patient satisfaction and increased QoL. ■

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(Continued from page 32)

trim it down, I don't aggressively scleral depress and try to shave down the anterior retina, as this increases the risk of iatrogenic choroidal hemorrhaging.

Next, I fill the eye with PFO, tilting away from the retinectomy site to push the subretinal fluid out and lower the risk of small PFCL bubbles entering the subretinal space. I laser under PFO with longer-duration burns (150 ms to 200 ms).

Finally, I remove the PFO during air infusion while tilting the eye toward the retinectomy; I meticulously drain any residual balanced salt solution before removing the PFCL below the edge of the retinectomy. In nearly all cases, I use silicone oil tamponade. In the rare situation where a retinectomy isn't necessary, I may use C_3F_8.

Upon studying factors associated with better visual outcomes in eyes with PVR undergoing retinectomy, we found that a shorter time to surgery after PVR redetachment (mean of 2.9 days) was associated with better outcomes, independent of whether the macula was on or off.[3] Therefore, surgeons should get these eyes back to the OR in a timely fashion. ■

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OCULAR BLACKOUT: A HARBINGER OF SICKLE CRISIS

This patient presented with a rare complication of sickle cell disease.

BY SIDRA ZAFAR, MD

A 21-year-old woman with a history of sickle cell disease (SCD) presented to the emergency department with complaints of bilateral vision loss. The patient reported a complete blackout in both eyes that lasted approximately 1 to 2 hours while she was drinking alcohol 3 days ago. Since then, her vision had gradually improved but had not returned to baseline.

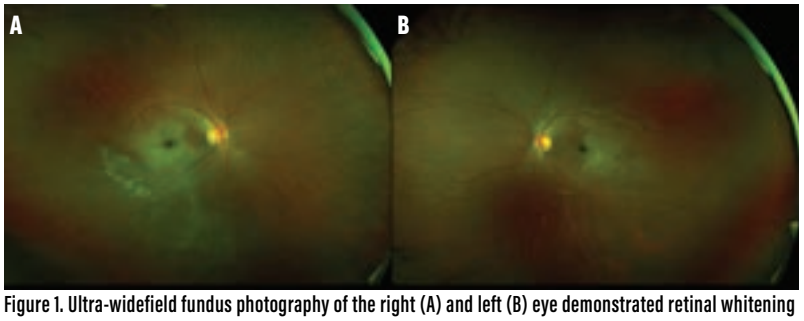

Figure 1. Ultra-widefield fundus photography of the right (A) and left (B) eye demonstrated retinal whitening secondary to CRAO.

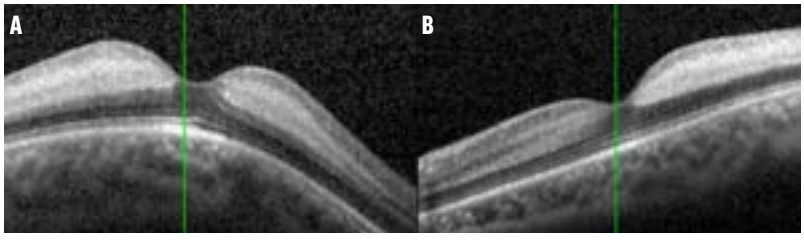

Figure 2. OCT of the right (A) and left (B) eye showed increased reflectivity and thickening of the inner retinal layers consistent with CRAO.

EXAMINATION

On examination, her VA was counting fingers OD and 20/25 OS. IOP was within normal limits. No relative afferent pupillary defect was noted. Anterior segment examination was unremarkable. Dilated fundus examination of each eye revealed a cherry red spot and retinal edema consistent with concurrent central retinal artery occlusion (CRAO; Figure 1). OCT imaging showed inner- and middle-layer hyperreflectivity and thickening (Figure 2).

The patient's arterial occlusions were thought to be secondary to her SCD, and she was admitted for emergent exchange transfusion. A stroke and hypercoagulability workup showed low protein C, protein S, and antithrombin III levels and elevated lipoprotein A and factor VIII. The hemoglobinopathy panel indicated elevated hemoglobin S (HbS) levels (90.7%). The day following the exchange transfusion, the patient's VA improved to 20/400 OD, and the left eye remained stable. The repeat hemoglobinopathy panel showed decreased HbS levels (19.5%). Given the patient's hypercoagulability workup and that her mother had a history of deep vein thrombosis and pulmonary embolism, the patient was started on anticoagulation.

DISCUSSION

Sickle cell retinopathy (SCR) is the most common manifestation of SCD and can be classified as nonproliferative (NPSCR) or proliferative (PSCR). The retinal changes in NPSCR are secondary to vascular occlusion and local ischemia.[1] Clinical findings include peripheral retinal vascular anastomoses, salmon patches, iridescent spots, and black sunbursts. Salmon patches are well-demarcated, superficial intraretinal or preretinal hemorrhages, whereas iridescent spots represent hemosiderin-filled macrophages in areas of old, resorbed hemorrhages and within the inner retina just beneath the internal limiting membrane. Sunburst lesions appear after resolution of the hemorrhages and are localized

THE EXACT PATHOGENESIS OF VASCULAR OCCLUSION IN SCD IS POORLY UNDERSTOOD, BUT SEVERAL MECHANISMS HAVE BEEN PROPOSED, INCLUDING ABNORMAL ENDOTHELIAL ADHESION BY SICKLED ERYTHROCYTES, ACTIVATION OF THE COAGULATION CASCADE, AND INTIMAL INJURY.

areas of retinal pigment epithelium hyperplasia and pigment migration. Central retinal changes can consist of arteriovenous tortuosity, foveal avascular zone enlargement, and arterial occlusions.[1,2] A foveal depression sign has also been described, characterized as a darkened foveal reflex due to thinning of the retinal layers in this region.[3]

PSCR is characterized by the development of peripheral retinal neovascularization, the hallmark sign being a sea fan configuration.[1,2] Sea fans have a high propensity to regress by autoinfarction, although they may lead to vision loss through vitreous hemorrhage or tractional retinal detachment.[2] Genotype is the risk factor most strongly associated with the development of PSCR.

Vision-threatening PSCR occurs earlier and is more likely to affect those with hemoglobin C SCD (HbSC) versus homozygous SCD (HbSS).[4] Several theories have been proposed for this, including higher hematocrit levels in HbSC, which may lead to increased red blood cell sludging and small vessel occlusion in the retinal vasculature.[5] Another theory is that vascular occlusion in HbSC may be less severe, resulting in low-grade chronic ischemia and release of proangiogenic growth factors, which creates a more favorable environment for neovascularization. In contrast, the vascular occlusion in HbSS is more complete, resulting in more profound infarction and retinal necrosis, which is less likely to generate an angiogenic response.[5]

Bilateral concurrent CRAO secondary to SCD is extremely rare. To the best of our knowledge, only three cases have been previously reported.[6-8] The exact pathogenesis of vascular occlusion in SCD is poorly understood, but several mechanisms have been proposed, including abnormal endothelial adhesion by sickled erythrocytes, activation of the coagulation cascade, and intimal injury. Renganathan et al reported a case of a 24-year-old woman with a history of SCD who presented with a VA of hand motion OU in the setting of CRAO during a sickle crisis. Immediate exchange transfusion was initiated and continued until her symptoms improved over 2 days.[6] Murthy et al similarly reported a case of a 37-year-old woman who presented with a VA of no light perception OU and had recently been started on a phosphodiesterase type 5 inhibitor for pulmonary hypertension. Although immediate exchange transfusion was initiated, the patient did not recover any vision.[7]

In our case, we believe that alcohol may have precipitated a sickle crisis, leading to bilateral occlusion of the central retinal artery.

The mainstay for treatment in SCD remains hydroxyurea or blood transfusion. Transfusions help to decrease the proportion of red sickle cells in circulation while simultaneously improving anemia and peripheral tissue oxygen delivery. For acute SCD complications, the goal of transfusion therapy is to reduce the posttransfusion HbS level to less than 30%.

WHILE RARE, BE AWARE

Concurrent retinal arterial occlusion in SCD is exceedingly rare. Exchange transfusion should be initiated emergently in cases that do present to attempt to reverse some of the vision loss in these patients. ■

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INFECTIVE ENDOCARDITIS DETECTED IN RETINAL EXAMINATION

Ocular findings led to the diagnosis of a rare but potentially fatal infection in the heart.

BY MAKENA PARKER, MPHYS, BA; SARAH SYEDA, MD; AND MATHEW W. MACCUMBER, MD, PHD

Infective endocarditis (IE) is a condition that can lead to significant morbidity and mortality if not addressed in a timely fashion. IE affects the inner lining of heart chambers and valves and is traditionally caused by infection with microorganisms, such as bacteria or fungi. It is characterized by the presence of multiple findings, rather than a single result, making it somewhat tricky to diagnosis; regardless, misdiagnosis can have serious consequences. Given the wide array of presentations, it is important to remain vigilant and always consider the possibility of this diagnosis.

Duke criteria were developed in 1994 to aid in the appropriate diagnosis of IE based on a constellation of findings,[1] categorized as either major criteria (ie, positive blood cultures, echocardiographic results) or minor criteria (ie, fever, predisposition, microbiological evidence, presence of vascular or immunologic phenomena). Based on the combination of criteria met, a patient's presentation may be classified as "definite IE," "possible IE," or "rejected IE." Since being established, the Duke criteria have faced criticism due to the overly broad categorization of "possible IE," as a patient would meet the requirements of this classification by satisfying only one minor criterion.

This case report demonstrates how retinal findings can fit within the diagnostic criteria for IE.

CASE REPORT

A 39-year-old man presented with a blind spot in his right field of vision that appeared 4 days prior. At onset, he initially presented to an optometrist, who referred him for a retinal evaluation due to the presence of retinal bleeding. His medical history was significant for a bicuspid aortic valve and was negative for intravenous drug use. Of note, he reported having an ongoing illness that had lasted for 5 weeks without improvement, including symptoms of muscle aches, subjective fevers, chills, night sweats, malaise, decreased appetite, and unexplained weight loss of 15 lbs. He underwent systemic workup with his primary care physician and was found to have a positive Epstein-Barr viral capsid antigen IgG test, which is typically associated with past infection. A blood culture that was taken at an outside hospital grew *Streptococcus mitis*, but this was thought to be a result of contamination, as only one culture was drawn; thus, no antibiotic treatment was initiated at that time.

Examination and Retinal Imaging

On examination, the patient's VA was 20/150 OD and 20/20 OS. Ophthalmoscopy, fundus photography, and fluorescein angiography (FA) revealed a preretinal hemorrhage in the right eye and scattered bilateral retinal hemorrhages (Figures 1 and 2). OCT showed a preretinal hemorrhage in the right eye (Figure 3). These findings prompted referral to hematology and infectious disease.

At 2-week follow-up, the examination and imaging were significant for the development of Roth spots (Figure 4). Evaluation by hematology noted an elevated prothrombin time (15.4; normal: 10-13 seconds), positive beta 2 glycoprotein (49.3; normal: < 20 units/mL), and elevated erythrocyte sedimentation rate and C-reactive protein.

Given the retinal changes, IE was suspected. A prompt outpatient transthoracic echocardiogram was obtained, which revealed a 1 cm x 1 cm circular echodensity with a narrow stalk noted on the ventricular aspect of the aortic valve, as well as severe aortic regurgitation.

To the Emergency Department

At this time, the patient was instructed to immediately present to the emergency department. Transesophageal echocardiogram showed a 1 cm x 2.5 cm mobile echodensity,

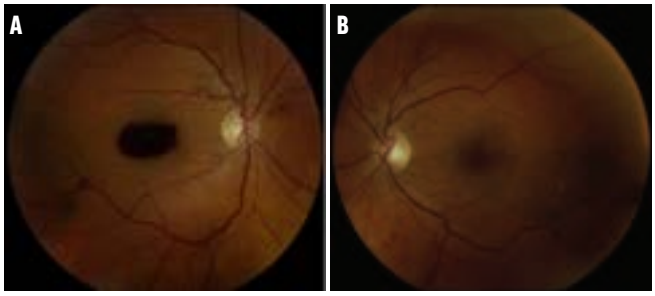

Figure 1. Fundus photography of the right (A) and left (B) eye showed preretinal hemorrhage in the right eye, causing a blockage.

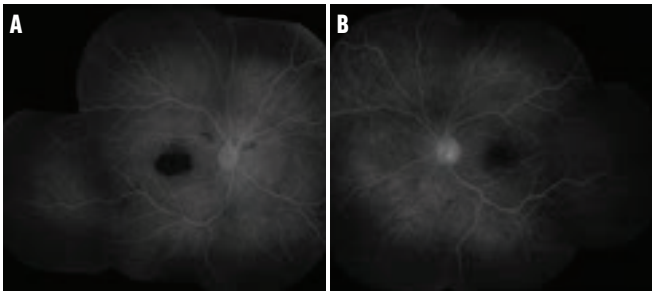

Figure 2. FA of the right (A) and left (B) eye demonstrated scattered retinal hemorrhages.

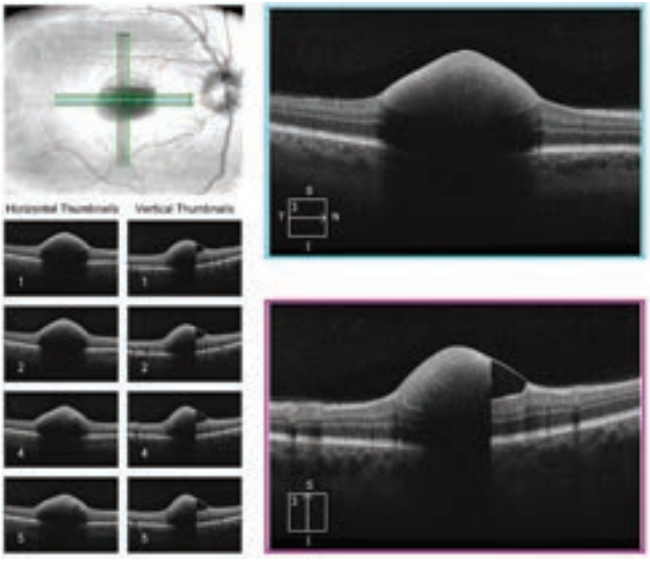

Figure 3. OCT imaging of the right eye showed a preretinal hemorrhage.

consistent with bacterial endocarditis (Figure 5). A single blood culture was taken, which grew *Streptococcus mitis*. Physical examination was significant for irregularly shaped macules of the lower extremities, consistent with Janeway lesions. The patient was initiated on intravenous ceftriaxone and vancomycin, which was later tapered to ceftriaxone alone. He received aortic valve replacement on day 5 of hospitalization, and intraoperative cultures were taken to determine the length of antibiotic therapy. He continued 4 weeks of antibiotic therapy with intravenous ceftriaxone from the time of the first negative blood culture, recorded on day 2 of hospitalization.

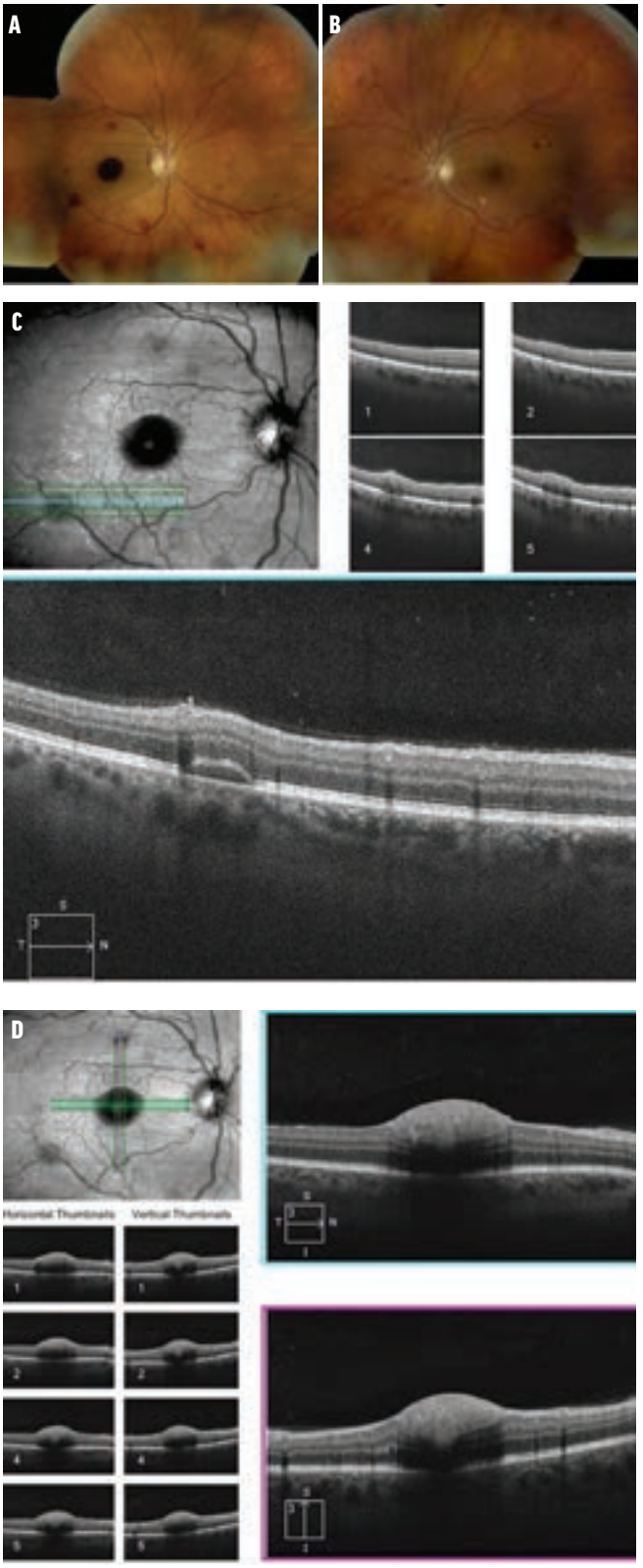

Figure 4. At the 2-week follow-up, fundus photography of the right (A) and left (B) eye showed Roth spots. OCT imaging of the right eye revealed Roth spots (C) and a preretinal hemorrhage (D).

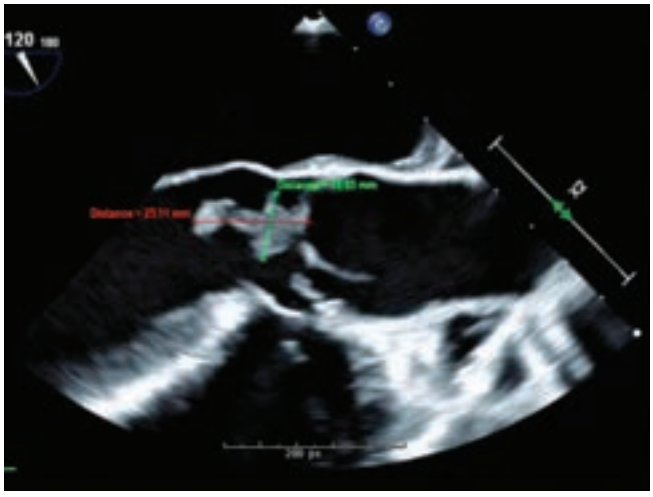

Figure 5. Transesophageal echocardiogram confirmed the presence of a mobile echodensity on the ventricular aspect of the aortic valve.

The patient was seen in clinic 2 months after the initial presentation. His VA had improved to 20/80 OD, and he noted a persistent but improving scotoma. Examination and fundus photography were significant for a resolving preretinal hemorrhage in the right eye, which was expected to continue to impair visual acuity until resolution (Figure 6). The patient was instructed to remain on daily warfarin to help prevent thrombus formation.

CONFIRMING IE

Since Duke established the criteria for IE, modifications have been made to increase the sensitivity of disease detection and more clearly delineate next steps based on patient presentation and test results.[2] This patient originally presented to an outside hospital, where a single blood culture was taken. The combination of a single positive blood culture and the presence of fever placed this patient in the "possible IE" category; however, no further interventions were performed until he followed up with ophthalmology 1 week later. The presence of Roth spots greatly increased the likelihood of IE, and once the transthoracic echocardiogram was performed, the diagnosis was confirmed. The use of algorithms and calculators for guidance in the diagnosis of IE is critical, as clinical presentation can vary widely, making accurate diagnosis difficult.

The patient's original placement in the "possible IE" category should have prompted additional testing to determine if the patient should then be moved to the "definite IE" or "rejected IE" category. Early suspicion for IE can aid in determining subsequent management, and close follow-up is critical for the detection of additional signs and symptoms that can complete the clinical picture. Roth spots are not specific for IE, and they can be associated with other conditions that should also be investigated, including antiphospholipid syndrome, diabetic retinopathy,

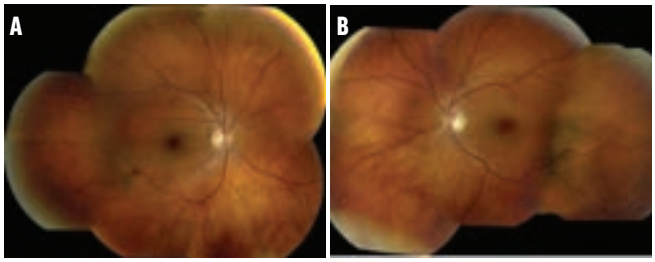

Figure 6. Fundus photography of the right (A) and left (B) eye 2 months after initial presentation demonstrated a resolving hemorrhage in the right eye after aortic valve replacement surgery and completion of a 4-week antibiotic course.

and various prothrombotic or autoimmune diseases.[3] This patient was already undergoing a full workup with his primary care physician, so other sources were being investigated in conjunction with suspicion for IE.

With prompt action and early testing, this patient quickly initiated treatment, resulting in the best visual prognosis. He also underwent aortic valve replacement within days of diagnosis, preventing the development of neurological sequelae, which can result from mobile thrombus formation.

NO ROOM FOR ERROR

IE is a can't-miss diagnosis, as it can be fatal if left untreated. Therefore, it is best to maintain a high index of suspicion for this condition as a potential differential. The Duke criteria and its proposed modifications serve as a means of stratifying that level of concern to determine the likelihood of IE and guide testing to confirm a diagnosis. ■

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RISING STARS IN RETINA

Get to know outstanding retina fellows from the class of 2024.

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REGENXBIO

Ellie Xiao Yi Zhou, MD

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

My fascination with retina began during my ocular pathology fellowship under the mentorship of Sander R. Dubovy, MD, at the Bascom Palmer Eye Institute. I joined Dr. Dubovy in the retina clinic and gained a deeper understanding of retina pathology. By participating in grand rounds and interacting with amazing retina surgeons, I realized that the creativity, fine motor skills, and pattern-recognition required to be a great vitreoretinal surgeon, combined with the dynamic and fast-paced technological advancements, are aspects that I really enjoy.

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

During my residency at Case Western Reserve University, I had outstanding mentors, including Warren Sobol, MD; Shree Kurup, MD; Jose J. Echegaray, MD; and Daniel Weidenthal, MD. Their contagious enthusiasm for retina and dedication to teaching influenced my decision to pursue a retina fellowship.

Throughout my fellowship, I learned from some of the most incredible retina mentors in the field. Lejla Vajzovic, MD, and Xi Chen, MD, PhD, provided invaluable mentorship throughout my fellowship, particularly during my first months. Glenn Jaffe, MD, and Dilraj Grewal, MD, showed me that being precise and adaptable are incredible traits to develop as a surgeon. Sharon Fekrat, MD, and Eric Postel, MD, taught me how to connect with patients and colleagues in more meaningful ways. Durga S. Borkar, MD, MMCi, guided me through complex surgical cases. Finally, Cynthia A. Toth, MD, and Dr. Chen were wonderful research mentors who inspired my passion for teaching and pediatric retina. All my mentors have been incredibly supportive, and I consider each of them life-long mentors.

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

While my fellowship offered numerous memorable clinical and surgical experiences, the vibrant and supportive culture at Duke really enhanced this experience. I enjoyed getting to know my attendings, co-fellows, and residents outside of the clinical setting. Whether it's bonding over Dr. Vajzovic's lively annual holiday axe throwing soiree, enjoying fruit picking and ice cream at a local farm, or gathering for journal club meetings, these moments have cultivated lasting friendships that I will cherish for years to come.

FIRST CAREER MILESTONE

Dr. Zhou has joined the faculty at the University of Chicago.

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

Seek out as many opportunities as possible to gain exposure to surgical and medical retina during residency. Find mentors who are passionate about the field and can offer you advice and help you assess if this is the right fit for you. Lastly, attend retina meetings; they are great networking opportunities. ■

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CODING ADVISOR
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KNOW YOUR E/M CODING IN RETINA

Medical decision making is usually the determining factor.

BY JOY WOODKE, COE, OCS, OCSR

As of 2021, the level of E/M for office visits is determined by either medical decision making (MDM) or total physician time on the day of the encounter. In retina practices, MDM is usually the determining factor. Upon documenting a medically relevant history and examination, any qualifying MDM elements are then analyzed.

The final determination for the level of E/M is guided by the MDM table, which can be accessed at aao.org/em, along with current guidance. The three components of MDM include:

- The number and/or complexity of problems addressed during the encounter.
- The amount and/or complexity of data to be reviewed and analyzed.
- The risk of complications and/or morbidity or mortality of patient management.

Complexity ranges from straightforward to low to moderate to high. To arrive at the E/M level, two of the three components must meet or exceed the same level of complexity. For example, a moderate problem and risk would be assigned CPT code 99204 for a new patient or 99214 for an established patient. Alternatively, a moderate problem with a low risk would be assigned CPT code 99203 or 99213, respectively.

The following examples build on each other to help you get a better sense of how to code these patient encounters.

EXAMPLE SCENARIO NO. 1

A patient presents with wet AMD with active choroidal neovascularization (CNV) and subretinal hemorrhage. Select the level of complexity for the problem category:

A. Low: one stable chronic illness
B. Moderate: one acute illness with systemic symptoms
C. Moderate: one or more chronic illnesses with exacerbation, progression
D. High: one or more chronic illnesses with severe exacerbation, progression

Answer: C. Although active CNV and subretinal hemorrhage are concerning, they do not typically meet the definition of *severe* as outlined by the AMA CPT 2024: "significant risk of morbidity and may require escalation level of care," such as hospitalization. Therefore, it is categorized as a moderate-complexity problem.

EXAMPLE SCENARIO NO. 2

A new patient is diagnosed with stable mild diabetic retinopathy with no macular edema in each eye. No treatment is prescribed, but the patient is asked to return in 1 month or sooner if they experience new symptoms or a change in vision. Select the level of complexity for the problem category:

A. Low: one stable chronic illness
B. Moderate: one undiagnosed new problem with uncertain prognosis
C. Moderate: one or more chronic illnesses with exacerbation, progression
D. High: one or more chronic illnesses with severe exacerbation, progression

Answer: A. Diabetic retinopathy is a chronic illness and can be categorized as stable (low) or progressing (moderate). In this case, there is no documentation of disease progression. Being that this disease can progress rapidly and is often not easily managed, why isn't it

AS OF 2021, THE LEVEL OF E/M FOR OFFICE VISITS IS DETERMINED BY EITHER MEDICAL DECISION MAKING (MDM) OR TOTAL PHYSICIAN TIME ON THE DAY OF THE ENCOUNTER. IN RETINA PRACTICES, MDM IS USUALLY THE DETERMINING FACTOR. UPON DOCUMENTING A MEDICALLY RELEVANT HISTORY AND EXAMINATION, ANY QUALIFYING MDM ELEMENTS ARE THEN ANALYZED.

considered an undiagnosed new problem with uncertain prognosis? The AMA definition of *an undiagnosed new problem with uncertain prognosis* is "a problem in the differential diagnosis that represents a condition likely with high risk of morbidity without treatment." A common misconception is that *undiagnosed new problem* means all new problems diagnosed during the encounter; however, if a diagnosis is confirmed during the encounter, it is not considered undiagnosed.

EXAMPLE SCENARIO NO. 3

A letter is sent to the referring physician, and OCT, fluorescein angiography, and B-scan findings are reviewed. Select the level of complexity for the data category:

A. Minimal or none
B. Limited: two reviewed/ordered tests
C. Moderate: three reviewed/ordered tests
D. High: three reviewed/ordered tests, discussion of management with external provider

Answer: A. Under the first category of the data component, the reviewing or ordering of each unique test does not include a test performed in the office that has a separate CPT code. Even bundled tests or reviewing tests performed previously within your practice does not count. What is included, for example, is lab tests, MRIs, and CT scans ordered and/or reviewed from an external source. Similarly, sending a letter to a referring physician does not qualify as discussion of management with an external provider; however, two-way coordination over the phone and/or secure messaging about patient care does qualify. Documentation should include the reason for the discussion and the effect on patient management.

EXAMPLE SCENARIO NO. 4

A new patient has worsening proliferative diabetic retinopathy, and panretinal photocoagulation is scheduled. Code this office visit:

A. E/M level two, CPT code 99202
B. E/M level three, CPT code 99203
C. E/M level four, CPT code 99204
D. E/M level five, CPT code 99205

Answer: C. For the problem component, the level of complexity would be moderate, as one chronic illness with progression is documented. For a moderate level of risk, the procedure would need to involve minor surgery with identified patient or procedure risk factors or major surgery without identified patient or procedure risk factors. The latter best describes our case. Identified risk factors include any risk that is greater than the usual risk associated with the procedure. Whether a procedure is minor or major is not based on the global period; instead, it is based on the mutual understanding of trained physicians in the same specialty. Ophthalmic lasers, which have varied global periods, have a moderate level of risk.

EXAMPLE SCENARIO NO. 5

An established patient has a worsening chronic retinal detachment, and next-available surgery is scheduled. Code this office visit:

A. E/M level two, CPT code 99212
B. E/M level three, CPT code 99213
C. E/M level four, CPT code 99214
D. E/M level five, CPT code 99215

Answer: C. To qualify for the high-level problem, there would need to be a threat to the body's functionality requiring immediate treatment; thus, this problem is considered moderate. The risk is also considered moderate, with a decision for major surgery without additional risk being scheduled urgently but not emergently. ■

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TISSUE GLUE-ASSISTED PLAQUE RADIOTHERAPY FOR UVEAL MELANOMA

A potentially safer approach for eyes with a thin sclera.

BY ROBERT J. MEDINA, BA; MADISON M. WOODS, BA; ROLIKA BANSAL, MD; AND CAROL L. SHIELDS, MD

Uveal melanoma is a rare intraocular tumor that most often arises from the choroid. The most common treatment modality for this malignancy is plaque radiotherapy,[1,2] which involves delivery of focal radiation to the tumor using radionucleotides, such as iodine-125, ruthenium-106, cobalt-60, iridium-192, and cesium-131.[3] In a meta-analysis of 14 cohorts (n = 21,263), the 5-year median local tumor control following plaque radiotherapy for uveal melanoma was excellent (94%).[4]

The surgical technique of plaque radiotherapy involves suturing a template device with precisely placed radioactive material onto the sclera to deliver radiation through the sclera to target the entire melanoma, with the apex dose of 70 Gy delivered to the area of greatest thickness. This requires accurate positioning of the plaque onto the surface of the eye, centered over the intraocular melanoma and covering all tumor margins. The plaque is secured with partial-thickness 5-0 nylon scleral sutures, as plaque displacement could potentially lead to poor delivery of radiation to the tumor. Additionally, if placement of the sutures is too deep or too shallow, especially in cases of a thin sclera, ocular complications such as scleral perforation with vitreous leakage, retinal detachment, choroidal or vitreous hemorrhage, endophthalmitis, or ultimate extraocular extension may occur.[5,6] Due to these risks, biologic tissue adhesive (ie, tissue/fibrin glue) has been proposed as a potential mode of assistance for plaque application in eyes with a thin sclera.[5,6]

Herein, we detail a case report using the technique of tissue glue-assisted plaque radiotherapy.

CASE REPORT

A 77-year-old White man was found to have a choroidal nevus in his left eye measuring 8 mm x 8 mm in base and 2.8 mm in thickness on ultrasonography that demonstrated growth into melanoma after 11 years of follow-up. The choroidal melanoma was located superotemporally, measuring 12 mm in base (Figure 1A) and 5.7 mm in thickness with no evidence of extrascleral extension (Figure 1B).

Local plaque radiotherapy with an 18-mm iodine-125 round plaque was advised. At the time of surgery, there was notable intraoperative scleral thinning evidenced by a bluish hue underlying the uveal tissue involving two quadrants (Figure 2A). Due to the risks of placing scleral sutures in such thin tissue, we decided to use tissue glue-assisted plaque securement (Tisseel [Fibrin Sealant], Baxter). One 5-0 nylon partial-thickness scleral suture was cautiously placed (Figure 2B), and glue was applied over the entire

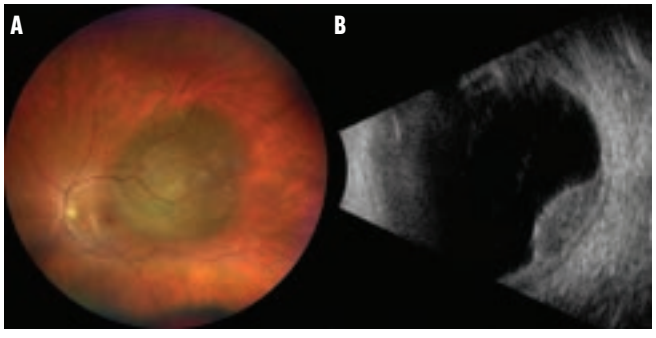

Figure 1. The choroidal melanoma (A) was 5.7 mm in thickness on ultrasonography (B).

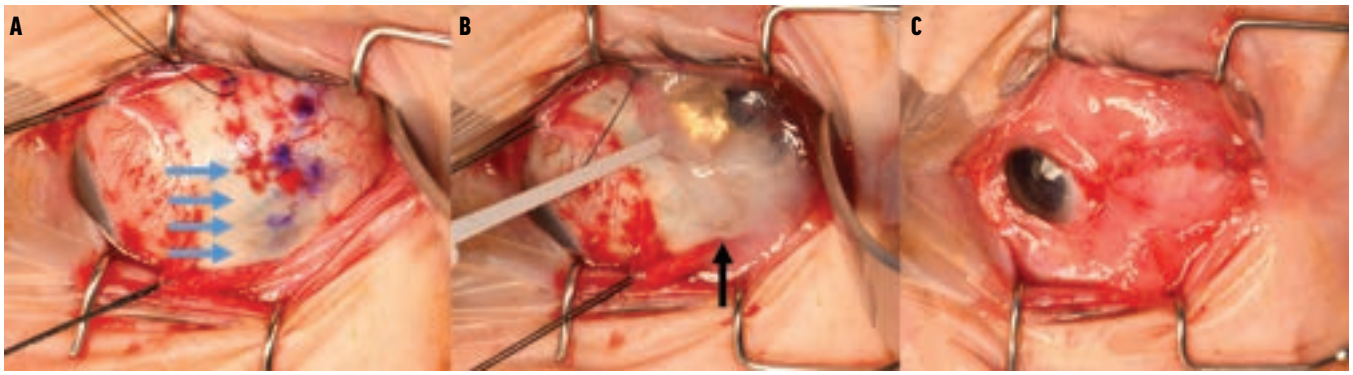

Figure 2. During surgery, scleral thinning (A, blue arrows) was noted; therefore, one suture was placed, and the remainder of the plaque was sealed with tissue glue to all margins covering both suture holes (B, black arrow). Closure of the overlying Tenon fascia and conjunctiva was performed (C).

plaque rim, including both suture holes. The Tenon fascia and then the conjunctiva were both carefully pulled over the glue for closure (Figure 2C) with the melanoma apex dose delivered at 70 Gy over 102 hours.

At the time of plaque removal, the device was secure and in place and could be safely peeled off the sclera. Eight months later, the radiation seed-induced local choroidal atrophy was in an ideal position, another sign of accurate plaque placement (Figure 3A), and the tumor demonstrated regression in thickness to 4.4 mm (Figure 3B).

THE USE OF TISSUE GLUE IN OPHTHALMIC PROCEDURES

Tissue glue is commonly used in eyelid and adnexal surgeries, conjunctival autograft with amniotic membrane transplantation, conjunctival closure in strabismus surgery, conjunctival port-closure in vitreoretinal and cataract surgery, corneal perforation, keratoplasty, corneal limbal stem cell transplantation, epikeratophakia, temporary keratoprosthesis, keratorefractive procedures, and as a substitute for sutures in trabeculoplasty and placement of drainage devices in glaucoma.[7-20] By using tissue glue, surgeons can avoid suture-related complications.

TISSUE GLUE-ASSISTED PLAQUE RADIOTHERAPY IN THE LITERATURE

In 2016, Zloto et al assessed the use of fibrin glue as an adhesive and urokinase as a dissolvent for tissue glue in the setting of plaque placement in six porcine eyes.[6] In this ex-vivo animal model, the feasibility of this technique and the glue adhesion strength were assessed and compared with a sutured plaque.[6] The tissue glue-assisted plaques were held tightly in place with post-placement stability over 5 days and could be removed with a force similar to that required with the suturing technique. The removal of each plaque in this study used saline and urokinase, with saline having no effect on the glue dissolvent and drops of urokinase having an immediate dissolving effect. However, the authors stated that the plaque-glue complex could be retrieved easily by gently grasping it along with side-to-side movement, with no damage to the underlying globe.[6]

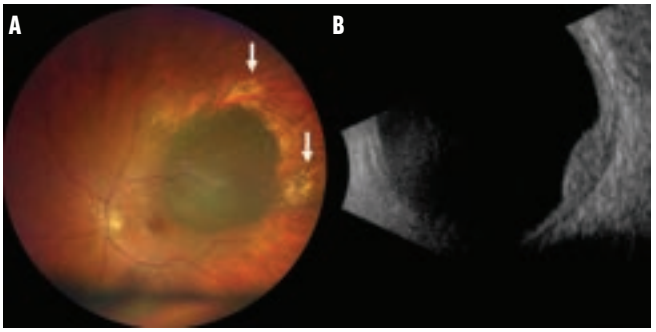

Figure 3. At the 8-month follow-up visit, the melanoma demonstrated regression, and choroidal atrophy at the site of the radiation seeds confirmed accurate placement (A, white arrows). Tumor thickness was reduced to 4.4 mm (B).

In 2023, our team reported on tissue glue-assisted plaque radiotherapy in six patients with choroidal melanoma who demonstrated intraoperative scleral thinning.[5] The tissue glue was applied over the plaque rim and suture holes. Precaution was taken to prevent fibrin glue from entering under the plaque to avoid lifting it off the sclera and reducing the apical radiation dose. In these six cases, the tumor apex dose was 70 Gy with a mean dose rate of 63.6 cGy/hour over a mean duration of 117.6 hours. Complete closure of the conjunctiva was achieved in each case.[5] At plaque removal, accurate plaque position was confirmed with no shifting, and the device was removed by lifting the glue and device off the globe without the need for urokinase. No glue-associated complications were noted.[5]

A NOVEL AND SAFER OPTION

Plaque radiotherapy is a primary treatment for uveal melanoma. In eyes with a thin sclera, fibrin tissue glue can serve as a novel alternative to sutures for a potentially safer surgical approach. ■

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 provided in part

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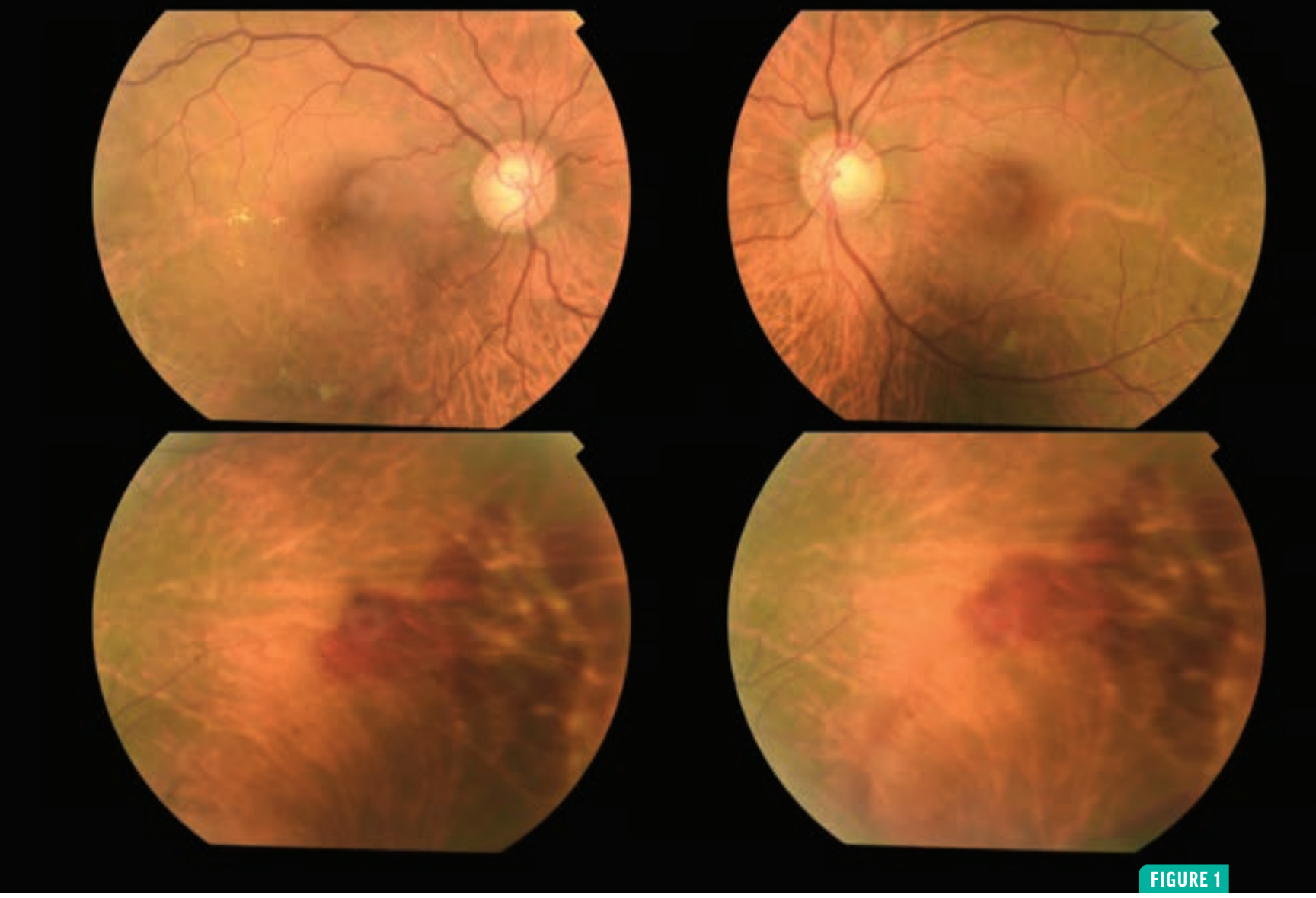

FIGURE 1

BULLETPROOF: A CASE OF CHORIORETINITIS SCLOPETARIA

Impact from a high-velocity object can lead to this rare condition.

BY INÊS CERDEIRA LUDOVICO, MD; PATRÍCIA SILVA, MD; AFONSO MURTA, MD; CATARINA BARÃO, MD; CARLOS BATALHA, MD; AND ARNALDO SANTOS, PHD

A 58-year-old man with no relevant medical or ocular history presented at our emergency department with a sudden decrease in visual acuity in his left eye after a shotgun injury near the globe. His BCVA was 20/100 OS. Slit-lamp examination revealed extensive periocular ecchymosis and a discrete temporal subconjunctival hemorrhage with no signs of penetrating injury. His ocular motility was unaffected, and his IOP measurements were unremarkable.

Fundoscopy showed a temporal subretinal hemorrhage

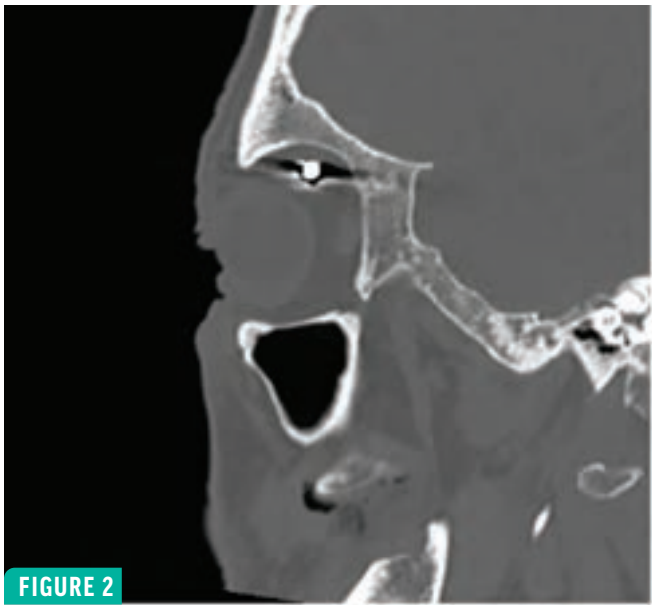

FIGURE 2

accompanied by discrete vitreous hemorrhage in the vicinity, as well as Berlin macular edema (Figure 1). No tears or signs of retinal detachment were noted. A CT scan of the orbits detected the presence of a metallic foreign body adjacent to the lateral wall with no signs of retrobulbar hemorrhage or damage to the globe or extraocular muscles (Figure 2). The surgeons who observed the foreign body opted for a conservative course, and thus, it was not removed from the orbital cavity at this time.

At the 2-week follow-up, the patient's VA had recovered to 20/20 OS. OCT of his left eye showed a disorder of the retinal pigment epithelium cells in the damaged area, with no signs of macular edema (Figures 3 and 4). Retinography revealed a resorbing lower temporal vitreous hemorrhage and a retinal hemorrhage that had already reabsorbed.

A SHOCK FELT AROUND THE GLOBE

Chorioretinitis sclopetaria is a rare disease characterized by a rupture of the neurosensory retina, the underlying choroid, and the sclera due to an impact from a penetrating high-velocity object into the orbit, such as a bullet.

The lesions observed in this case were the result of differences in elasticity of the various layers of the eye. The Bruch membrane, attached choriocapillaris, and retinal pigment epithelium are all rigid and more prone to injury and rupture. Because the sclera and neurosensory retina are more elastic, a much greater force is necessary to cause disruption and damage to this area.

There is no consensus on the management of chorioretinitis sclopetaria due to the low number of reported cases, as well as the variability in injury. If surgery is not indicated, patients may be carefully observed, as was the case for our patient, as the lesions will heal gradually in many cases as a result of the large degree of glial proliferation at the injury site. ■

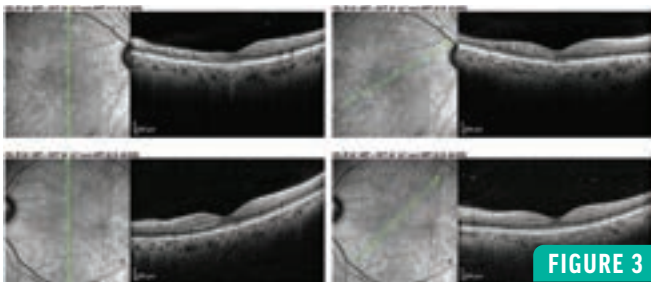

FIGURE 3

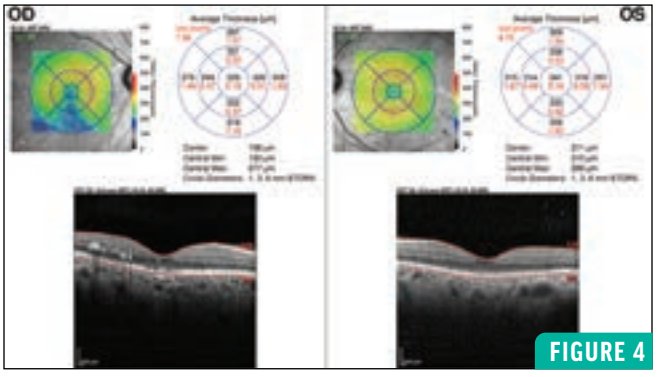

FIGURE 4

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If you have images you would like to share, email Manish Nagpal, MS, FRCS, FASRS, at drmanishnagpal@yahoo.com.

Note: Photos should be 400 dpi or higher and at least 10 inches wide.

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

SYFOVRE®
(pegcetacoplan injection)
15 mg / 0.1 mL

Save more retinal tissue

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

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

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

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

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

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

Discover more at SyfovreECP.com

INDICATION

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

IMPORTANT SAFETY INFORMATION

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.

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